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The impact of coffee on mental health

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121 ST SESSION OF THE International Coffee Council
MÉXICO 9-13 DE ABRIL DE 2018

Associação Brasileira ABIC da Indústria de Café

PROS AND CONS OF COFFEE CONSUMPTION

COFFEE CONTAINS ANTIOXIDANTS, VITAMINS AND MINERALS AND A FEW DIETARY PROTEINS.

Research shows coffee consumption has reduced the risk of some diseases and ailments, including:

- Parkinson's
- Alzheimer's
- Type 2 diabetes
- Gallstones
- Cancer - oral, esophageal and pharyngeal
- Asthma attacks
- Heart rhythm problems
- Strokes
- Cirrhosis of the liver
- Caffeine increases the effectiveness of certain types of painkillers; act as a stimulant

GOOD FOR THE GARDEN: Used coffee grounds benefit many plants, adding nitrogen to the soil.

EVEN THOUGH CAFFEINE CAN HAVE POSITIVE EFFECTS, OVERCONSUMPTION MAY CAUSE NEGATIVE RESULTS.

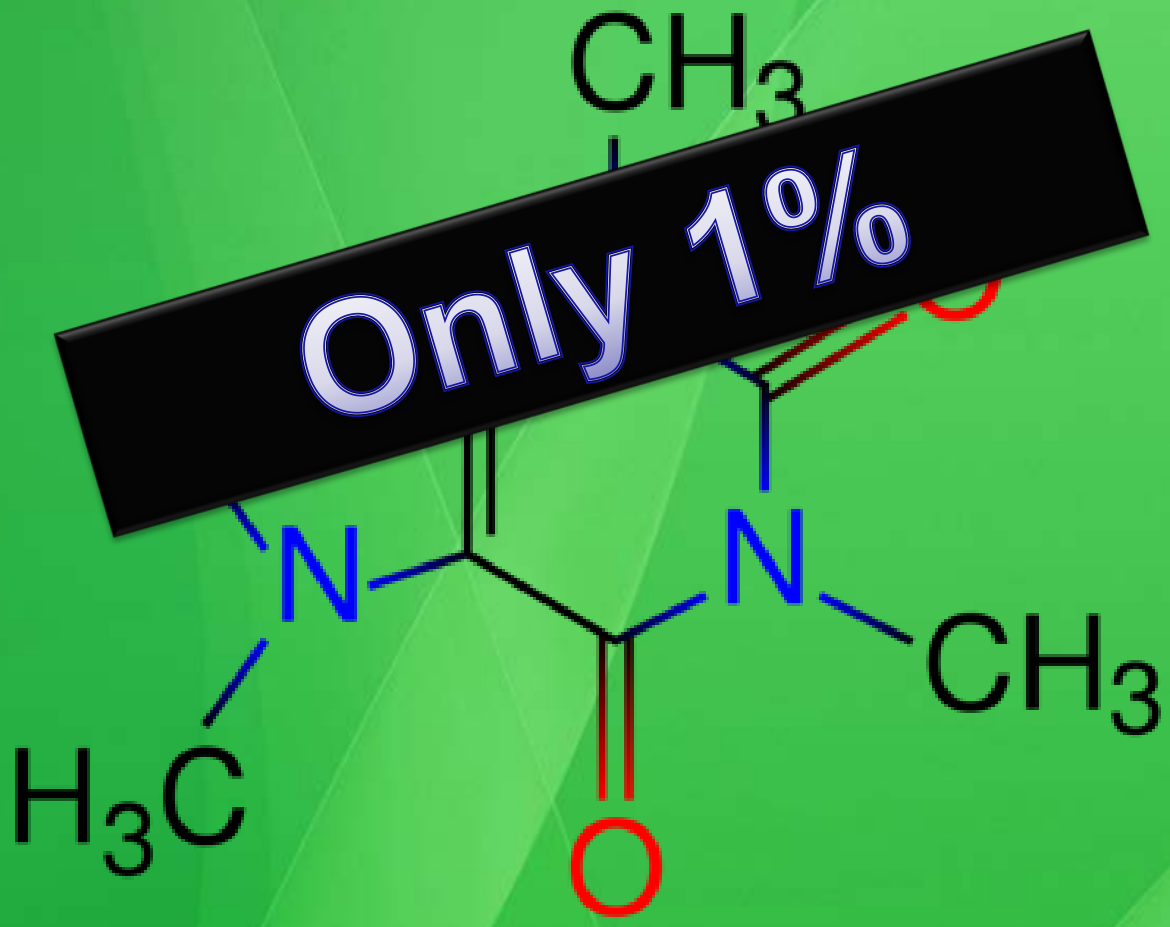
Negative effects may include:

- Changes in sleep pattern
- May cause auditory hallucinations
- Hampers absorption of some minerals and vitamins, such as magnesium, zinc and iron
- Can raise blood pressure
- Mild diuretic could lead to dehydration and a loss of vitamins B and C as well as calcium, iron and zinc
- Can stain teeth
- Acids can aggravate heartburn

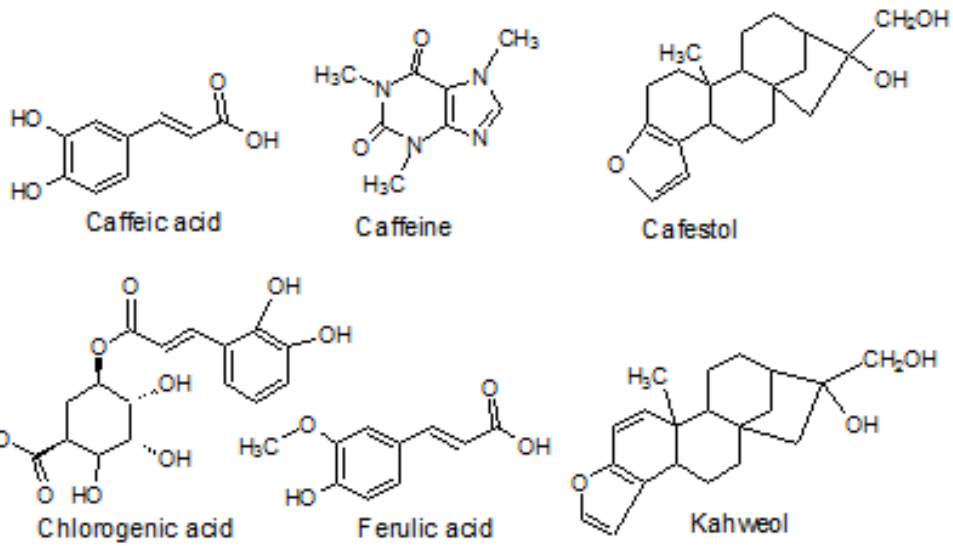
ROASTING THE BEANS: Coffee contains hundreds of compounds, some brought out during the roasting process; some of the carcinogens produced by the high heat of roasting include cresote, pyrimidine, tars and polycyclic aromatic hydrocarbons.

SOURCES: Harvard School of Public Health, e-importz.com, National Coffee Association, The Specialty Coffee Association of America, Stroke: Journal of the American Heart Association.

Caffeine



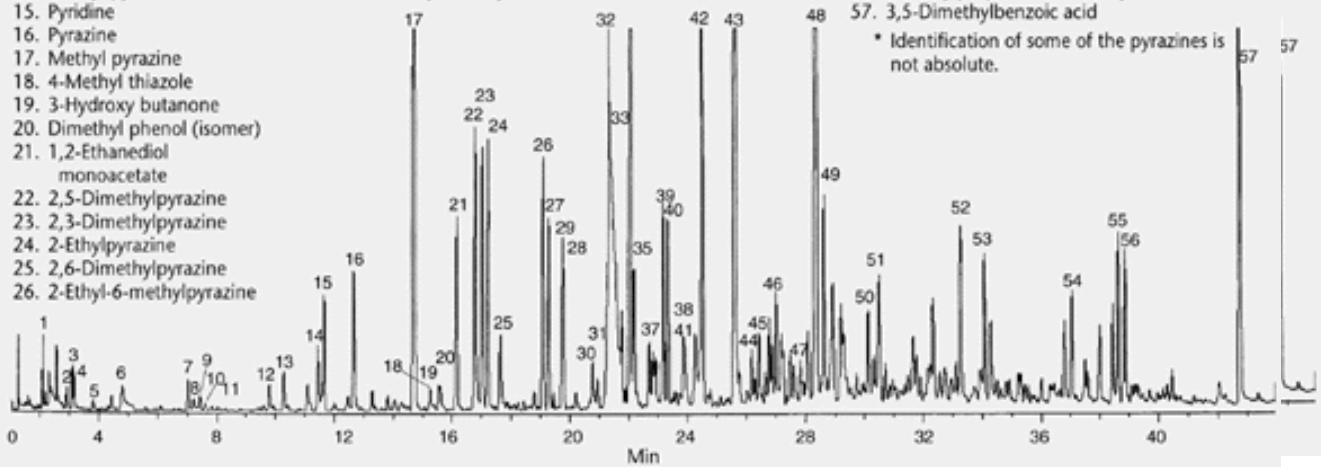

And about the other 99%?



Coffee Components*

1. 2-Methyl furan
2. 2-Butanon
3. 2-Pentanone
4. 3-Methyl butanal
5. 2,5-Dimethylfuran
6. 2-Acetyloxy-2-propanone
7. 2-Ethyl hexanol
8. Dimethylsulfoxide
9. Phenol
10. Hexanal
11. 2-Methyl thiophene
12. n-Methyl pyrrole
13. 4-Methylphenol
14. 2-Ethyl pyrrole
15. Pyridine
16. Pyrazine
17. Methyl pyrazine
18. 4-Methyl thiazole
19. 3-Hydroxy butanone
20. Dimethyl phenol (isomer)
21. 1,2-Ethanediol monoacetate
22. 2,5-Dimethylpyrazine
23. 2,3-Dimethylpyrazine
24. 2-Ethylpyrazine
25. 2,6-Dimethylpyrazine
26. 2-Ethyl-6-methylpyrazine
27. 2-Ethyl-5-methylpyrazine
28. Trimethylpyrazine
29. 2-Ethyl-3-methylpyrazine
30. 2,6-Diethylpyrazine
31. 2-Ethenylpyrazine
32. 2-Ethyl-3,5-dimethylpyrazine
33. Glycerol
34. 2,3-Diethylpyrazine
35. 2-Ethyl-3,6-dimethylpyrazine
36. 2-Furancarboxaldehyde
37. 2-Isopropenylpyrazine
38. 3,5-Diethyl-2-methylpyrazine
39. Furfural formate
40. 2-Furonyl ethanone
41. Methyl benzoylformate
42. Furanmethanol acetate
43. 5-Methyl-2-furancarboxaldehyde
44. Furanmethanol propionate
45. Furfanyl furan
46. Pyridine methanol
47. 2-Methyl-5-propenylpyrazine
48. Furanmethanol
49. 3-Ethyl-4-methyl-2,5-furandione
50. Pyrazine carboxamide
51. 2-Ethyl-3-hydroxy-4H-pyran-4-one
52. 1-(2-Furanylmethyl)pyrrole
53. 2-Methoxyphenol
54. 1-(1H-Pyrrole-2-yl)ethanone
55. 4-Ethyl-2-methoxy phenol
56. 3-Phenylpropenal or 2-Methylbenzofuran
57. 3,5-Dimethylbenzoic acid

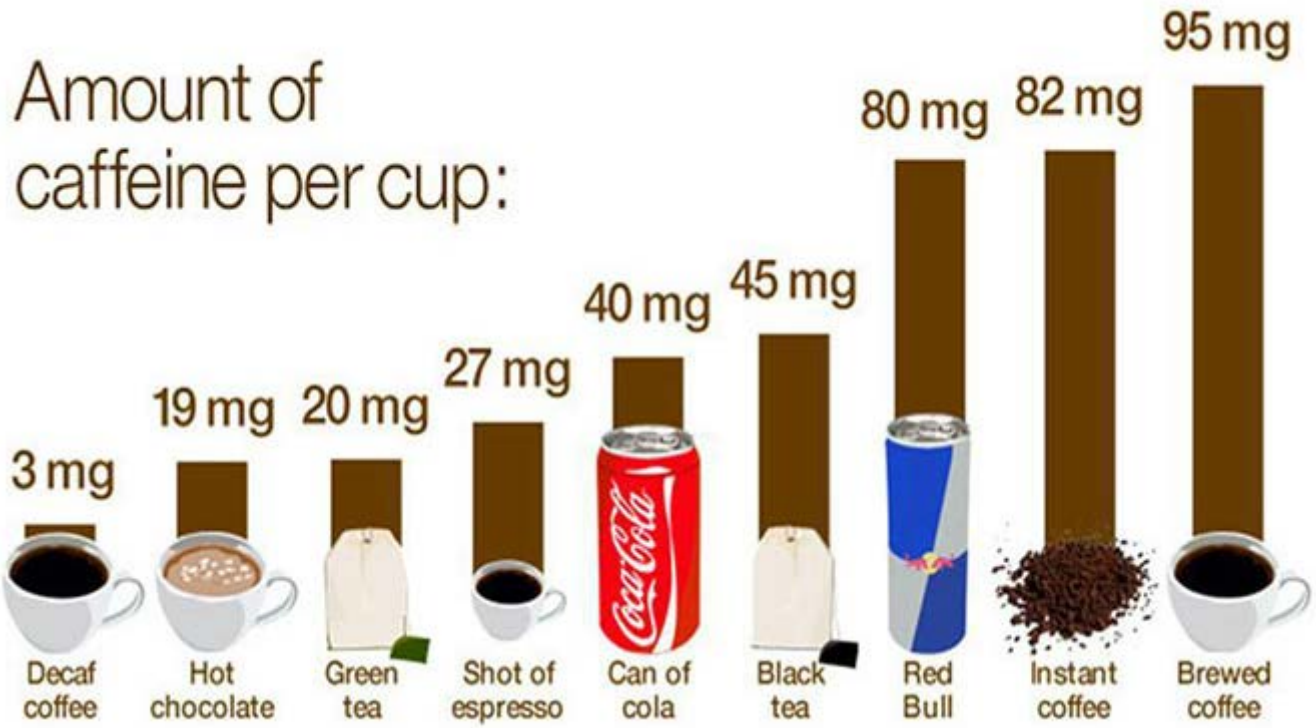
* Identification of some of the pyrazines is not absolute.



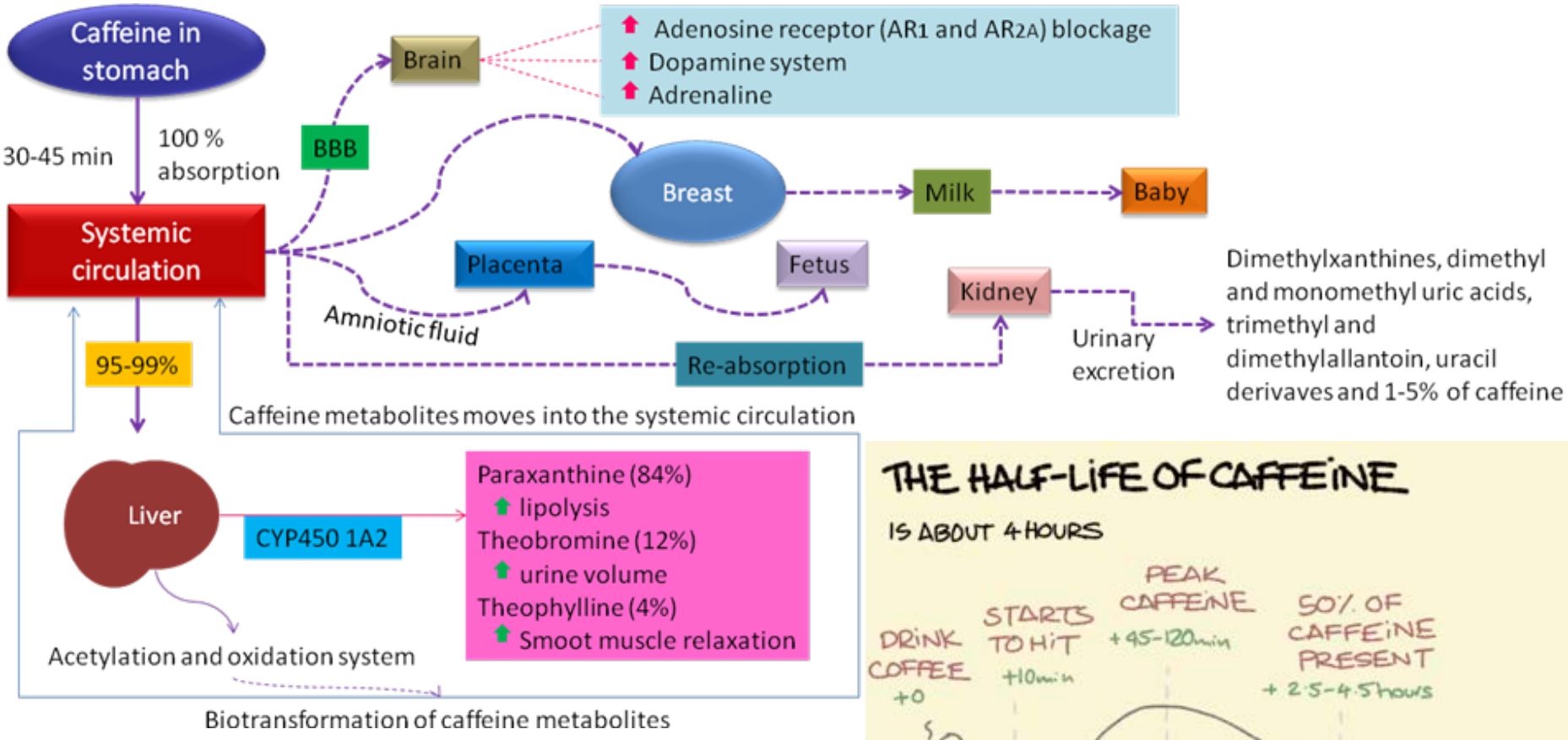
Caffeine

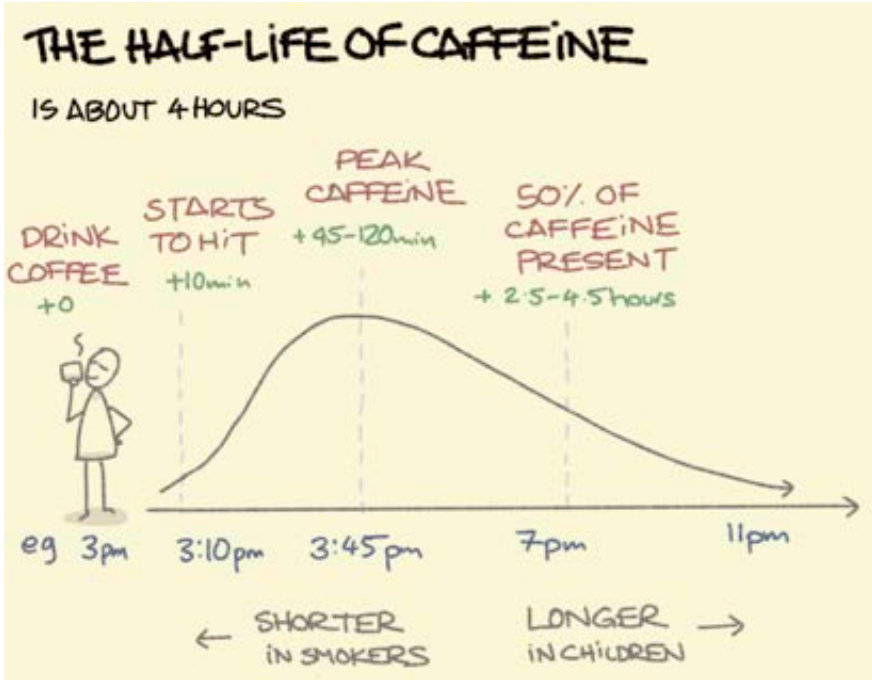
√ Is the most consumed psychoactive substance worldwide;

√ **Moderate safety daily caffeine consumption (**EFSA, 2015)**:**
Adults: 4-5 cups of coffee (± 400 mg/day)
Pregnant women: 2 cups of coffee (± 200 mg/day)
Children and adolescents: 2.5 - 3 mg/kg per day



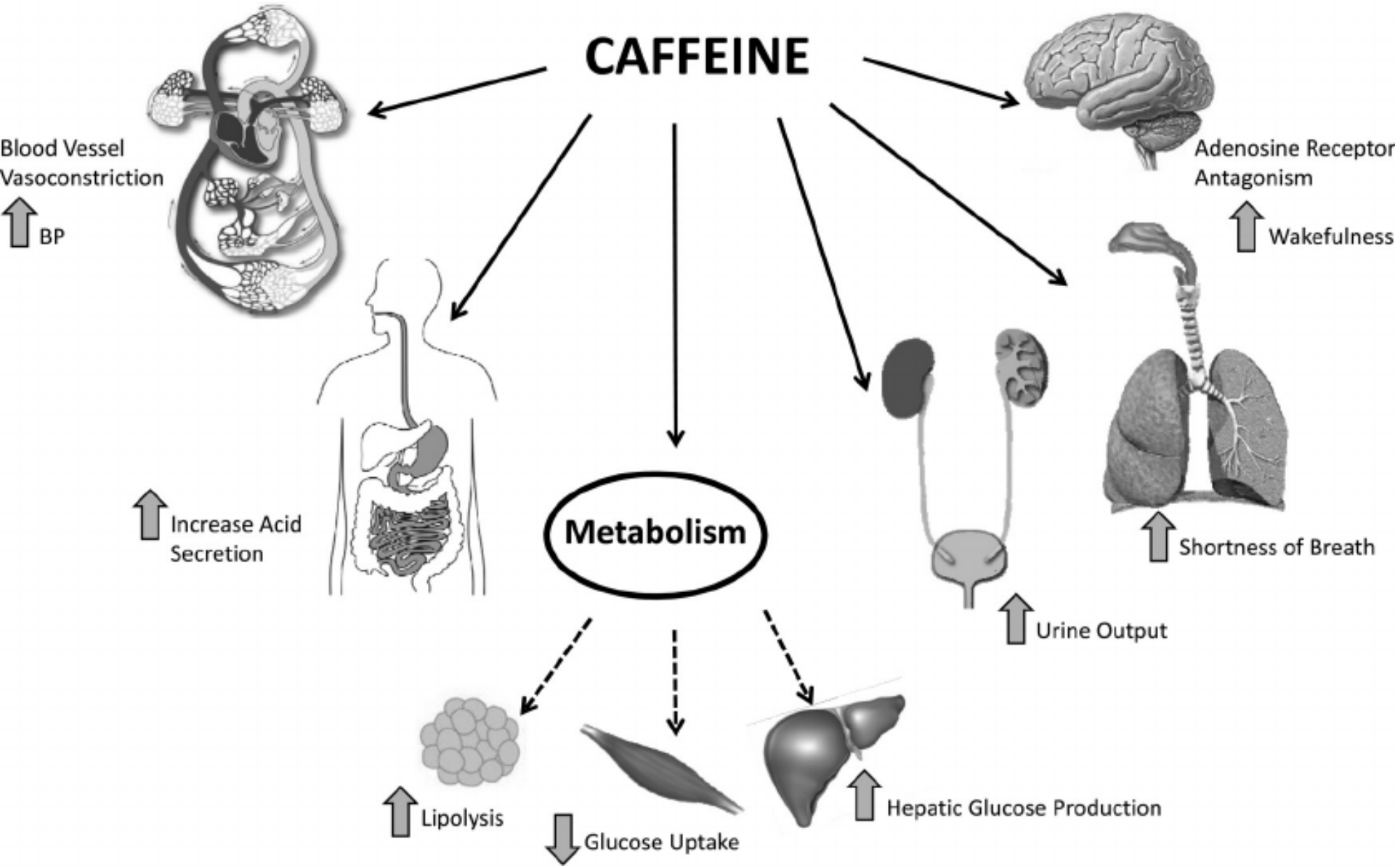
Caffeine kinetics in the body



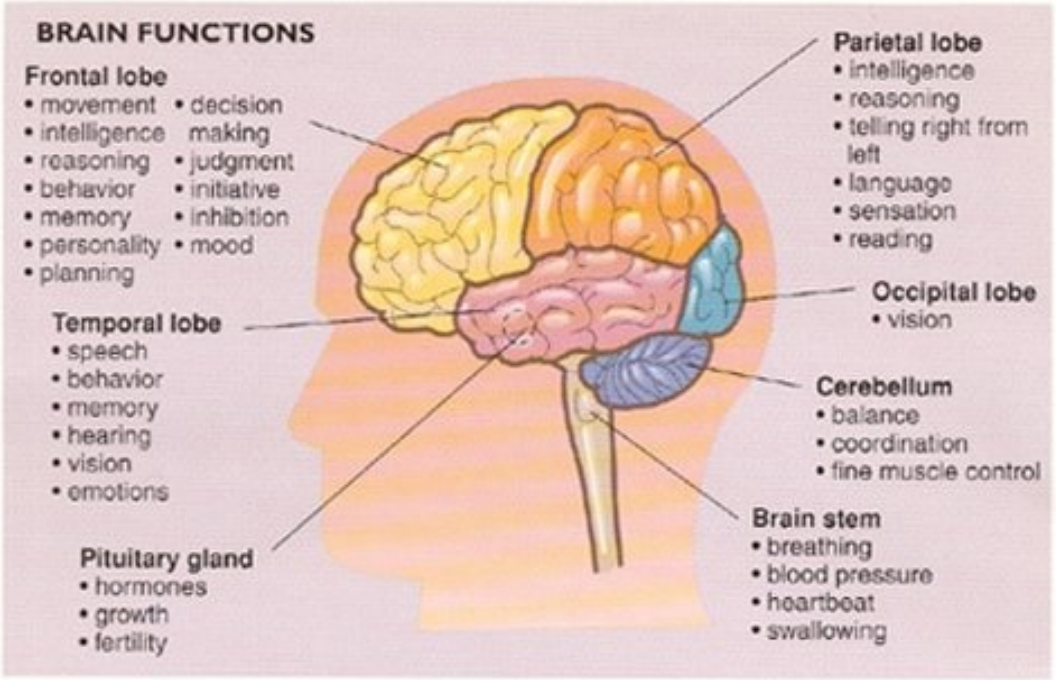


Islam et al. Int J Pharm Pharm Sci, 2016

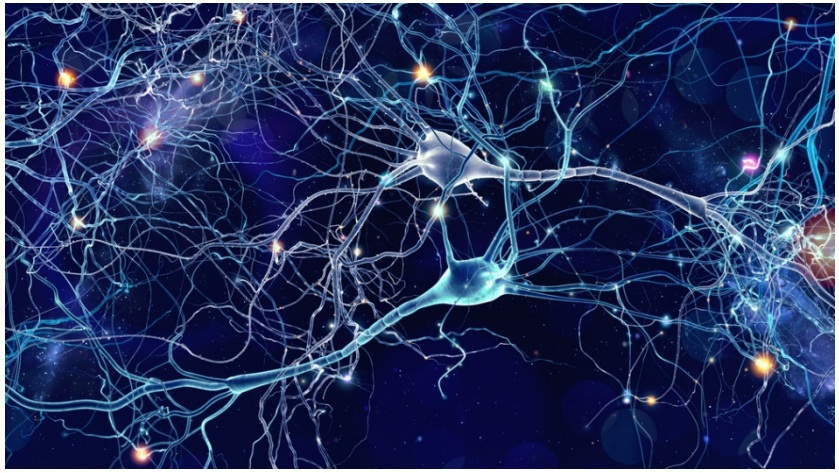
Effects of caffeine on the body

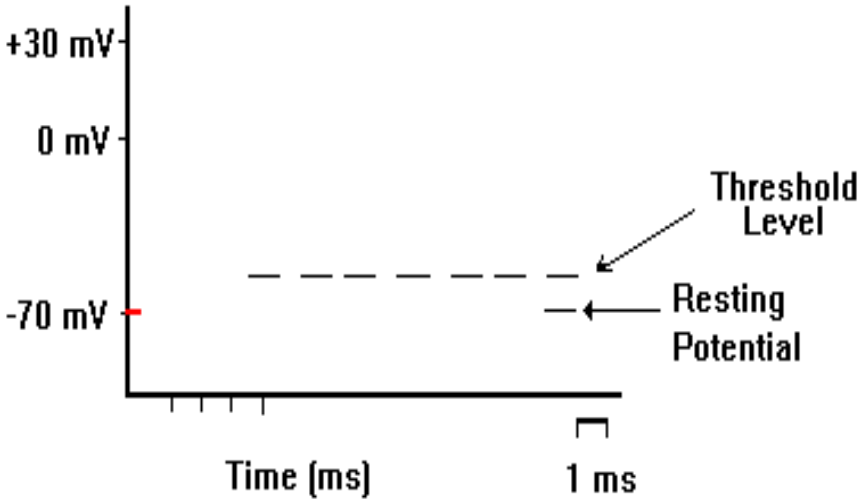


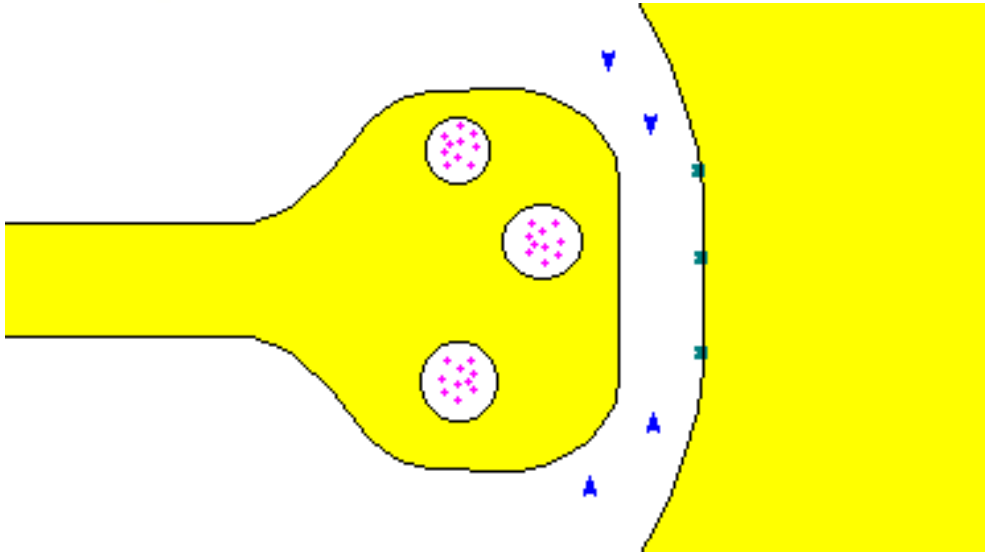
Inside the Brain



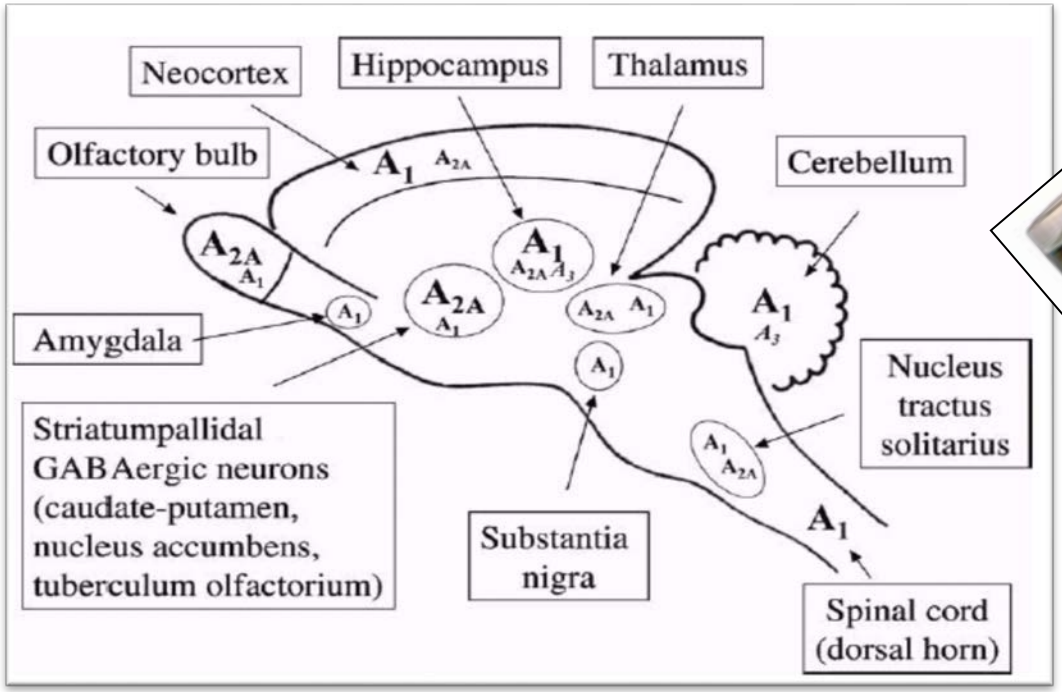
100 billion neurons that can have up to 15,000 connections with other neurons via synapses

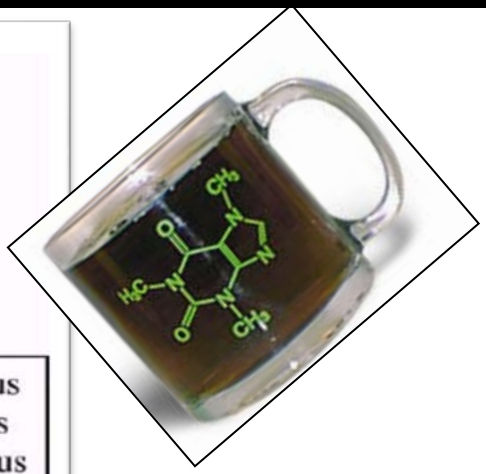


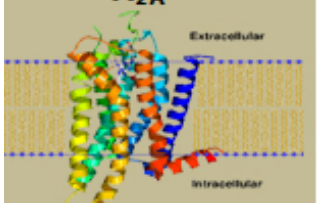




“Caffeine (Adenosine) receptors”

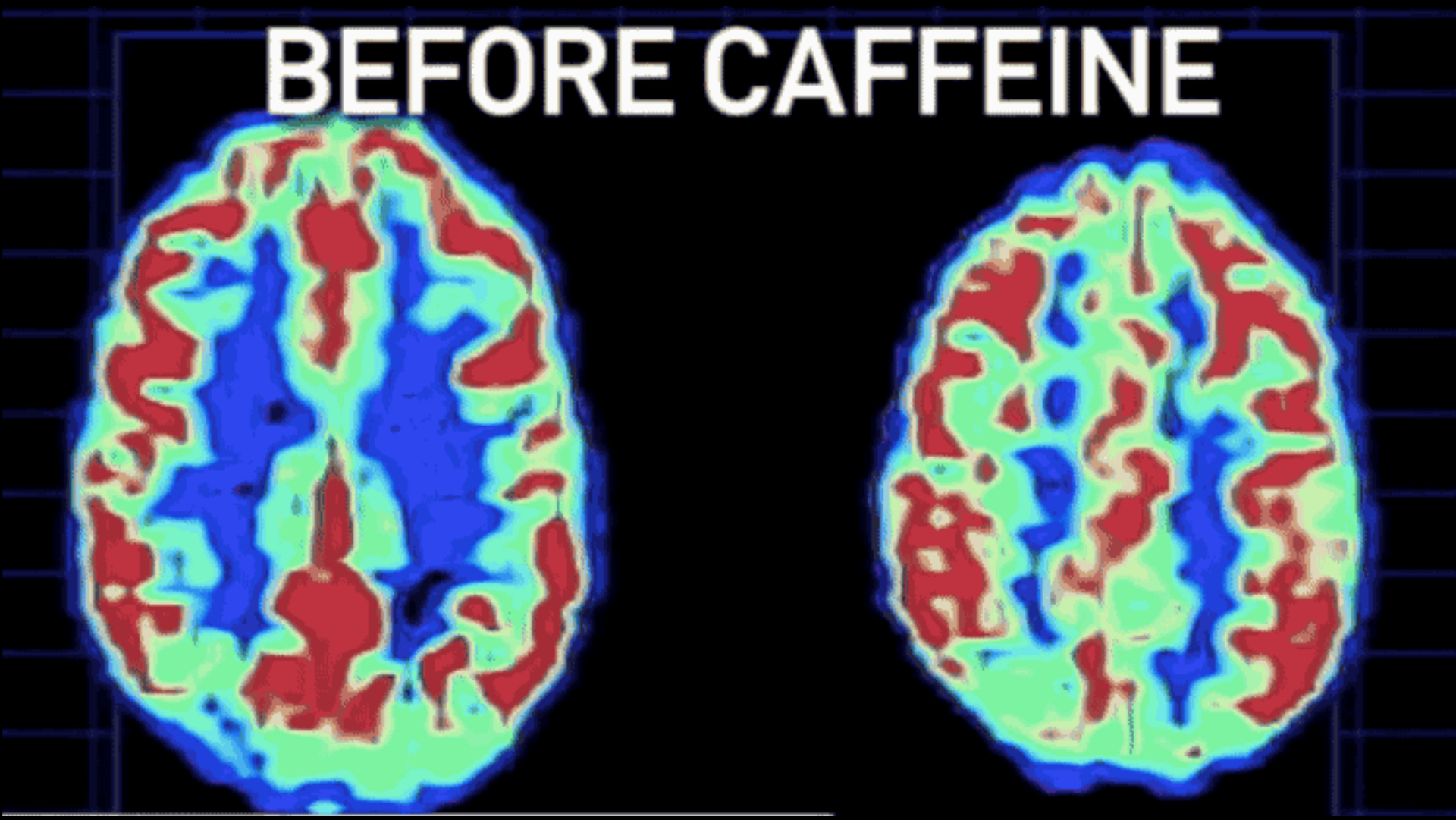




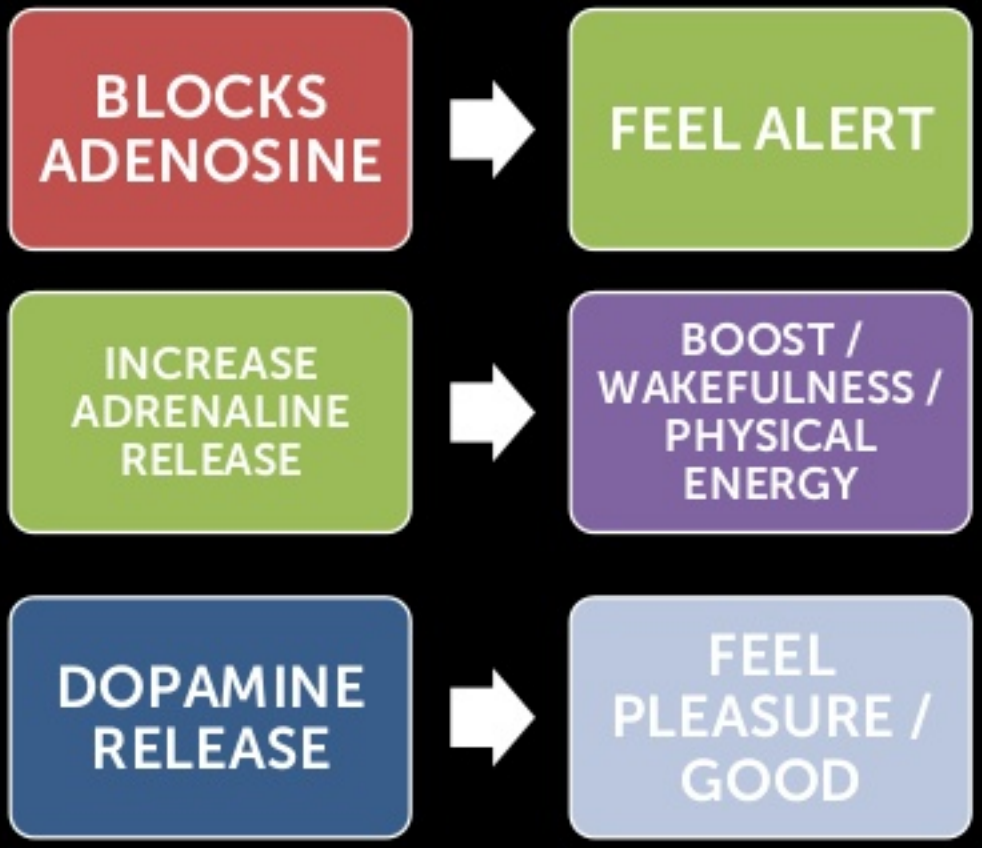
Receptor	Localization	Xanthines action
A_1	Almost all brain areas, especially hippocampus, cerebral and cerebella cortex, certain thalamus nuclei	Disinhibition of transmitter release
A_{2A} 	Dopamine rich regions: striatum, nucleus accumbens, tuberculum olfactorium, hippocampus, cortex	Increase transmission via dopamine D2 receptors

Ribeiro et al., Progress in Neurobiology, 2003
Kolahdouzan & Hamadeh, CNS Neuroscience & Therapeutics, 2017

“Caffeine (Adenosine) receptors”



CAFFEINE AND YOUR NEUROTRANSMITTERS



Brain disorders

Mental Disorders

- Anxiety disorders
- Insomnia
- Unipolar depression
- Dementia
- ADHD
- Alcohol dependence
- Conduct disorders
- PTSD
- Personality disorders
- Cannabis dependence
- Eating disorders

Neurological Disorders

- Headache
- Sleep Apnea
- Stroke
- Dementia
- Traumatic brain injury
- Epilepsy
- Parkinson’s disease
- Multiple Sclerosis
- Neuromuscular disorders
- Brain tumors

Brain disorders in US (Population 325 million)

Insomnia (60 million)

Depression (20 million)

Anxiety (19 million)

Attention Deficit Hyperactivity Disorder (ADHD) (6,2 million)

Alzheimer’s disease (4 million)

Schizophrenia (3 million)

Parkinson’s disease (1,5 million)

The impact of Brain Disorders

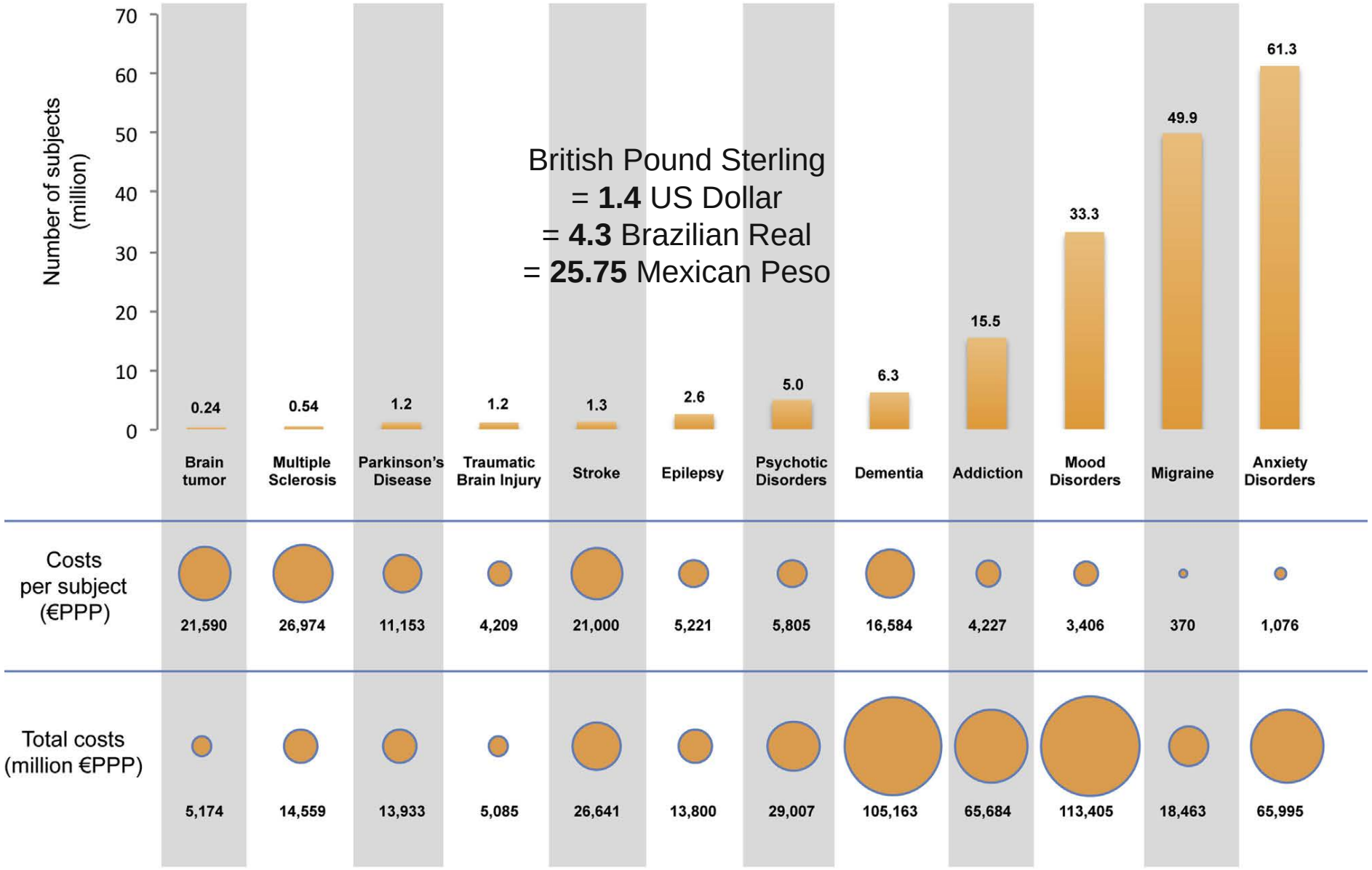
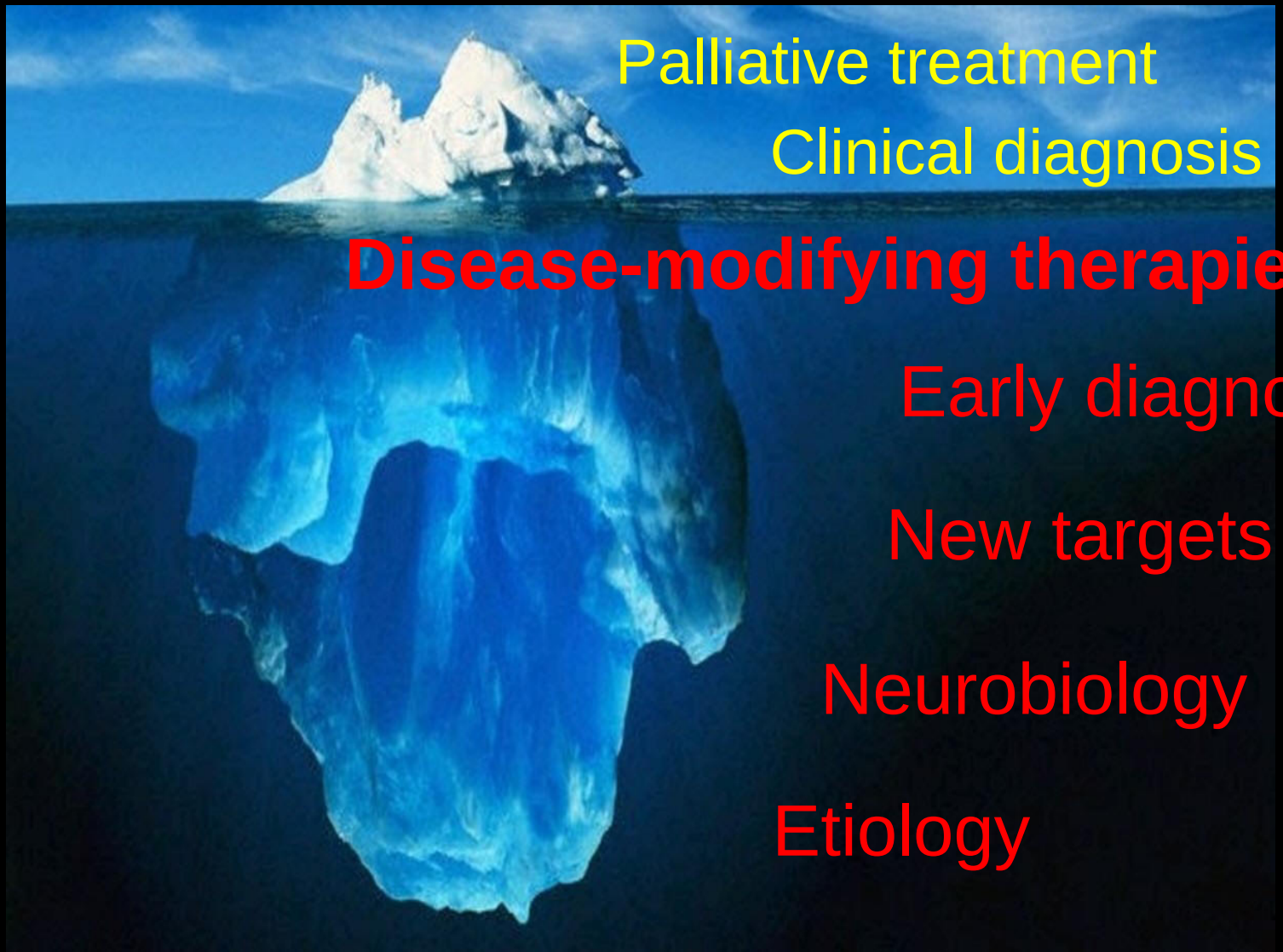


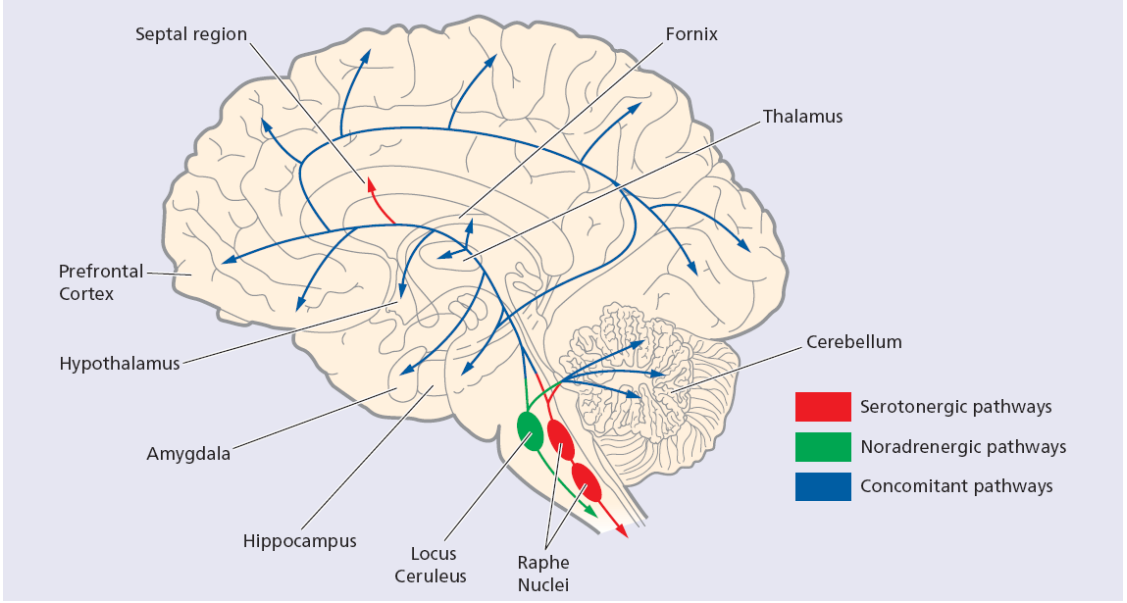
Figure 1. Cost of Disorders of the Brain in Europe in 2010

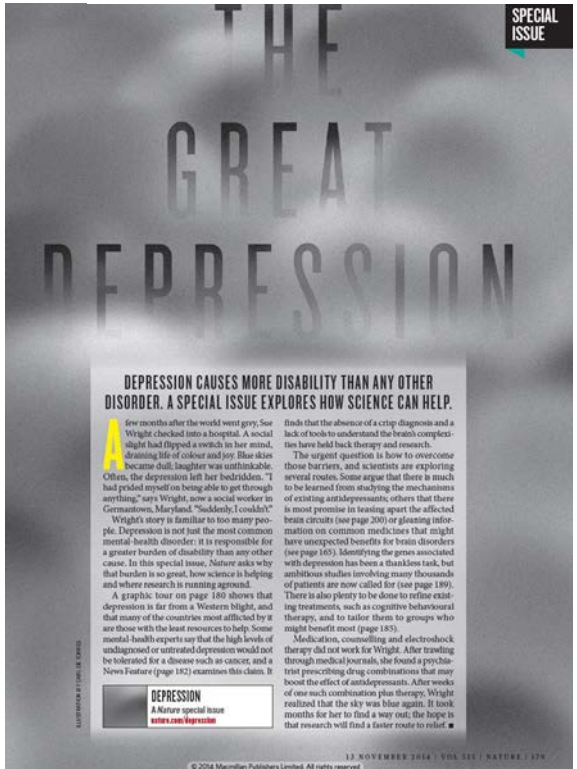
DiLuca & Olesen, Neuron , 2014

Big Challenges in Brain Disorders



Depression



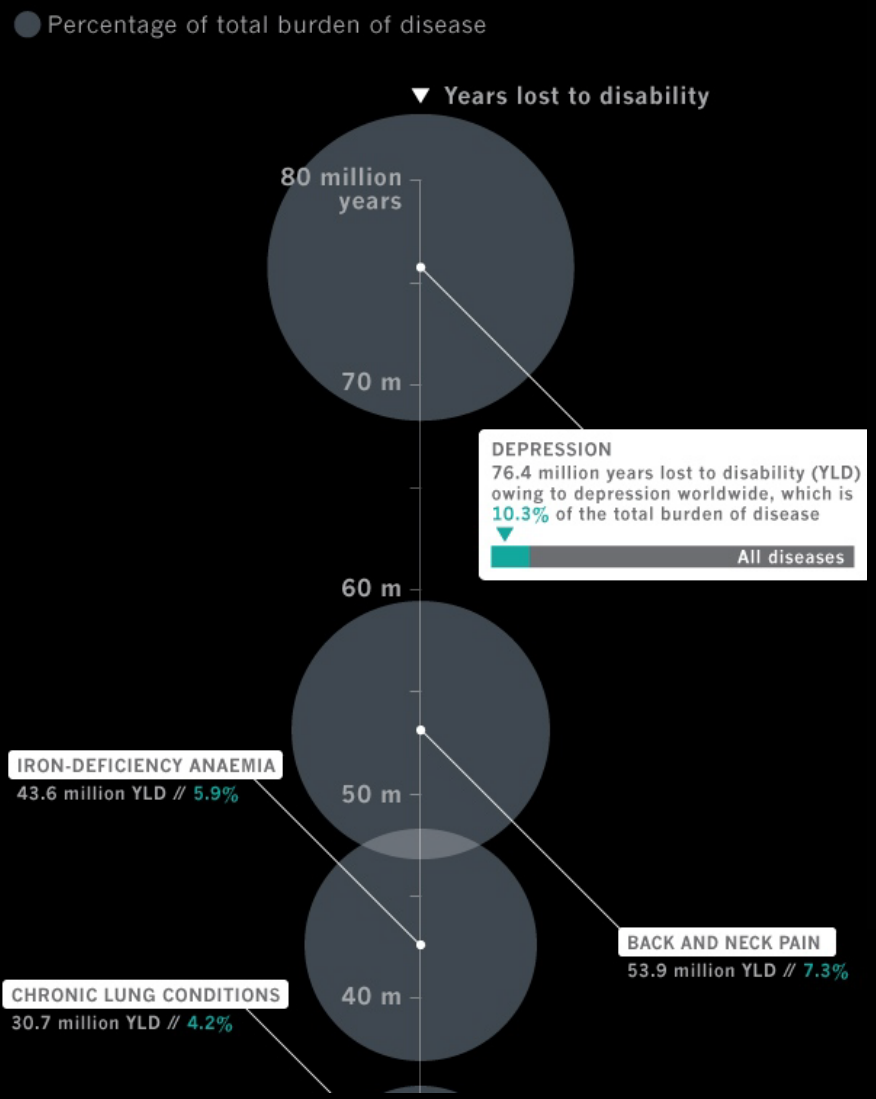


- WHO: Over 350 million people around the world have depression;
- Affects people of all ages, countries, cultures, religions, financial conditions;
- More frequent in women;
- Top cause of functional incapacitation;
- Antidepressant drugs failure in 50% of patients.

Special Issue, Nature, 2014

Top ten causes of disability

Depression accounts for the biggest share of the world's burden of disease, measured by years lost to disability (YLD): healthy years 'lost' because they are lived with a physical or mental disability.



Afghanistan 22.5% 0.16

This war-torn country reports the world's highest prevalence of depression, and yet it is among the least equipped to deal with it. Conflict is a well-established risk factor for depression, as are child sexual abuse and domestic violence.

Switzerland 6.16% 41.42

Switzerland's universal health care offers some of the best support for mental health, with more than 40 psychiatrists per 100,000 people. But studies estimate that even the best available treatments can reduce the burden of disability from depression by only 10–30%.

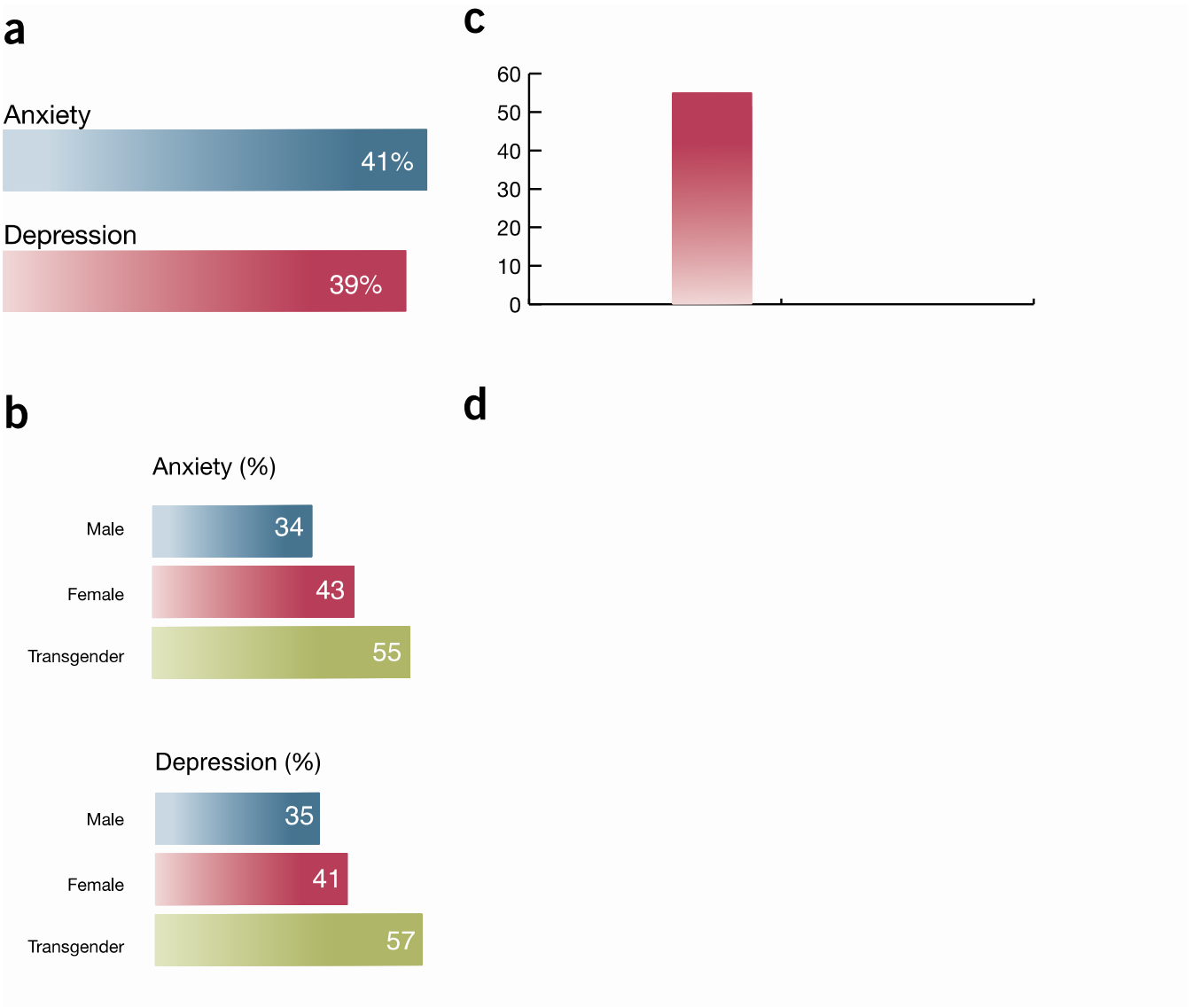
United States 4.45% 7.79

Depression receives significantly less in research funds from the US National Institutes of Health than do cancer or heart disease. That is partly because of a lack of patient advocates and the stigma that surrounds the condition.

Special Issue, Nature, 2014

Evidence for a mental health crisis in graduate education

Teresa M Evans[1], Lindsay Bira[2], Jazmin Beltran Gastelum[3], L Todd Weiss[4] & Nathan L Vanderford[4,5]



Coffee/Caffeine x Depression

try. 2014 July ; 15(5): 377–386. doi:10.3109/15622975.2013.795243.

Coffee, caffeine, and risk of completed suicide: results from 3 prospective cohorts of American adults

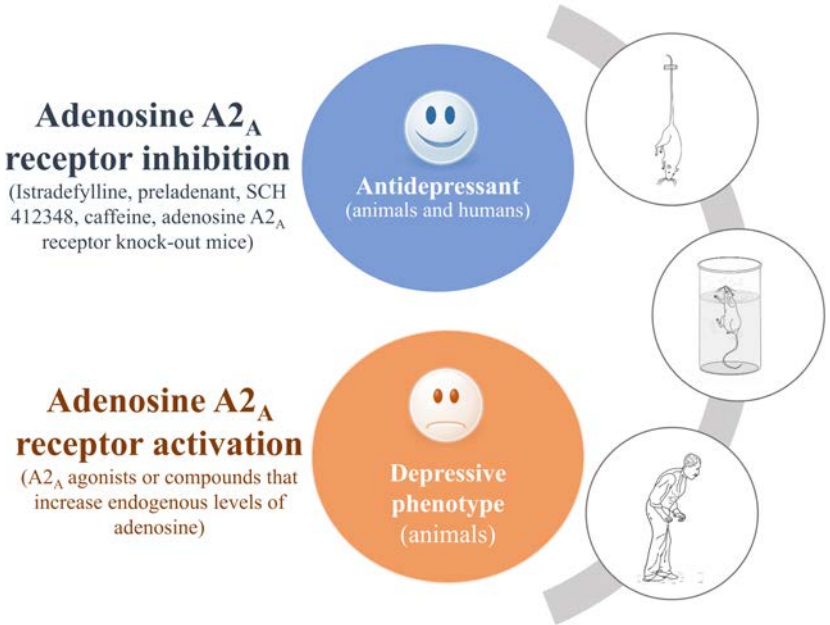
Michel Lucas[1], **Eilis J. O'Reilly**[1], **An Pan**[1], **Fariba Mirzaei**[1], **Walter C. Willett**[1,2,3], **Olivia I. Okereke**[2,3,4], and **Alberto Ascherio**[1,2,3,*]

[1]Department of Nutrition, Harvard School of Public Health, Boston, MA, US

[2]Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA

[3]Channing Division of Network Medicine Department of Medicine, Harvard Medical School, Boston, MA, USA

[4]Department of Psychiatry, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA



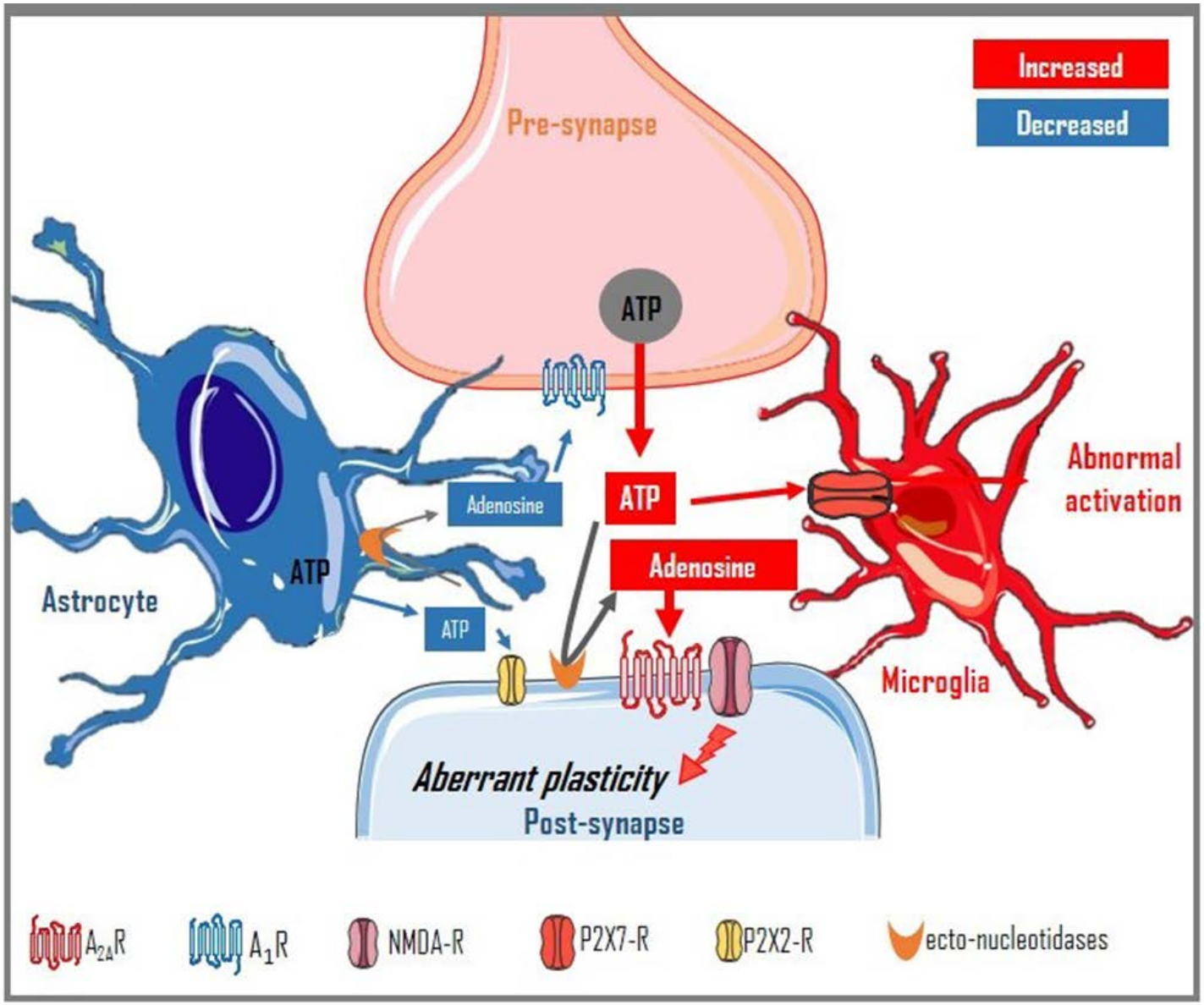
Prediger et al, 2015

√ Several studies on large cohorts have associated daily coffee drinking (**≥4 cups**) with a **decreased risk of depression (9-20%)** (Smith, 2009; Lucas et al., 2011) and **suicide (53%)** (Kawachi et al., 1996; Lucas et al., 2014);

√ **Caution:** One study showed **increased suicide risk (58%)** in those drinking **≥8 cups** of coffee daily (Tanskanen et al., 2000);

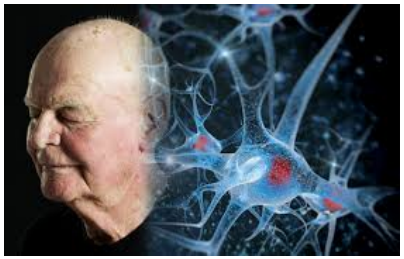
√ Many pre-clinical studies have demonstrated the antidepressant effects of caffeine in rodents (El Yacoubi et al., 2003; Yamada et al., 2014; Kaster et al., 2015).

Coffee/Caffeine x Depression

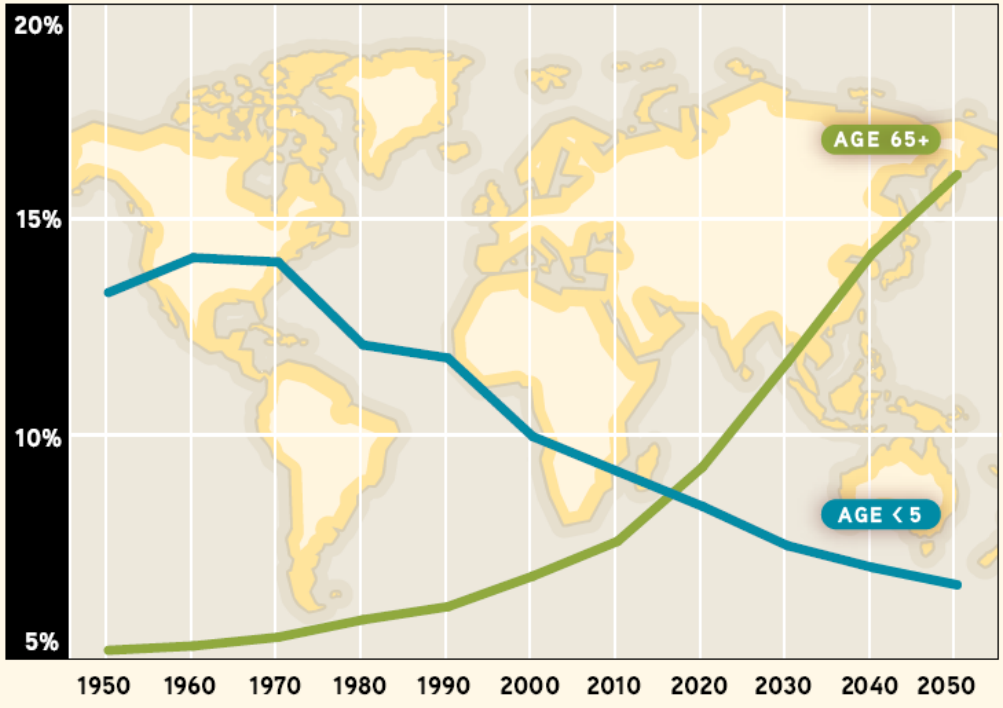


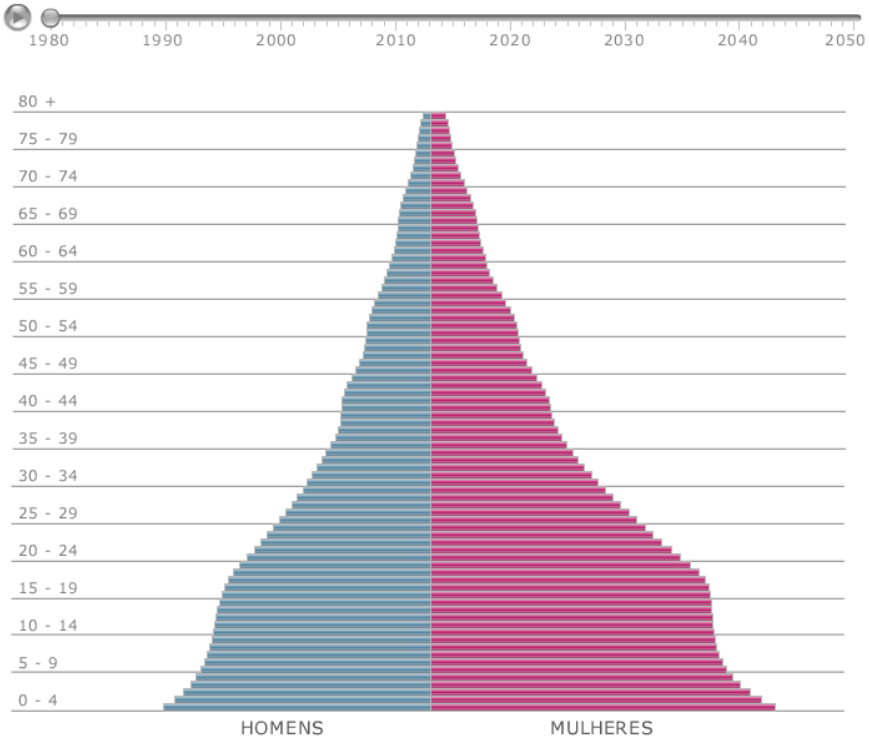
Rial et al, Frontiers in Cellular Neuroscience, 2016

Aging World: Neurodegenerative diseases



Parkinson's disease: 1-2% over 65 years
Alzheimer's disease: 5% over 65 years
40% over 80 years





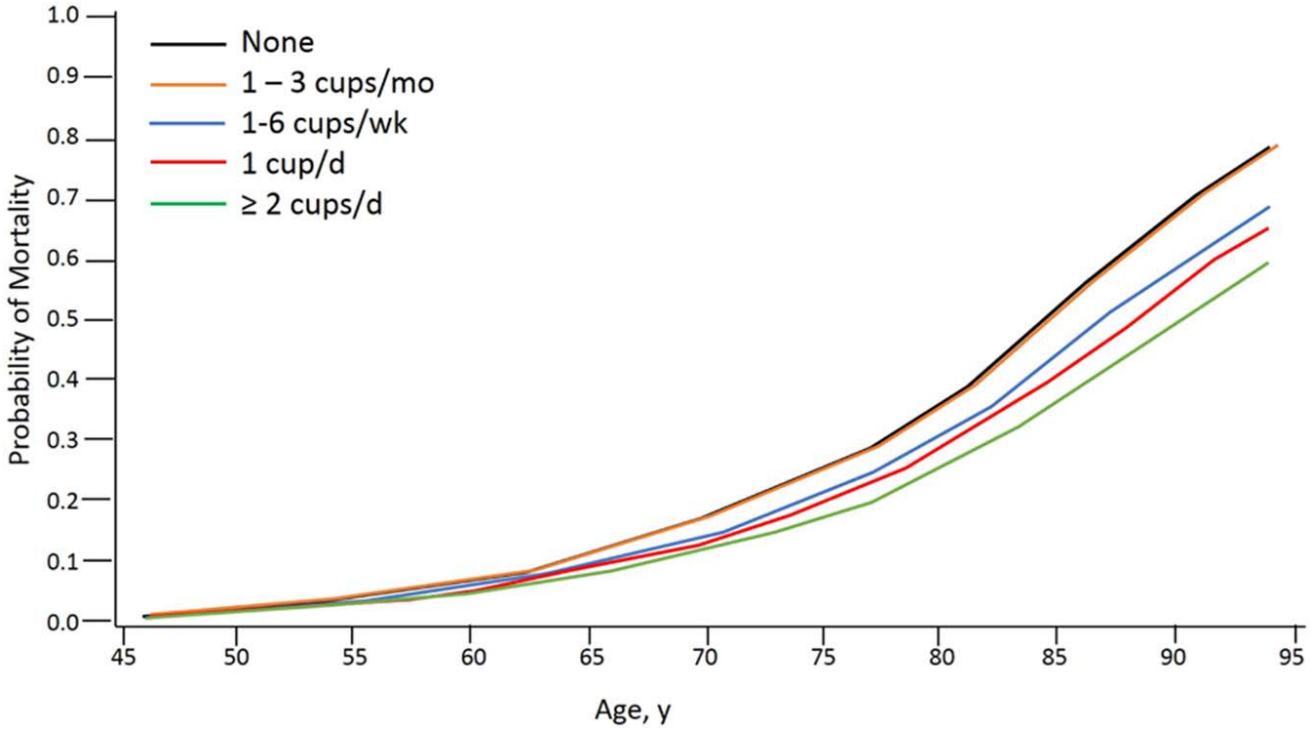
Example: Brazil (IBGE)

Dobriansky et al.; US National Institute on Aging (http://www.state.gov/g/oes/rls/or/81537.htm).

Aging World: Coffee for longevity

√ A multicenter prospective cohort study of **521,330 adults** who were recruited **from 10 European countries** and followed for 16 years showed that **the intake of at least 3 cups of coffee per day was associated with a lower risk (7-12%) of all-cause mortality** (Gunter et al, 2017);

√ Similar findings were described by Park et al. (2017) in a multi-ethnic prospective cohort study comprised of **185,000 non-white participants including African-Americans, Native Americans, Hawaiians, Japanese-Americans, and Latinos.**



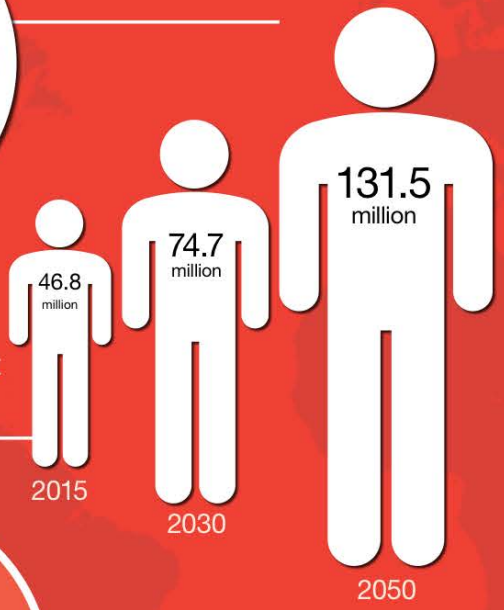
O'Keefe et al., Progress in Cardiovascular Diseases, 2018 (*In press)*

INFOGRAPHIC

The global impact of dementia

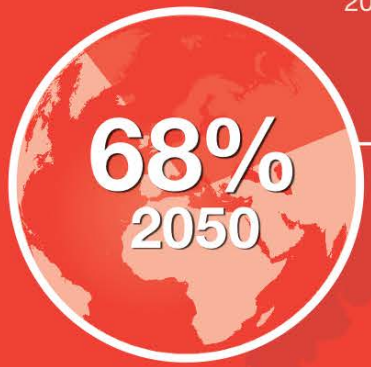
Around the world, there will be 9.9 million new cases of dementia in 2015,

one every 3 seconds



46.8 million people worldwide are living with dementia in 2015.

This number will almost double every 20 years.



Much of the increase will take place in low and middle income countries (LMICs): in 2015, 58% of all people with dementia live in LMICs, rising to 63% in 2030 and 68% in 2050.

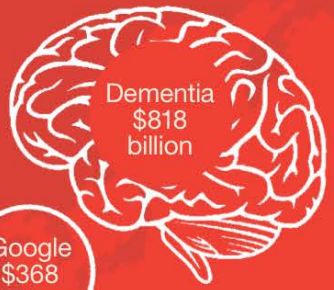
The total estimated worldwide cost of dementia in 2015 is US$ 818 billion. By 2018, dementia will become a trillion dollar disease, rising to

US$ 2 trillion by 2030

If global dementia care were a country, it would be the

18th largest economy

in the world exceeding the market values of companies such as Apple and Google



(source: Forbes 2015 ranking).

This map shows the estimated number of people living with dementia in each world region in 2015.

We must now involve more countries and regions in the global action on dementia.

The World Alzheimer Report 2015: The global impact of dementia, Alzheimer's disease international (ADI).

Alzheimer’s disease

Coffee/Caffeine x Alzheimer's disease

Alzheimer's disease (AD)—human epidemiological studies

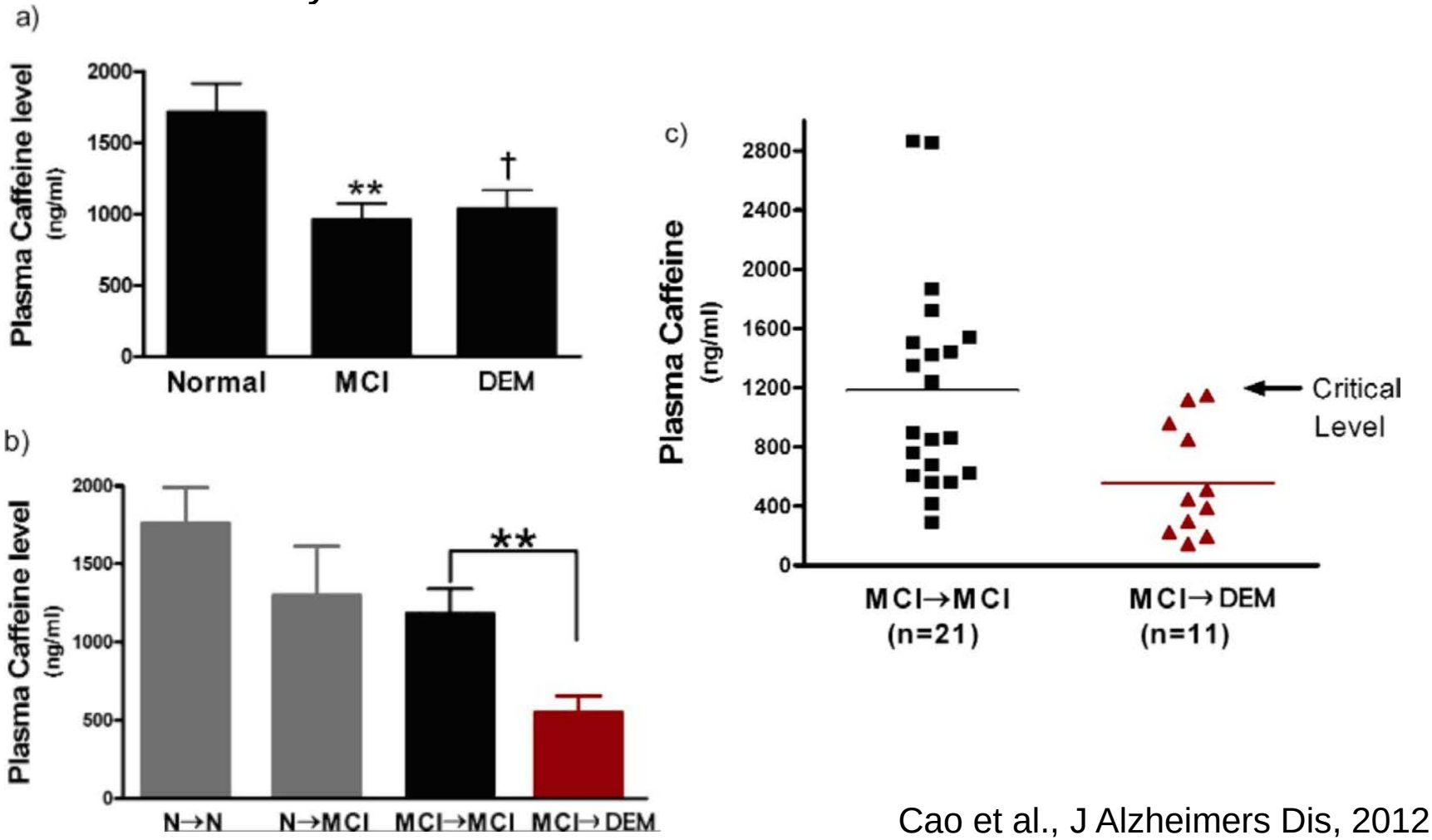
Reference	Participants	Duration	Main results	Conclusion
van Gelder et al., 2007	676 healthy men from Finland, Italy and the Netherlands 75-77 y	10 y Mini-mental state examination to assess global cognitive function	Coffee: ↓ cognitive decline (54%) Without coffee: 2.6 points of cognitive decline, 1 cup: 1.4 point of cognitive decline 2 cups: 1.3 points of cognitive decline 3 cups: 0.6 points of cognitive decline 4 cups: 1.6 points of cognitive decline Cognitive decline was not reduced for men who consumed >4 cups.	Consuming coffee was associated with slower cognitive decline in men. Consumption of 3 cups/d was most beneficial.
Eskelinen et al., 2009	1409 healthy participants 875 women 534 men Midlife: 50.4 y Later in life: 70.1 y	21 y	3-5 cups of coffee: ↓ 65%-70% risk of dementia and ↓ 62-64% risk of AD vs 0-2 cups 3-5 cups/d of coffee: ↓ risk of dementia in men (OR=0.27, CI=0.08-0.89) and women (OR=0.51, CI=0.17-1.52) vs 0-2 cups/d. In men, >5 cups: ↓ risk of dementia vs low coffee consumption (OR=0.36, CI=0.13-0.97).	Moderate coffee consumption at midlife may decrease the risk of developing AD and dementia later in life.
Maia & Mendoca, 2002	54 patients with probable AD 26 women 28 men 71.2 y 54 healthy controls 26 women 28 men 70.4 y	20 y preceding diagnosis	AD patients: average caffeine intake of 74±98 mg Healthy controls: average caffeine intake 199±136 mg Caffeine exposure: ↓ 60% risk of AD (OR=0.40, CI=0.25-0.67)	There is an inverse association between caffeine intake and AD
Lindsay et al., 2002	10 263 Canadian women and men >65 y	5 y	Daily coffee consumption: ↓ 31% risk of AD (OR=0.69, CI=0.5-0.96)	Coffee consumption is associated with lower risk of AD in Canadian population.

Most epidemiological studies suggest that a lifetime of regular coffee/caffeine consumption reduces the risk (30-70%) of developing Alzheimer's disease**.** Caffeine improves the attention and memory, decreases the production of amyloid-beta, however is not able to reverse the symptoms of Alzheimer's disease patients.

Kolahdouzan & Hamadeh, CNS Neuroscience & Therapeutics, 2017

Coffee/Caffeine x Alzheimer's disease

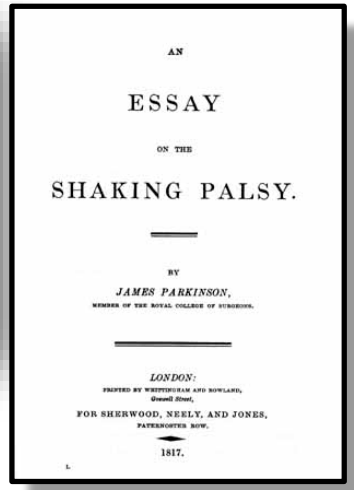
A study on 124 subjects aged 65–88 years reported that persons **evolving from 'moderate cognitive decline' (MCI) to Alzheimer's disease** during the 2–4 years follow-up **had 51% lower blood caffeine concentrations** than those who stayed at the MCI.



Cao et al., J Alzheimers Dis, 2012

Parkinson's disease – 200 years of study

James Parkinson
(1755-1824)



AN

ESSAY

ON THE

SHAKING PALSY.

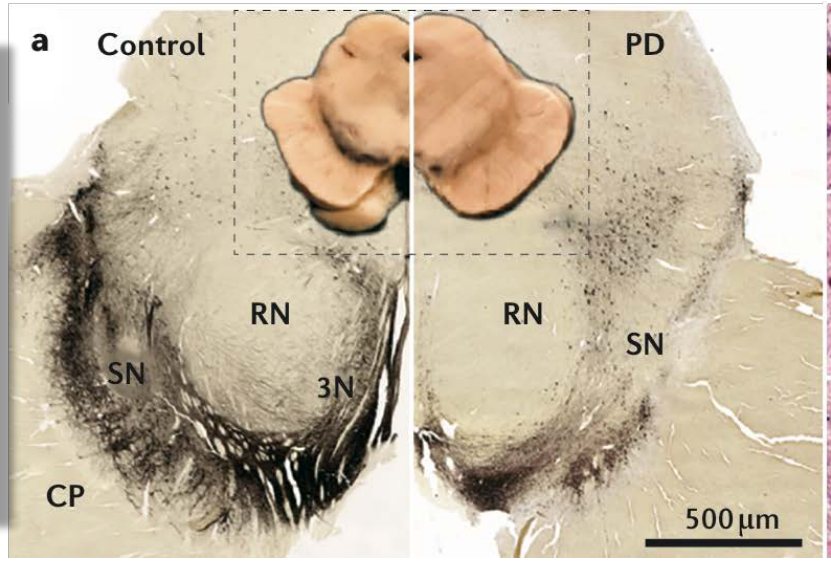
BY

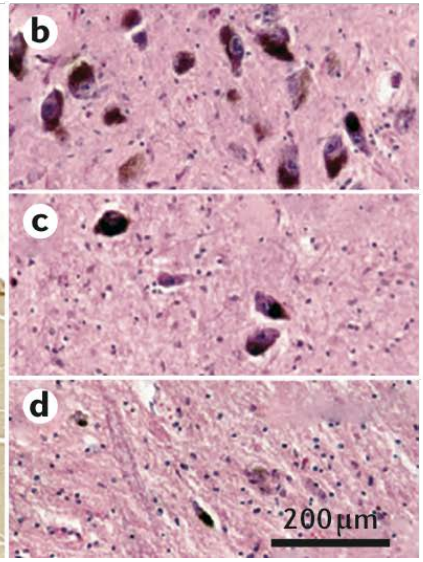
JAMES PARKINSON,

LONDON:

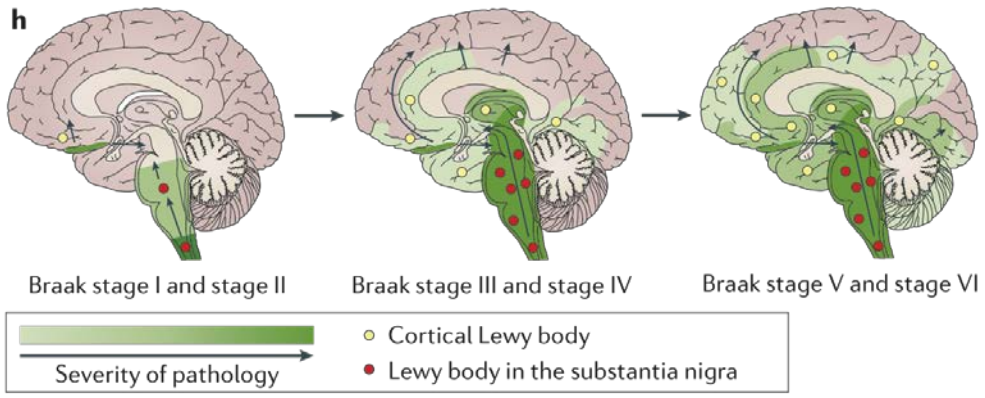
FOR SHERWOOD, NEELY, AND JONES,

1817.



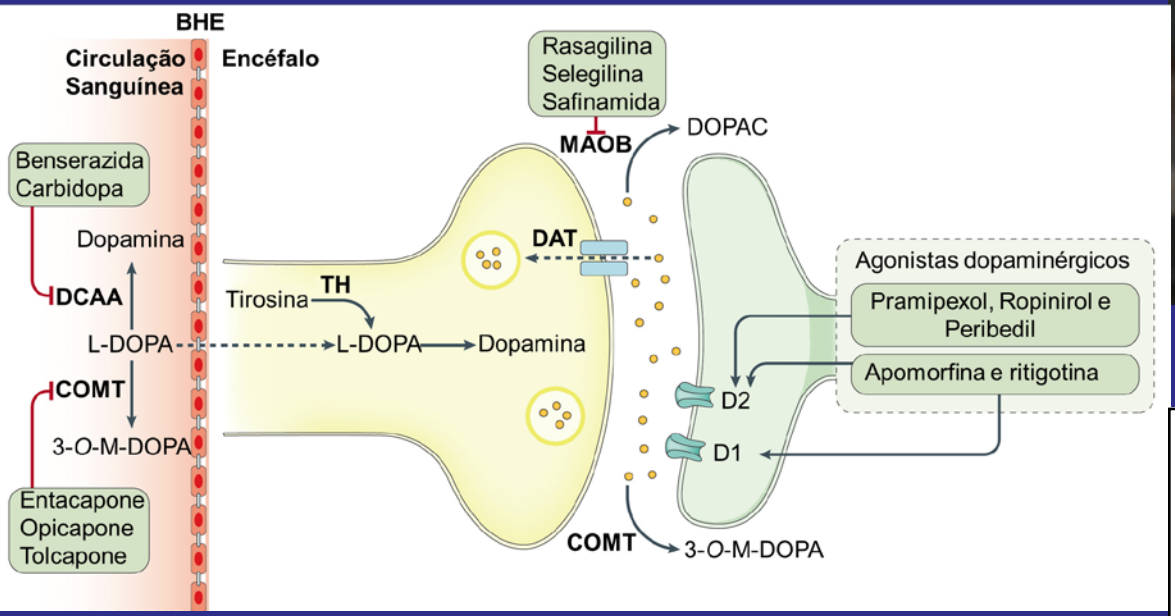


Non-motor symptom	Implicated brain region
Hyposmia	Olfactory bulb and amygdala
Impaired colour vision	Retina
Hallucinations	Occipital cortex
Pain	Basal ganglia, locus coeruleus, raphe nucleus, amygdala and thalamus
Anxiety	Basal ganglia
Depression	Limbic and cortical areas
Early cognitive dysfunction	Frontal cortex
Dementia	Temporal, parietal and occipital lobes
Sleep disturbance	Hypothalamus and reticular formation
Bladder hyper-reflexia	Basal ganglia



Motor symptoms

CHALLENGES OF PHARMACOLOGICAL TREATMENT



Poewe et al., Nat Rev Dis Primers, 2017

Awakenings, 1990

Journal of Alzheimer's Disease 20 (2010) S205–S220
DOI 10.3233/JAD-2010-091459
IOS Press

Review Article

Effects of Caffeine in Parkinson's Disease: From Neuroprotection to the Management of Motor and Non-Motor Symptoms

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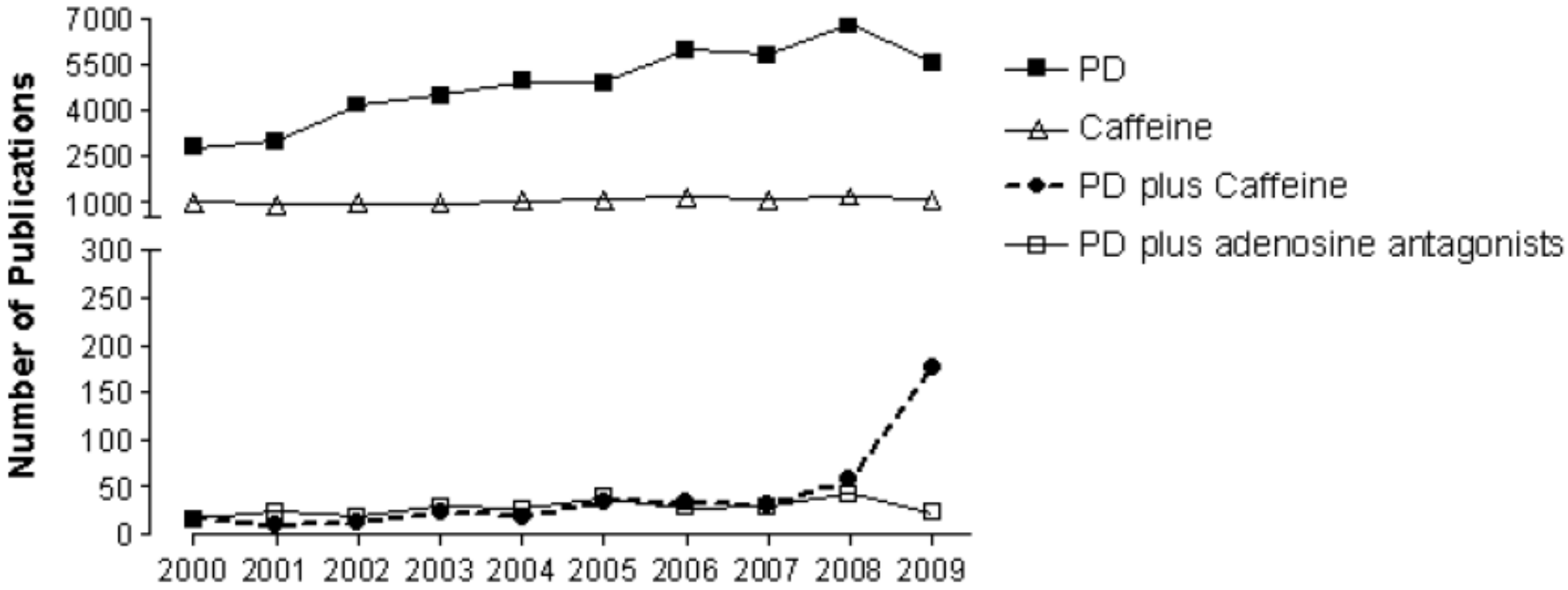


Caffeine and adenosine A2A receptors x Parkinson's disease – Animal models

Table 2 | Effects of non-dopaminergic therapies in animal models.

Drug class	Subclass	Effect in animal models	References
Adenosine receptor antagonists	A_{2A} antagonists Preladenant, Istradefylline, SCH58261, SCH412348, MSX-3	↓ catalepsy in reserpine and haloperidol models ↑ L-Dopa-induced contralateral turning behavior in 6-OHDA model ↓ behavioral sensitization induced by L-Dopa ↑ locomotion in MPTP and reserpine models ↑ survival of DA neurons in 6-OHDA model ↓ striatal DA nerve terminal loss and gliosis in MPTP model	Mandhane et al., 1997; Kanda et al., 1998; Shiozaki et al., 1999; Ikeda et al., 2002; Salamone et al., 2008; Hodgson et al., 2009; Trevitt et al., 2009
	Non-specific Caffeine, Theophylline, DMPX	↓ catalepsy in reserpine and haloperidol models ↑ survival of DA neurons in MPTP, paraquat and maneb models	Mandhane et al., 1997; Chen et al., 2001; Xu et al., 2002; Bishnoi et al., 2006; Kalda et al., 2006; Singh et al., 2009; Trevitt et al., 2009; Kachroo et al., 2010

Stayte and Vissel, Frontiers in Neuroscience, 2014

Caffeine and adenosine A2A receptors x Parkinson's disease – Animal models

- Pre-clinical studies indicate that caffeine may confer neuroprotection against the underlying dopaminergic neuron degeneration and can influence the onset and progression of PD.

- Caffeine, through the blockade of adenosine A2A receptors in striatopallidal neurons, can improve the motor deficits of PD and adenosine A2*A* receptor antagonists such as istradefylline reduce OFF time associated to chronic L-dopa therapy.

Coffee/Caffeine x Risk of Parkinson's disease

Parkinson's disease (PD)—human epidemiological studies

Reference	Participants	Duration	Main results	Conclusion
Postuma et al., 2012	61 PD patients Placebo: n=31 (19 M, 12 F) Caffeine: n=30 (25 M, 5 F) 65-68 y	6 wk 1st three wk: 100 mg caffeine, 2×/d 2nd three wk: 200 mg caffeine, 2×/d	Improved the total UPDRS (unified Parkinson's disease rating scale) by 4.7 points Improved the motor manifestation by 3.2 points	Caffeine treatment in PD patients has potential motor benefits
Ross et al., 2000	8004 American Japanese men 53 y	27 y	Caffeine >421 mg of caffeine: 5× ↓ risk of developing PD vs nondrinkers, 2.6× ↓ risk vs 124-208 mg/d, 3.8× ↓ risk vs 209-287 mg/d, and 2× ↓ risk vs 288-420 mg/d.	Caffeine has an inverse association with the risk of developing PD.
Liu et al., 2012	318 260 participants 187 499 women 130 761 men 61 y	9-11 y	Coffee at >5 cups/d: ↓ risk of PD in men (OR=0.70, CI=0.47-1.04) and women (OR=0.74, CI=0.42-1.29) vs nonusers Women on hormone therapy: ↓ risk of PD development upon caffeine consumption 129-511 mg/d OR=0.66 (CI=0.42-1.05) vs intakes <17.4 mg/d 511-590 mg/d OR=0.64 (CI=0.39-1.04) vs intakes <17.4 mg/d >590 mg/d OR=0.53 (CI=0.28-0.98) vs intakes <17.4 mg/d	Caffeine has an inverse association with the risk of developing PD.
Qi et al., 2014	492 722 participants for caffeine Women and men 901 764 participants for coffee Women and men		For every 200 mg/d increment of caffeine, risk of PD ↓ by 17% Coffee at ~ three cups/d (volume not identified): ↓ risk of PD (RR=0.72, CI=0.65-0.81) Coffee at two cups/d: 26% ↓ risk of PD vs nonusers Coffee consumption (3 cups/d) ↓ PD risk in men (RR=0.68, CI=0.59-0.78) and women (RR=0.76, CI=0.63-0.93) vs nonusers	Coffee and caffeine consumption have inverse associations with the risk of developing PD.
Palacios et al., 2012	63 590 women 69 y 48 532 men 71 y	8 y	Men—caffeine at 120 mg/d: ↓ risk of PD by 38% (RR=0.62, CI=0.40-0.95) vs 9.2 mg/d Men—caffeine at ≥274 mg/d (≥2 cups coffee/d) ↓ risk of PD by ~50% (RR=0.54, CI=0.37-0.80) vs 9.2 mg/d Men—caffeine at 478 mg/d ↓ risk of PD (RR=0.43, CI=0.26-0.71) vs 9.2 mg/d Women—caffeine at 435 mg/d (3.2 cups coffee/d) ↓ risk of PD by 40% (RR=0.61, CI=0.34-1.09) vs 5.6 mg/d.	Caffeine has a protective effect against the risk of developing PD.
Hu et al., 2007	15 042 women 64.0 y 14 293 men 62.2 y	12.9 y	In men, 0, 1-4 cups, and >5 cups of coffee (100 mL/cup) had a hazard ratio of 1.00, 0.55 (CI=0.26-1.15) and 0.41 (CI=0.19-0.88), respectively, of PD In women, 0, 1-4 cups and >5 cups of coffee (100 mL/cup) had a hazard ratio of 1.00, 0.50 (CI=0.22-1.12) and 0.39 (CI=0.17-0.89), respectively, for PD.	Coffee drinking is associated with lower risk of developing PD
Ascherio et al., 2003	77 713 women 30-55 y	18 y	Postmenopausal hormone users + ~1/2 a cup of coffee/d (68 mg/d of caffeine): ↓ 34% risk of PD Postmenopausal hormone users + five cups of coffee/d (688 mg/d of caffeine): ↑ 55% risk among	Use of postmenopausal hormone therapy was associated with a lower risk of PD in women with low caffeine intake, but it was associated with higher risk of PD in women with high caffeine intake.

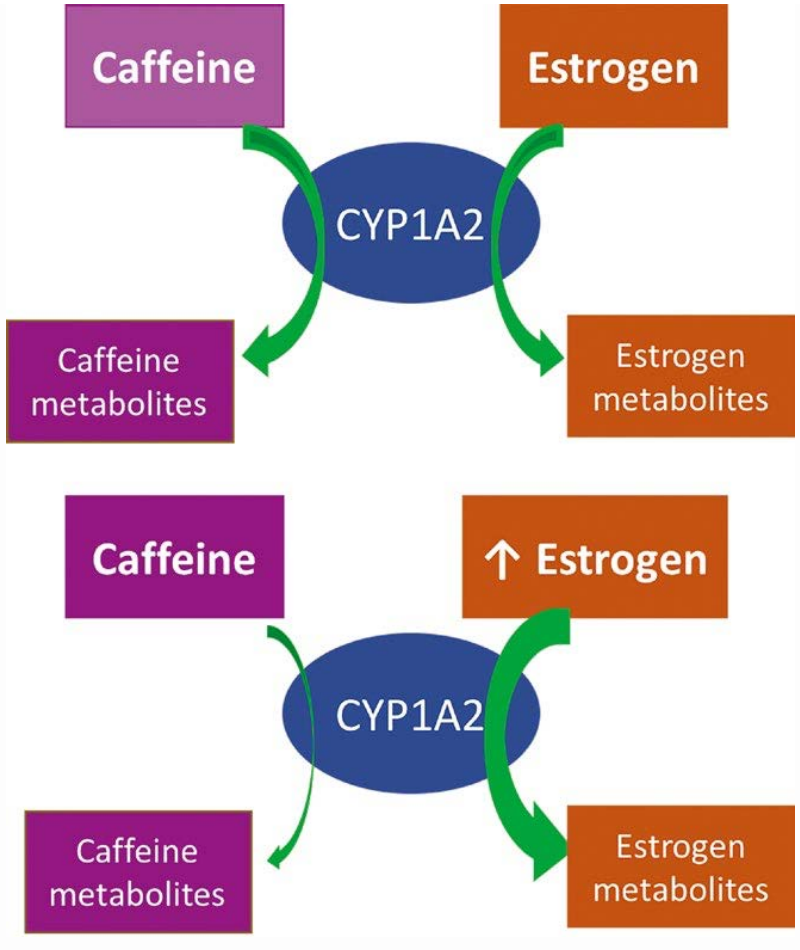
Kolahdouzan & Hamadeh, CNS Neuroscience & Therapeutics, 2017

Coffee/Caffeine x Risk of Parkinson's disease

O'Keefe et al., Progress in Cardiovascular Diseases, 2018 (*In press)*
Costa et al., J Alzheimers Dis, 2010

Prospective Study of Caffeine Consumption and Risk of Parkinson's Disease in Men and Women

Alberto Ascherio, MD, DrPH,[1,2] Shumin M. Zhang, MD, ScD,[1,3] Miguel A. Hernán, MD, DrPH,[2] Ichiro Kawachi, MD, PhD,[3,4] Graham A. Colditz, MD, DrPH,[2,3] Frank E. Speizer, MD,[3,5] and Walter C. Willett, MD, DrPH[1–3]



ASCHERIO et al., Neurology, 2003

Ronald B. Postuma, MD, MSc
Julius Anang, MD
Amelie Pelletier, MD
Lawrence Joseph, PhD
Mariana Moscovich, MD
David Grimes, MD
Sarah Furtado, MD
Renato P. Munhoz, MD
Silke Appel-Cresswell, MD
Adriana Moro, MD
Andrew Borys, MD
Douglas Hobson, MD
Anthony E. Lang, MD

Caffeine as symptomatic treatment for Parkinson disease (Café-PD)

A randomized trial

Methods: 121 PD patients with 1–8 years disease duration were randomized to caffeine-containing capsules 200 mg twice daily vs placebo capsules for 6–18 months. The outcomes included safety and tolerability, motor symptoms, sleep, cognition and quality of life.

Exclusion criteria included caffeine intake ≥150 mg per day

Conclusion:

- **Caffeine did not provide clinically important improvement of motor manifestations of PD.**
- Epidemiologic links between caffeine and lower PD risk do not appear to be explained by symptomatic effects.

Clinicaltrials.gov identifier: NCT01738178

Postuma et al., Neurology, 2017

Serum caffeine and metabolites are reliable biomarkers of early Parkinson disease

Motoki Fujimaki, MD, Shinji Saiki, MD, PhD, Yuanzhe Li, PhD, Naoko Kaga, PhD, Hikari Taka, PhD, Taku Hatano, MD, PhD, Kei-Ichi Ishikawa, MD, PhD, Yutaka Oji, MD, Akio Mori, MD, Ayami Okuzumi, MD, Takahiro Koinuma, MD, Shin-Ichi Ueno, MD, Yoko Imamichi, BS, Takashi Ueno, PhD, Yoshiki Miura, PhD, Manabu Funayama, PhD, and Nobutaka Hattori, MD, PhD

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Neurology® 2018;90:e404-e411. doi:10.1212/WNL.0000000000004888

Methods

Levels of caffeine and its 11 metabolites in serum from 108 patients with PD and 31 age-matched healthy controls were examined by liquid chromatography–mass spectrometry. Mutations in caffeine-associated genes were screened by direct sequencing.

Table 2 Alterations in caffeine and metabolite levels in patients with Parkinson disease (PD) and controls

Compounds	Controls, mean ± SD (LLD)	Patients with PD, mean ± SD (LLD)	*p* Value
Caffeine	79.10 ± 91.5 (2)	23.53 ± 22.4 (4)	<0.0001

Conclusion

Absolute lower levels of caffeine and caffeine metabolite profiles are promising diagnostic biomarkers for early PD. This is consistent with the neuroprotective effect of caffeine previously revealed by epidemiologic and experimental studies.

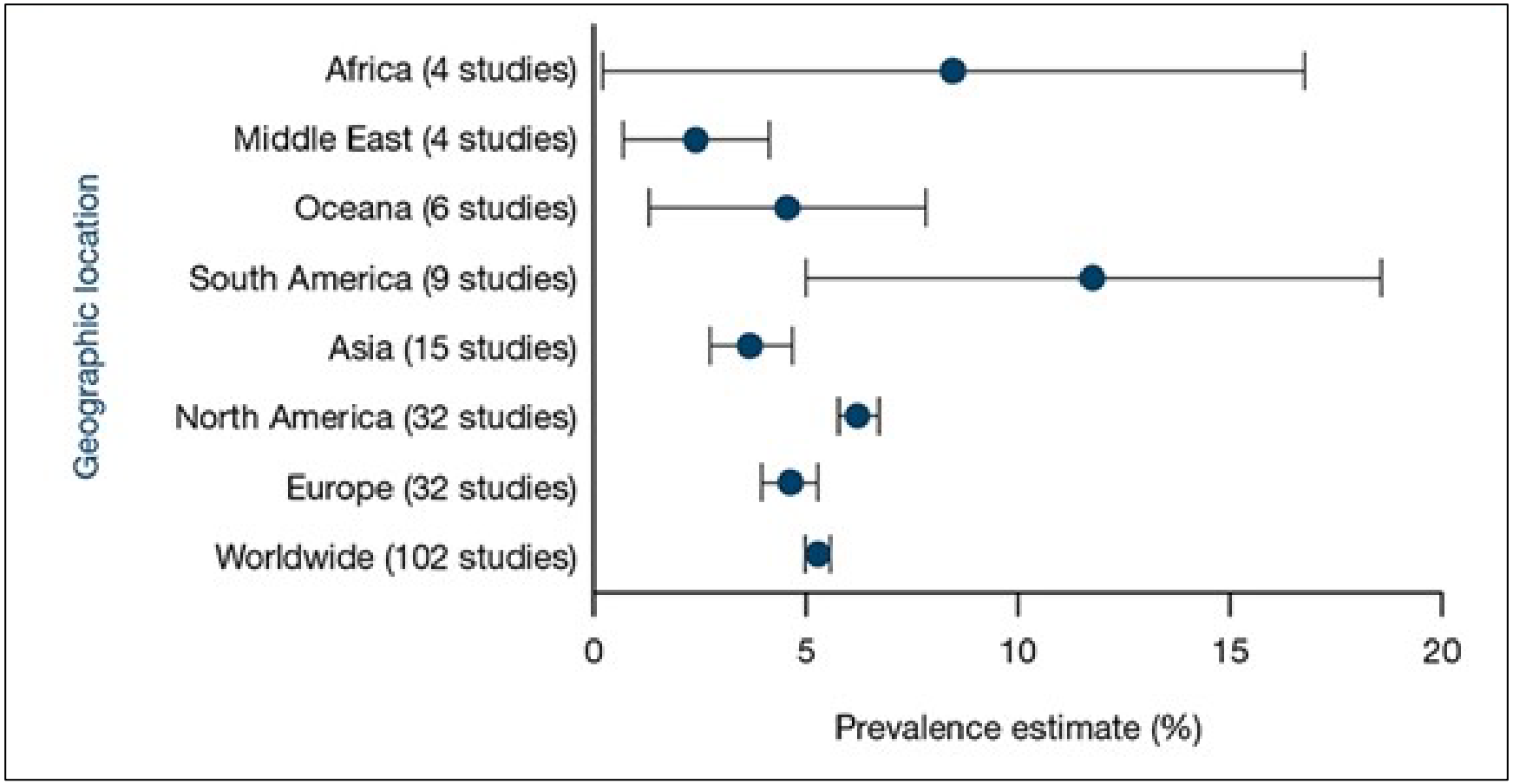
Attention-deficit hyperactivity disorder (ADHD)

ADHD is a chronic neurobehavioral disorder that begins in childhood and is characterized by a persistent pattern of:

- Inattention
- Hyperactivity
- Impulsivity

Diagnostic and Statistical Manual of Mental Disorders (DSM–V), 2013

Prevalence of ADHD in children and adolescents

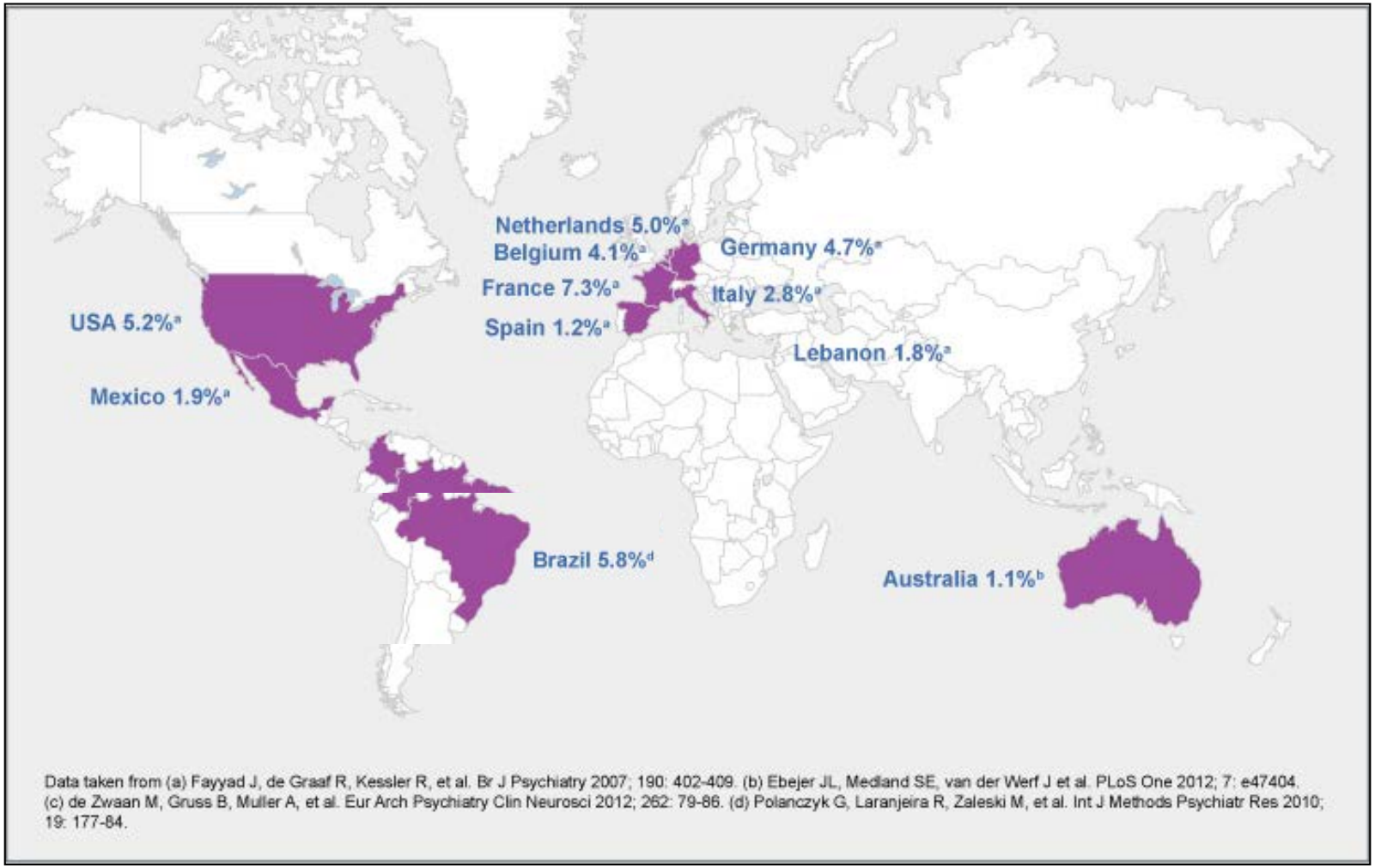


A meta-analysis of 102 studies on children and adolescents diagnosed with ADHD, found that the prevalence of ADHD in individuals aged ≤18 years varies among countries worldwide.

The estimated prevalence worldwide is 5%.

Polanczyk, G. et al. Am J Psychiatry, 2007

Prevalence of ADHD in adults

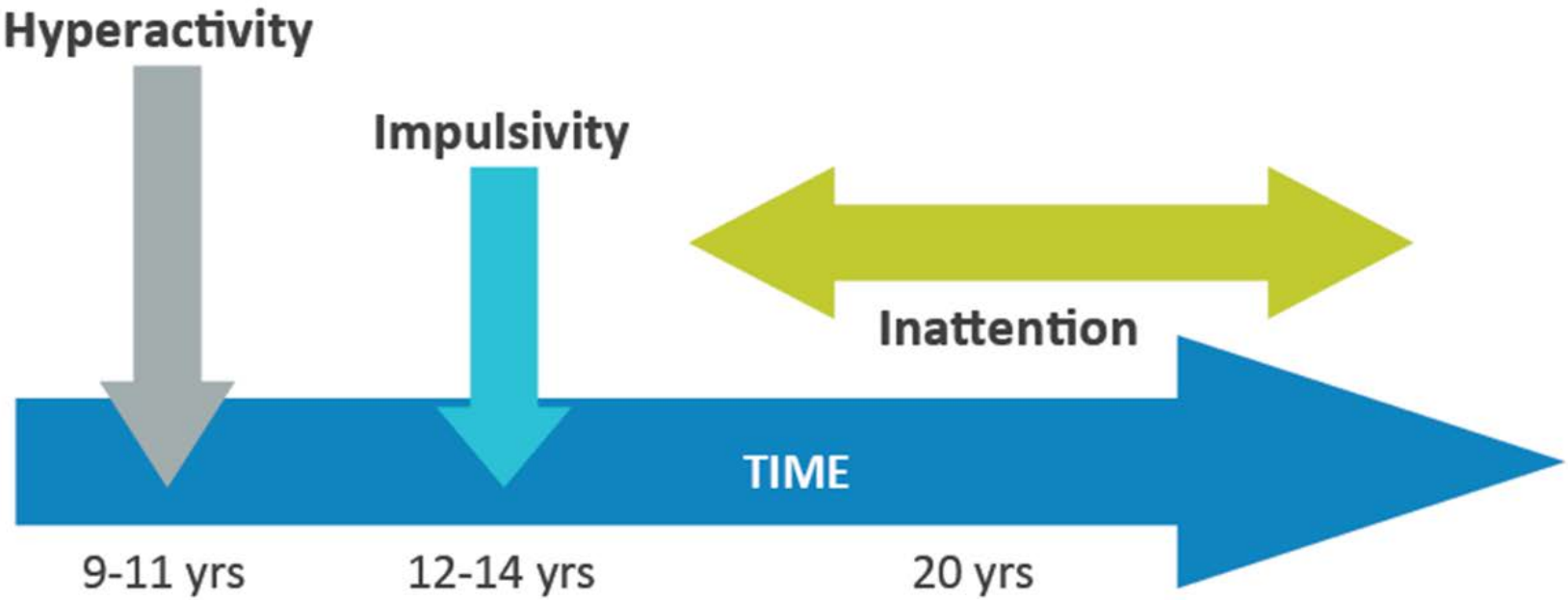


Data taken from (a) Fayyad J, de Graaf R, Kessler R, et al. Br J Psychiatry 2007; 190: 402-409. (b) Ebejer JL, Medland SE, van der Werf J et al. PLoS One 2012; 7: e47404. (c) de Zwaan M, Gruss B, Muller A, et al. Eur Arch Psychiatry Clin Neurosci 2012; 262: 79-86. (d) Polanczyk G, Laranjeira R, Zaleski M, et al. Int J Methods Psychiatr Res 2010; 19: 177-84.

The global prevalence of ADHD in adults ranges from 1.1% in Australia to 7.3% in France.

http://adhd-institute.com/burden-of-adhd/epidemiology/

Symptoms persist into adolescence and adulthood for majority of patients



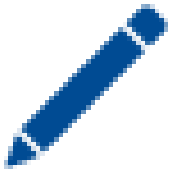
Child Mind Institute

Hyperactivity and impulsivity may diminish at a higher rate than inattention.

Negative impact of ADHD on multiple domains

Daily activities at home

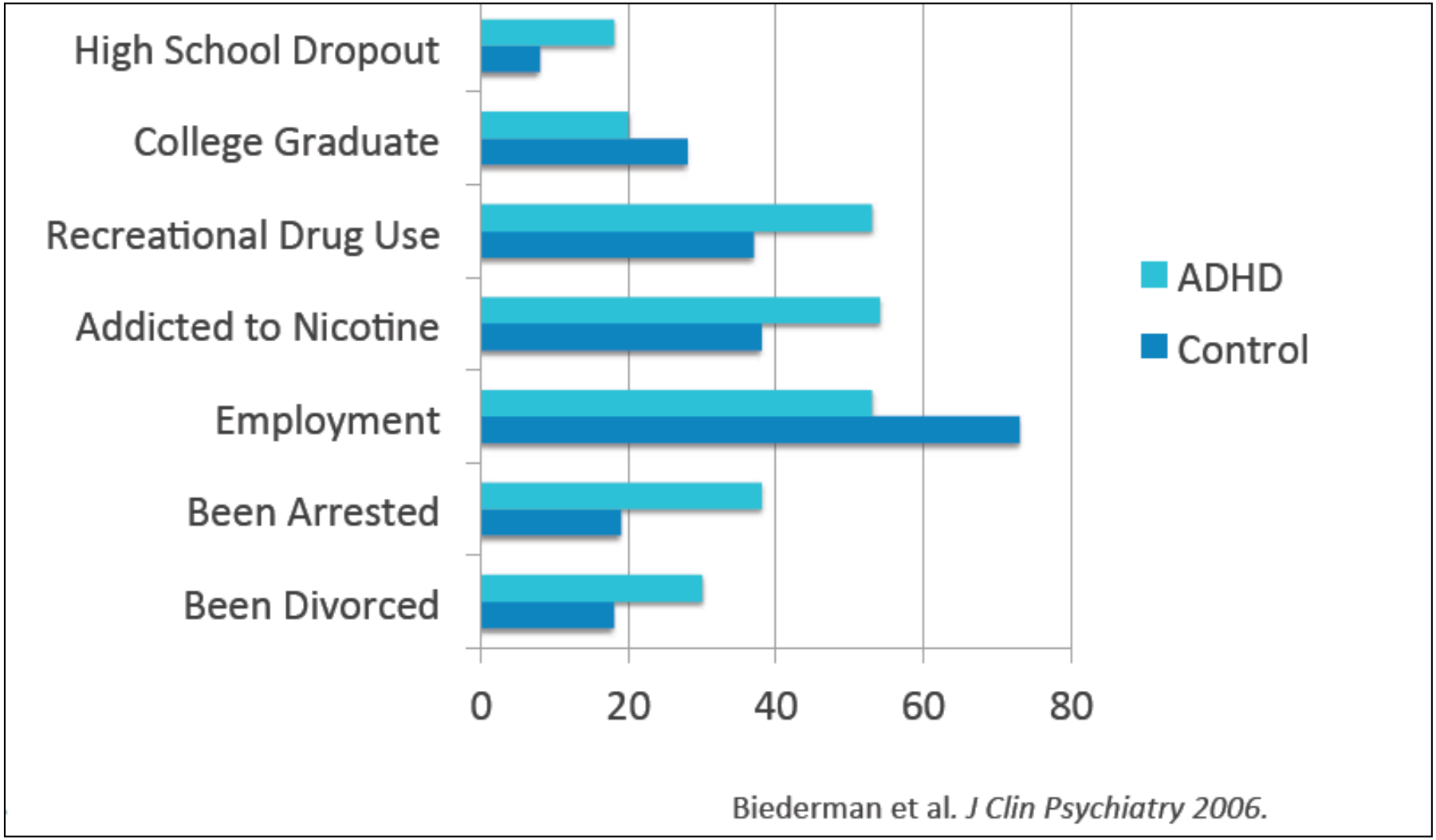
Parents, careers and siblings



School and homework

Teachers and friends

Real-Life Consequences



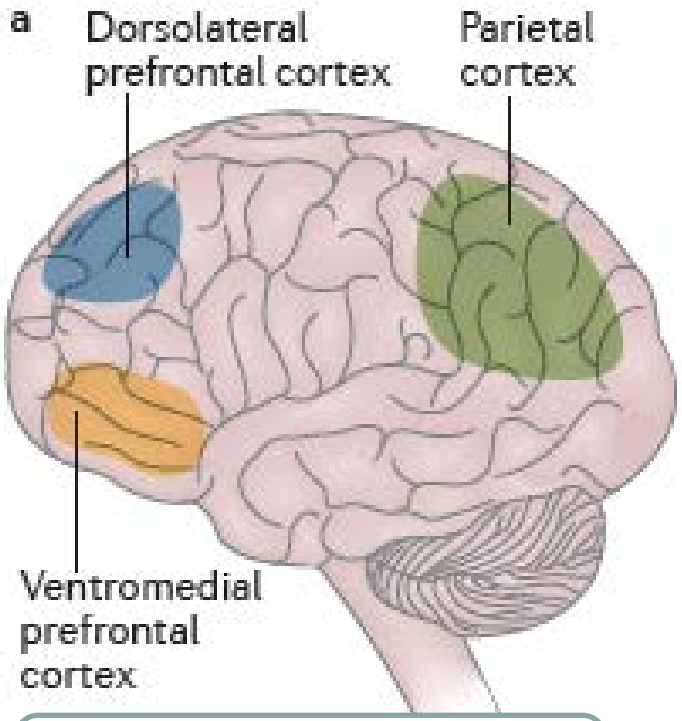
Biederman et al. *J Clin Psychiatry 2006.*

Neurobiology of ADHD

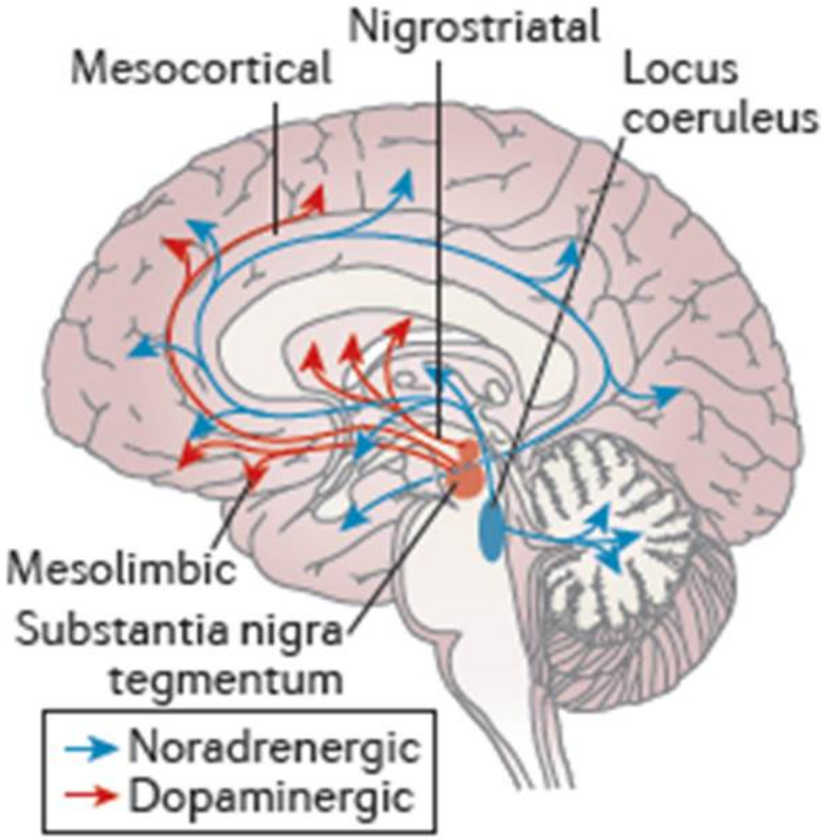
ADHD is associated with structural, functional and neurotransmitter alterations in many brain regions, including cortical and subcortical structures.

Working memory

Orientation



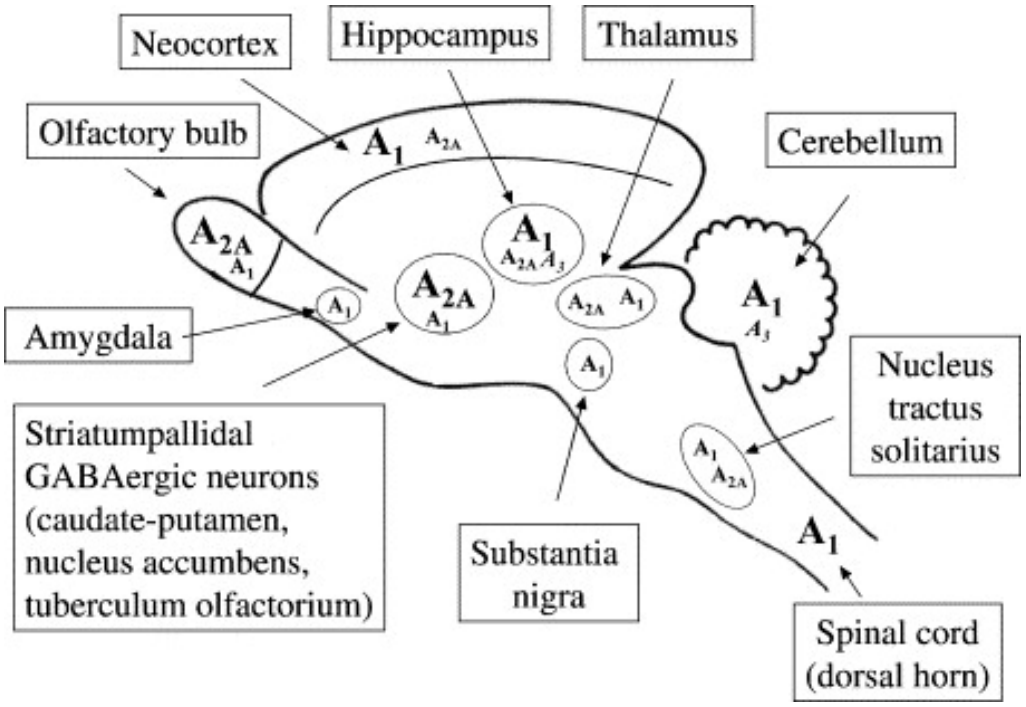
Decision making and strategic planning

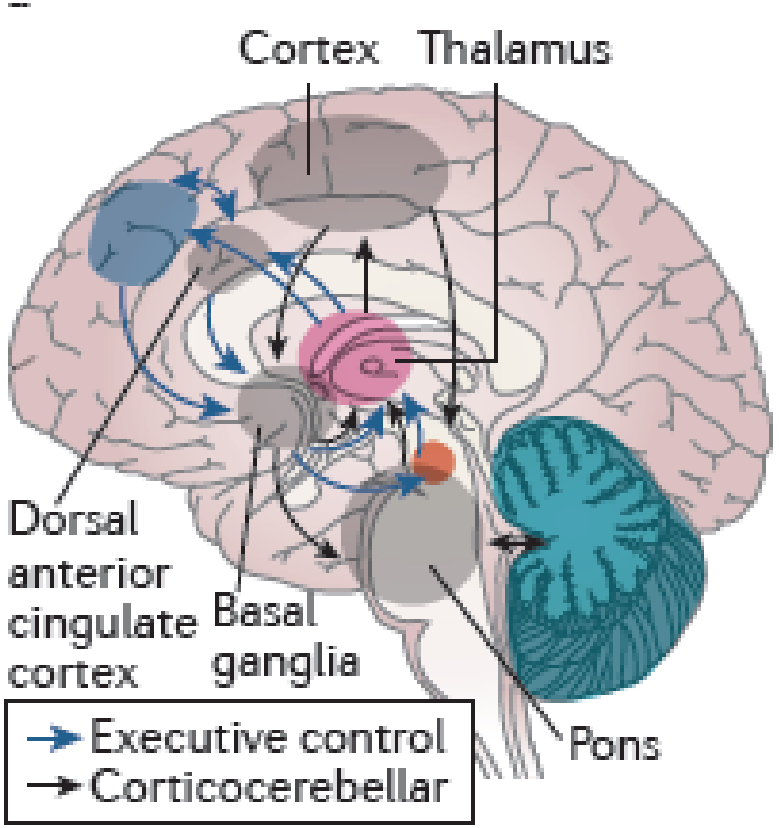


Faraone et al., Nat Rev Dis Primers, 2015

“Caffeine (Adenosine) receptors”

Adenosine receptors are widely distributed in brain areas with marked alterations in ADHD

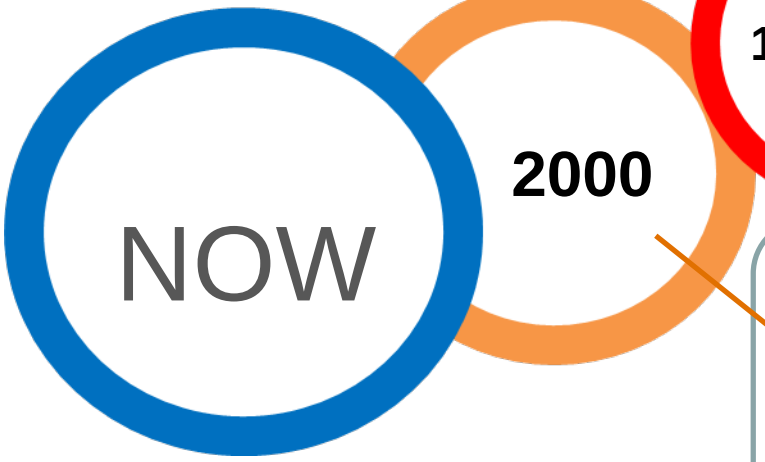




Ribeiro et al., Progress in Neurobiology, 2003

Faraone et al., Nat Rev Dis Primers, 2015

Coffee/Caffeine x ADHD



Schnackenberg: positive effects of coffee consumption in 11 hyperactive children.

1973

Kupietz & Winsberg: caffeine improves hyperactivity but not attention deficits.

1977

Garfinkel et al.; Schechter & Timmons: caffeine improves the effects of methylphenidate.

1978

Harvey & Marsh: superior effects of caffeine in comparison to placebo.

1981-1985

2000

Leon: meta-analysis study:

- small number of studies;
- mean study size was very small (14.4)
- different caffeine dose.

Reviewed in: Ioannidis et al., Journal of Psychopharmacology, 2014

Available online at www.sciencedirect.com
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Behavioural Brain Research 159 (2005) 197–205
BEHAVIOURAL BRAIN RESEARCH
www.elsevier.com/locate/bbr

Research report

Blockade of adenosine A_{2A} receptors reverses short-term social memory impairments in spontaneously hypertensive rats

Rui D.S. Prediger, Daniel Fernandes, Reinaldo N. Takahashi*

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International Journal of Neuropsychopharmacology (2005), **8**, 1–12. Copyright © 2005 CINP
doi:10.1017/S1461145705005341

Caffeine improves spatial learning deficits in an animal model of attention deficit hyperactivity disorder (ADHD) – the spontaneously hypertensive rat (SHR)

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Behavioural Brain Research 215 (2010) 39–44

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Chronic caffeine treatment during prepubertal period confers long-term cognitive benefits in adult spontaneously hypertensive rats (SHR), an animal model of attention deficit hyperactivity disorder (ADHD)

Vanessa A. Pires[a], Fabrício A. Pamplona[a,b], Pablo Pandolfo[a], Rui D.S. Prediger[a,b], Reinaldo N. Takahashi[a,*]

[a] *Departamento de Farmacologia, Centro de Ciências Biológicas, Universidade Federal de Santa Catarina, Campus Universitário Trindade, 88049-900 Florianópolis, SC, Brazil*
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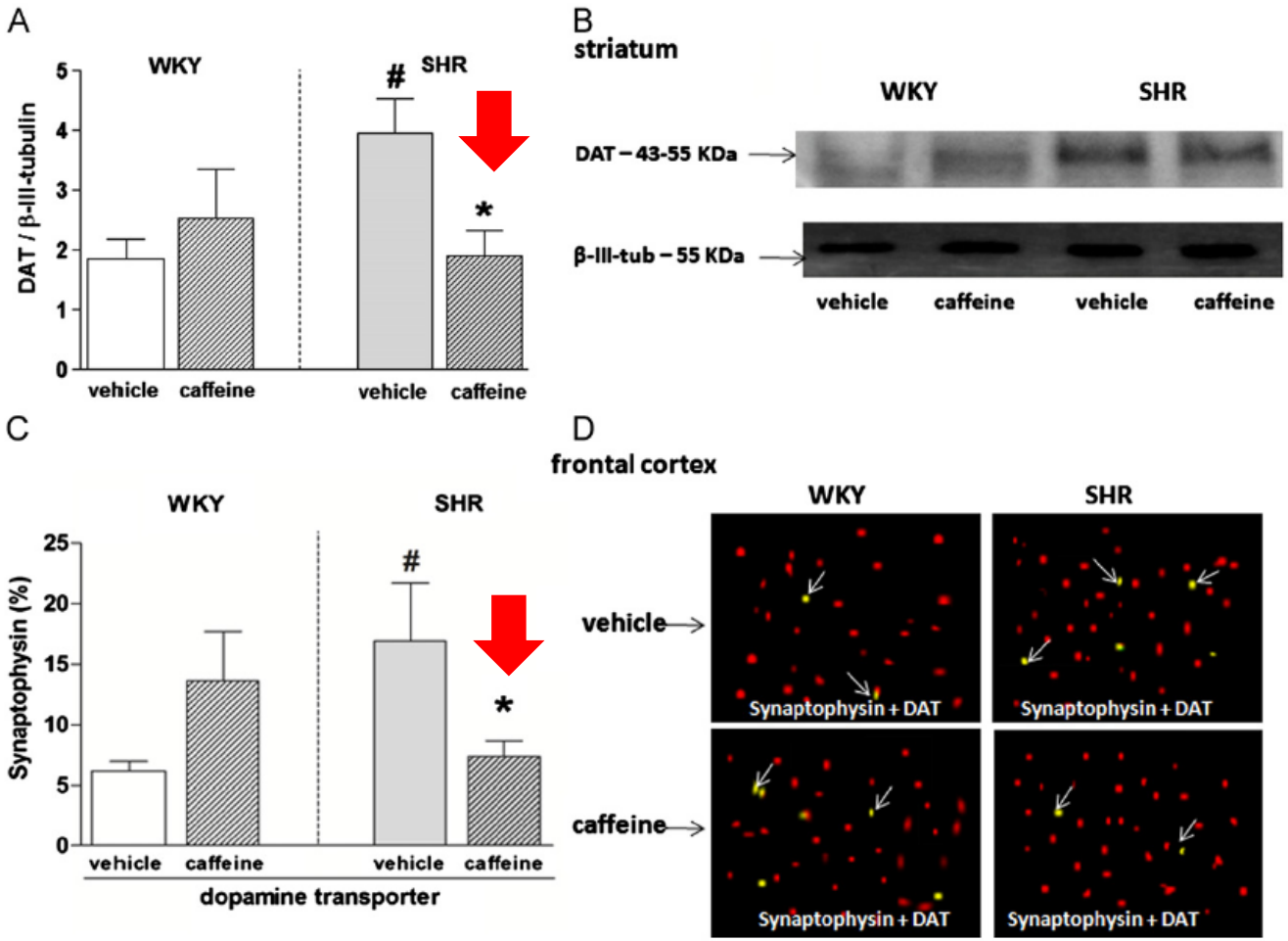
Behavioural Pharmacology 2009, **20**:134–145

Adenosine receptor antagonists improve short-term object-recognition ability of spontaneously hypertensive rats: a rodent model of attention-deficit hyperactivity disorder

Vanessa A. Pires, Fabrício A. Pamplona, Pablo Pandolfo, Daniel Fernandes, Rui D.S. Prediger and Reinaldo N. Takahashi

Chronic caffeine treatment normalizes dopaminergic function in the striatum and the frontal cortex



Chronic treatment with caffeine during adolescence (2 mg/kg, i.p.; twice daily for 21 day) in male SHR.

Pandolfo et al., European Neuropsychopharmacology 23 (2013) 317–328.

Conclusion

√ **Moderate safety daily caffeine consumption:**
Adults: 4-5 cups of coffee (± 400 mg/day)
Pregnant women: 2 cups of coffee (± 200 mg/day)
Children and adolescents: 2.5 - 3 mg/kg per day

√ Coffee/caffeine consumption improves attention, memory, mood and decreases the risk of depression and suicide;

√ Lifelong coffee/caffeine consumption prevents age-related cognitive decline and increases the longevity;

√ Despite ineffective for the improvement of Alzheimer's and Parkinson's diseases symptoms, lifelong coffee/caffeine consumption decreases the risk of these diseases and may represent a blood marker of diseases progression;

√ ADHD symptoms in children, adolescents and adults may be improved by coffee/caffeine consumption and future controlled clinical trials are welcome!

Caution in caffeine consumption

Systematic review of the potential adverse effects of caffeine consumption in healthy adults, pregnant women, adolescents, and children

Daniele Wikoff [a, *], Brian T. Welsh [b], Rayetta Henderson [c], Gregory P. Brorby [d], Janice Britt [e], Esther Myers [f], Jeffrey Goldberger [g], Harris R. Lieberman [h], Charles O'Brien [i], Jennifer Peck [j], Milton Tenenbein [k], Connie Weaver [l], Seneca Harvey [m], Jonathan Urban [b], Candace Doepker [n]

√ Risk pregnancy

√ Gastritis or ulcer

√ Insomnia

√ Anxiety disorders

(Panic attacks and generalized anxiety)

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Dr. Daniel Rial
Dr. Morgana Moretti
Dr. Jofre Freitas
Marissa Schamne
Angela França
Josiel Mack
Andréia Cunha
Samantha Lopes
Katiane Roversi
Tuane Sampaio
Ana Elisa Speck
Marina Magnini
Marcelo Falchetti
Gislaine Olescowicz
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Smell & Taste Center, US

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CAPES

CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico

FAPESC Fundação de Apoio à Pesquisa Científica e Tecnológica do Estado de Santa Catarina

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