3,4-Methylenedioxymethamphetamine
Ecstasy or MDMA

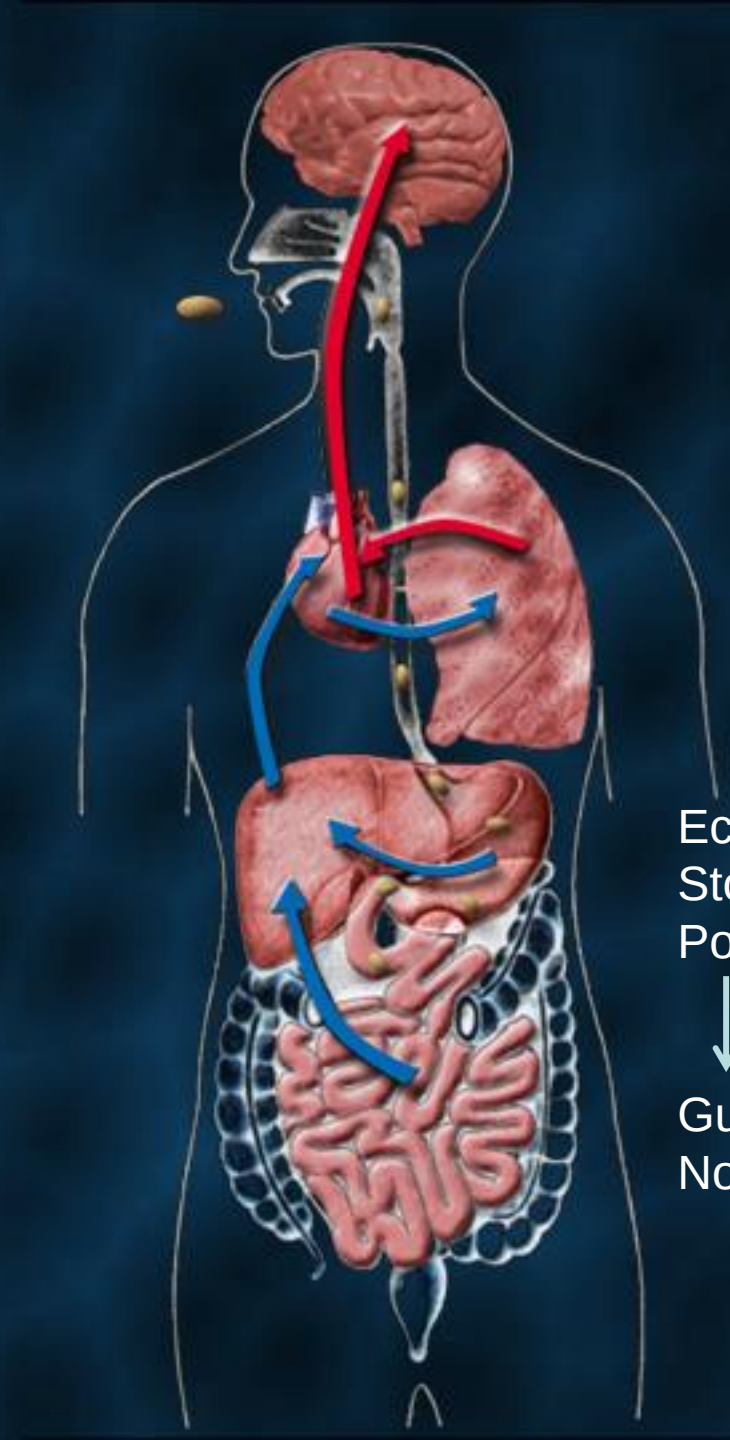
“… MDMA produces a state of relaxation and euphoria, a state of emotional openness, empathy, reduction of negative thoughts, reduction of inhibitions "

Sounds and colors may appear more intense

Defining Ecstasy

A derivative of amphetamine

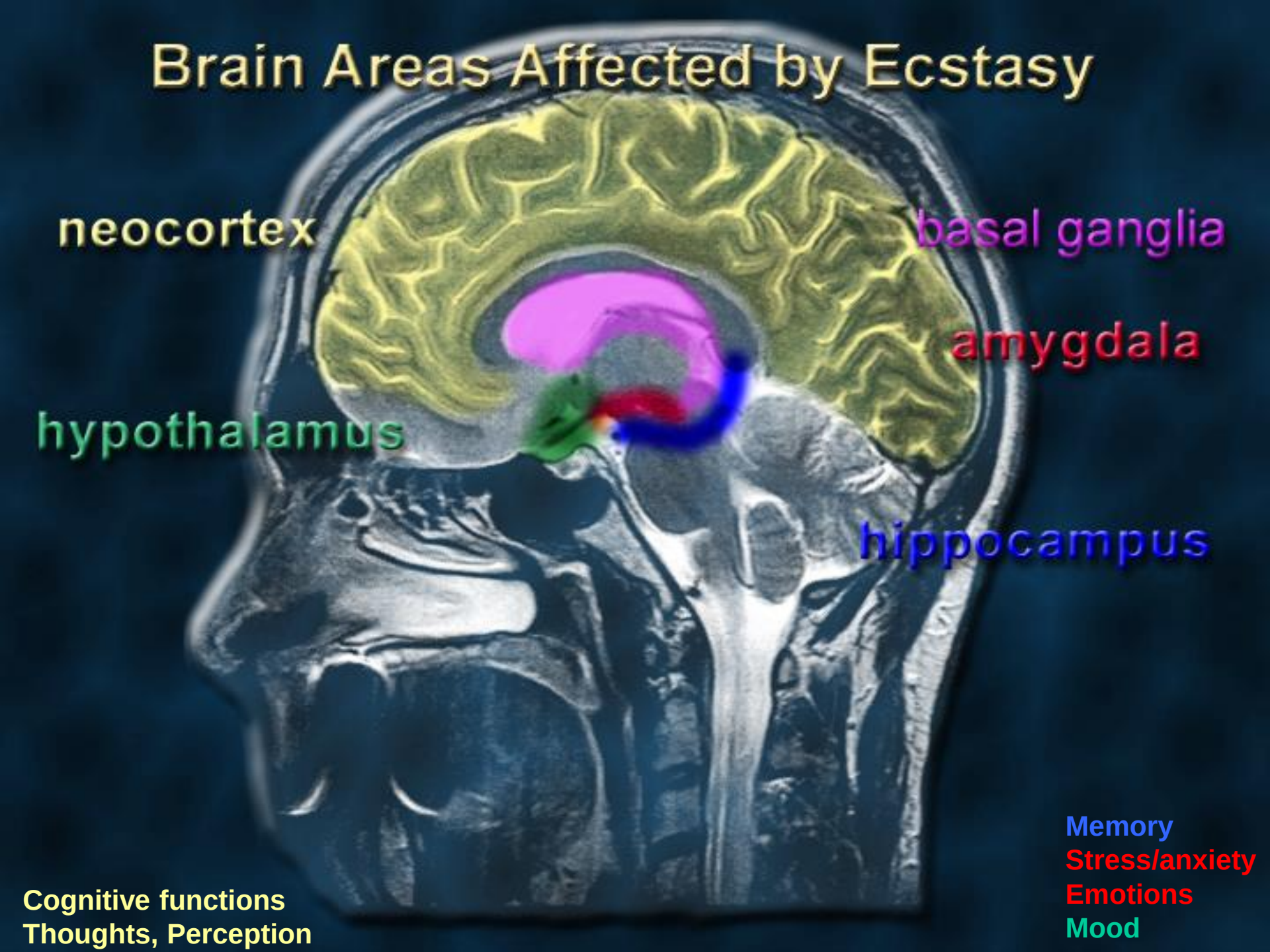
MDMA, XTC, E, essence, Adam

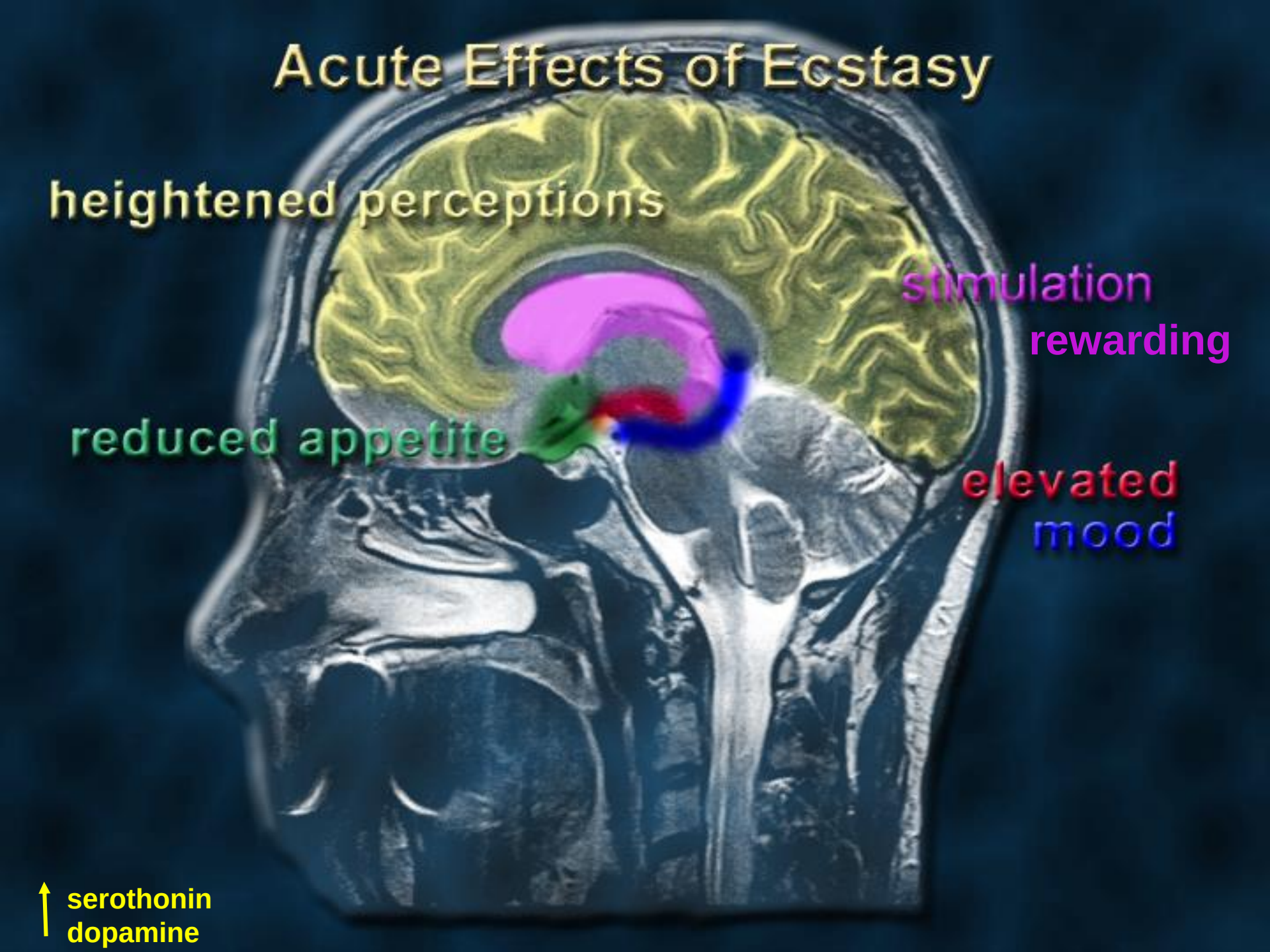


Ecstasi (weak base)
Stomac H+
Polar

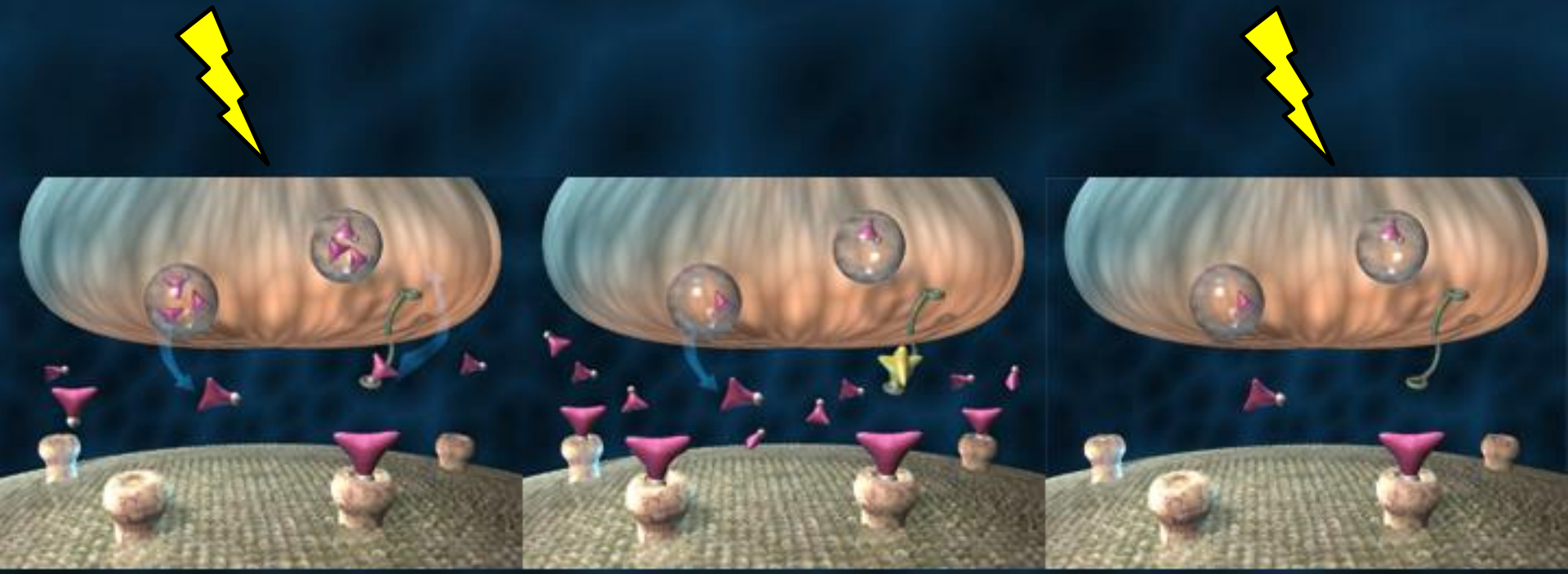
↓

Gut (alkaline)
Non polar


Brain Areas Affected by Ecstasy
neocortex
basal ganglia
amygdala
hypothalamus
hippocampus
Cognitive functions
Thoughts, Perception
Memory
Stress/anxiety
Emotions
Mood


Acute Effects of Ecstasy
heightened perceptions
stimulation
rewarding
reduced appetite
elevated
mood
serothonin
dopamine

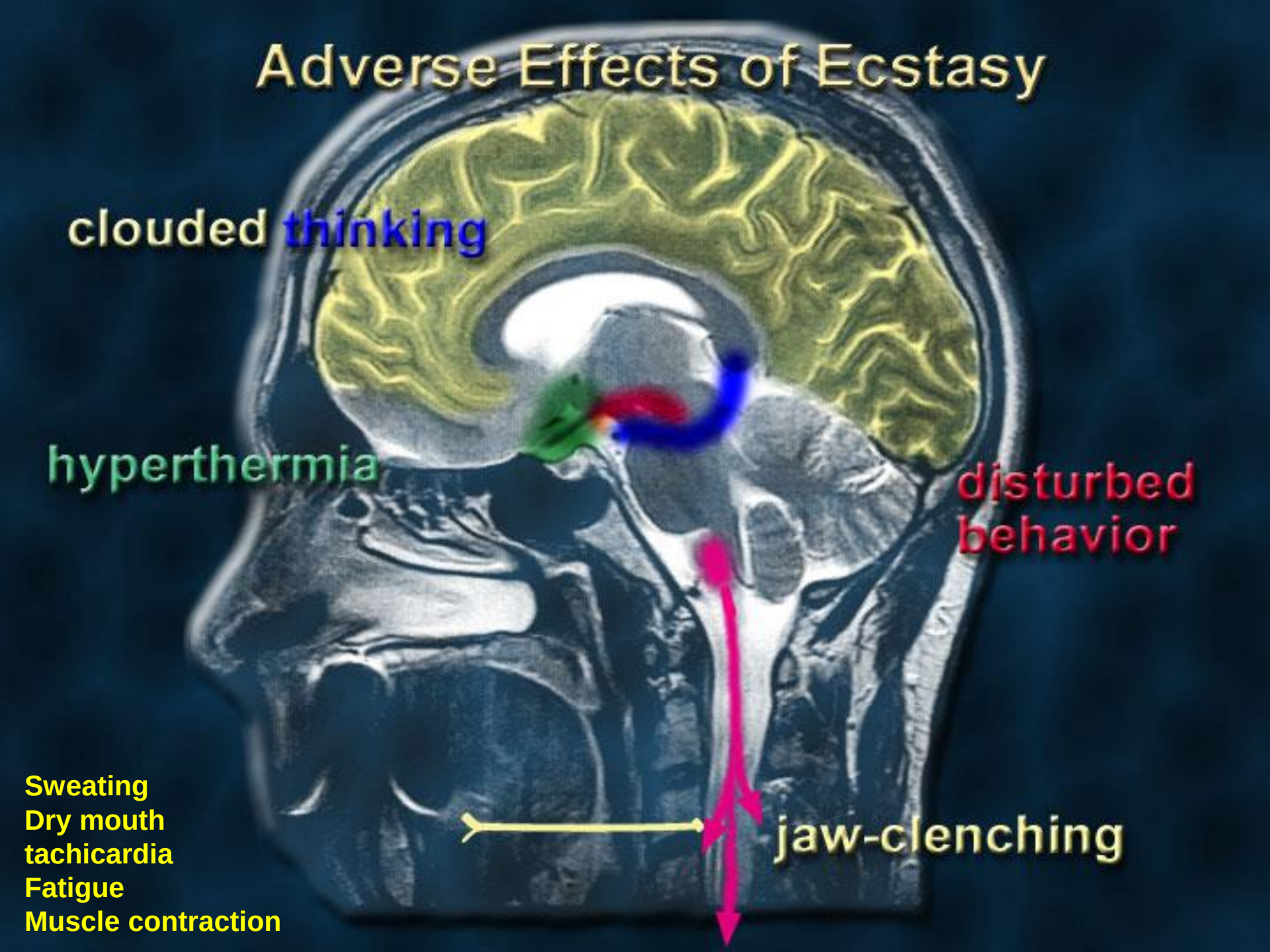
Short Term Effects after Ecstasy is Gone



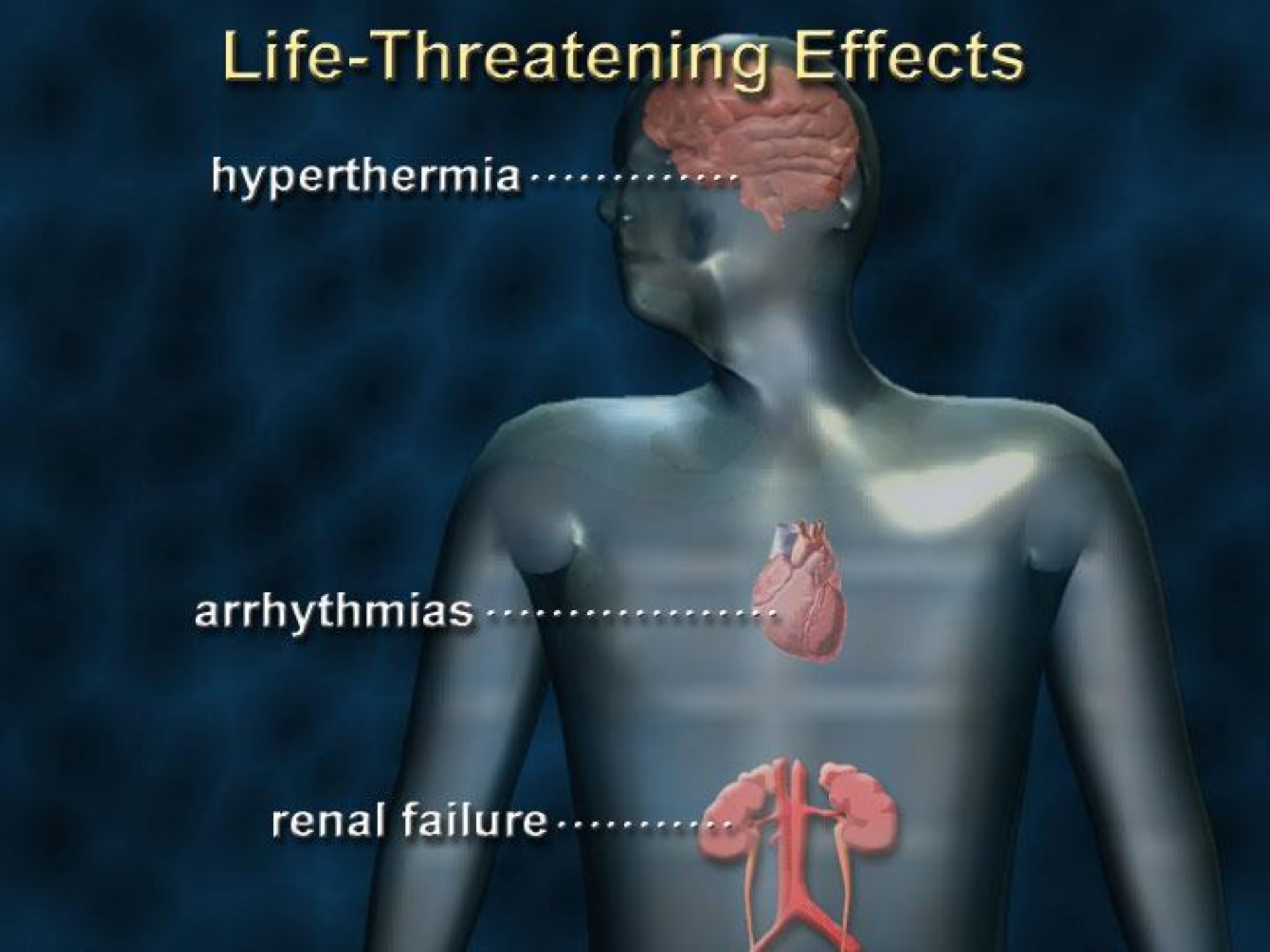
Normal

During Ecstasy
elevated mood

After Ecstasy
depression-like
feelings, irritablilty


Adverse Effects of Ecstasy
clouded thinking
hyperthermia
disturbed behavior
jaw-clenching
Sweating
Dry mouth
tachicardia
Fatigue
Muscle contraction

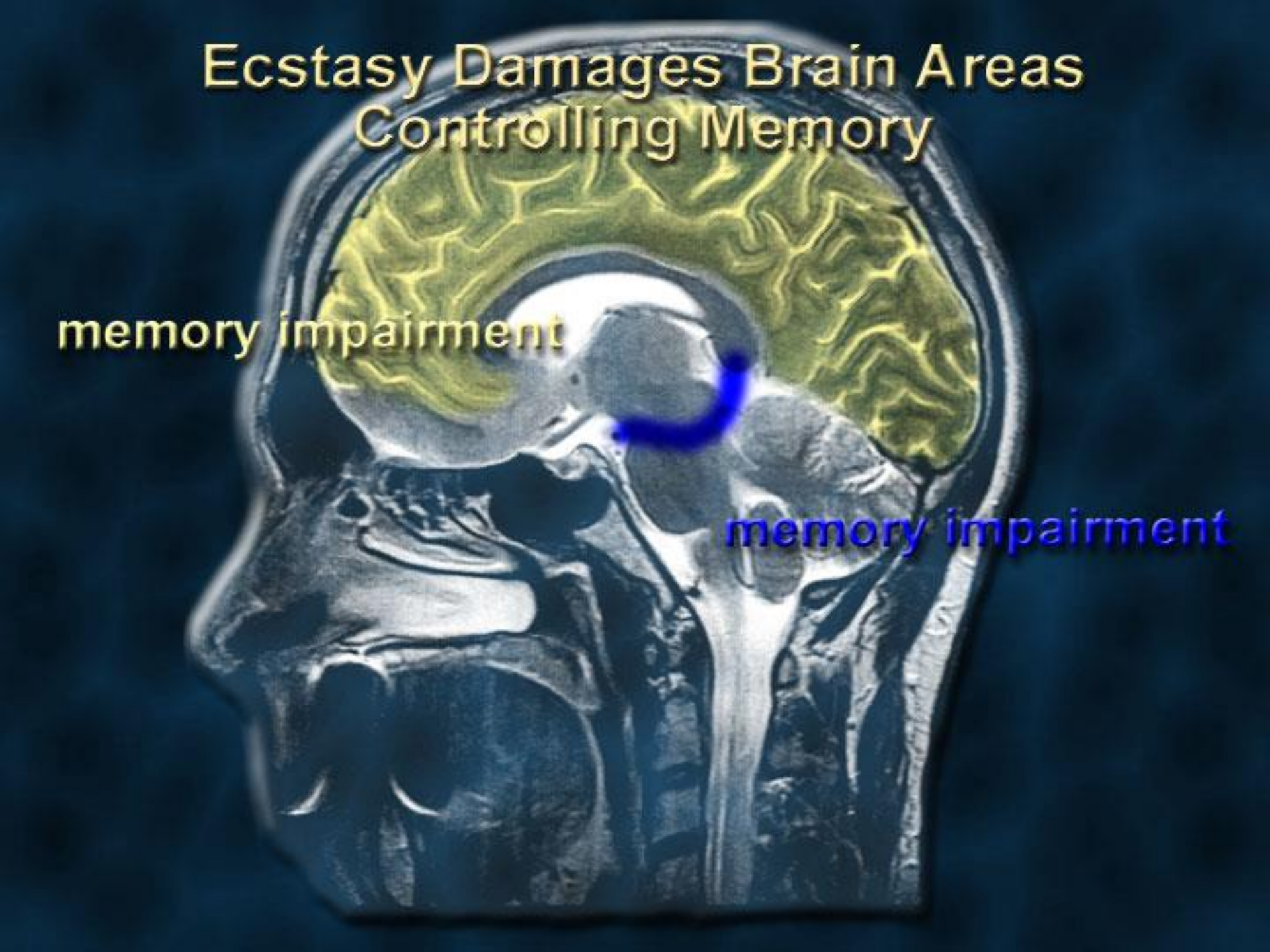
Life-Threatening Effects



Neuropsychiatric side effects following use of MDMA

ACUTE EFFECTS (IN 24 hrs)	SUB-ACUTE EFFECTS (IN 1 months)
Alteration of decision-making skills	Decrease of sleep
Decreased desire to perform physical / mental activities	Decrease of appetite
Difficulty performing mathematical operations	Drowsiness
Panic	Depression
Flashback	Anxiety
Anxiety	Irritability
Insomnia	**Chronic EFFECTS (over 1 month)**
Psychosis	
Bruxism	Panic
Decreased libido	Psychosis
Decrease appetite	Flashback
Intensification of unrest / agitation	Severe depression
Disorientation / confusion	Memory impairment
Nausea/vomiting	

Ecstasy Damages Brain Areas Controlling Memory



The Journal of Neuroscience, June 15, 1999, 19(12):5096–5107

Altered Serotonin Innervation Patterns in the Forebrain of Monkeys Treated with (±)3,4-Methylenedioxymethamphetamine Seven Years Previously: Factors Influencing Abnormal Recovery

George Hatzidimitriou,[1] Una D. McCann,[2] and George A. Ricaurte[1]

[1]Department of Neurology, The Johns Hopkins Medical Institutions, Baltimore, Maryland 21205, and [2]Unit on Anxiety Disorders, Biological Psychiatry Branch, National Institute of Mental Health, Bethesda, Maryland 20892

Long-term Toxic effects

Micro-photographs of sagittal sections of the frontal, parietal and primary visual cortex showing the serotonergic axons:

A
D **controls**
G

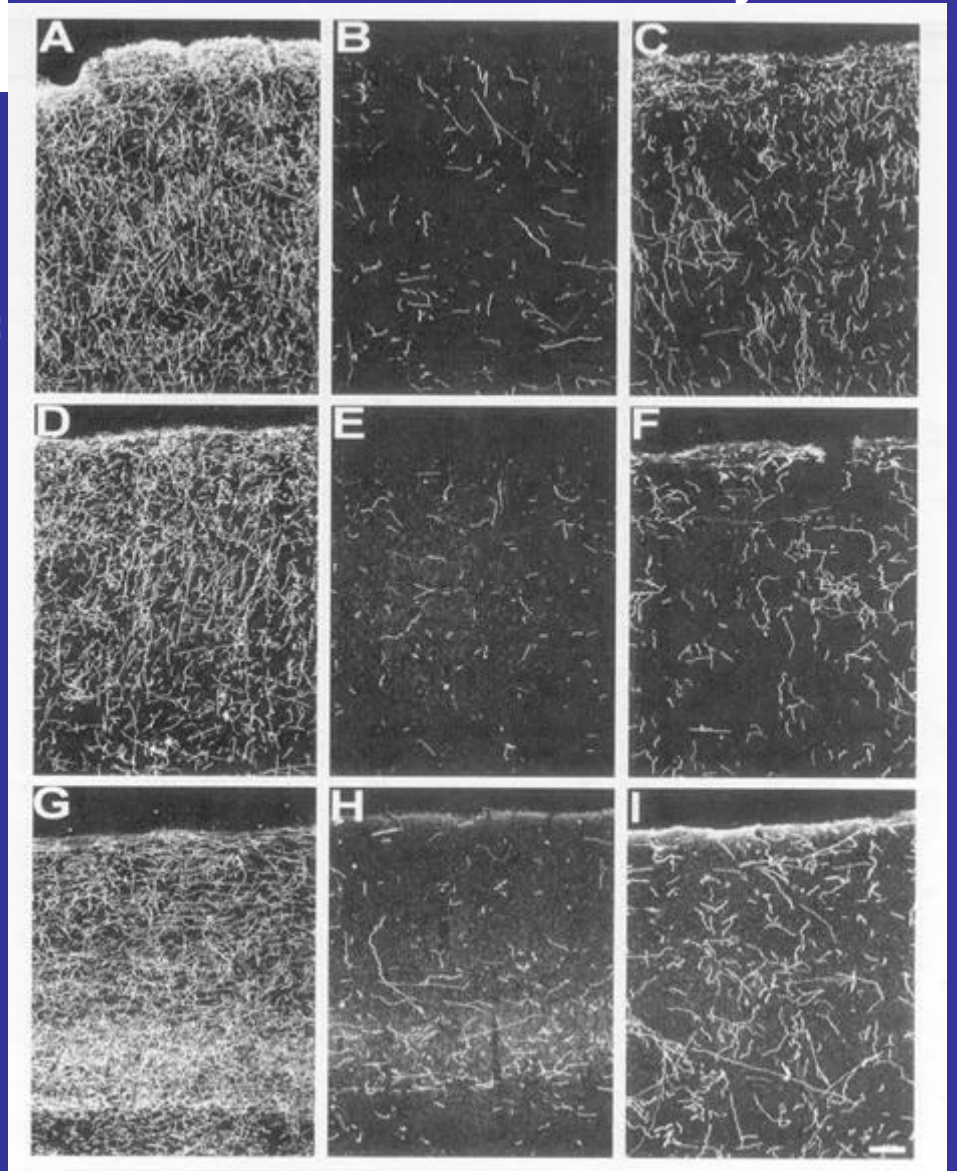
B
E **ecstasy**
2 weeks before
(5 mg/Kg 2vv/day for 4 days)

H

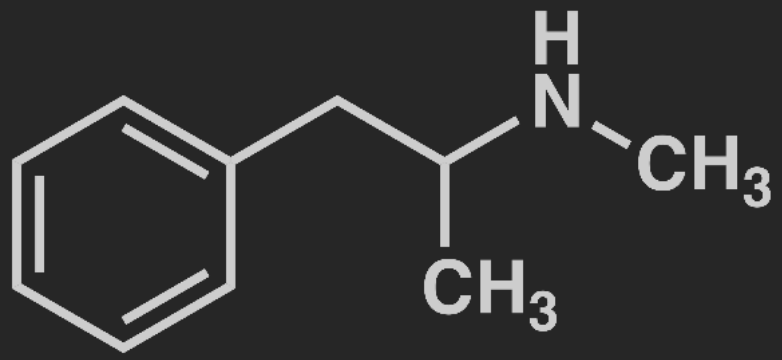
C
F **ecstasy**
7 years before
(5 mg/Kg 2vv/day for 4 days)

I

controls 2 weeks 7 years



Methamphetamine



"Ice" , "Shaboo" o " Crystal meth"

Effects

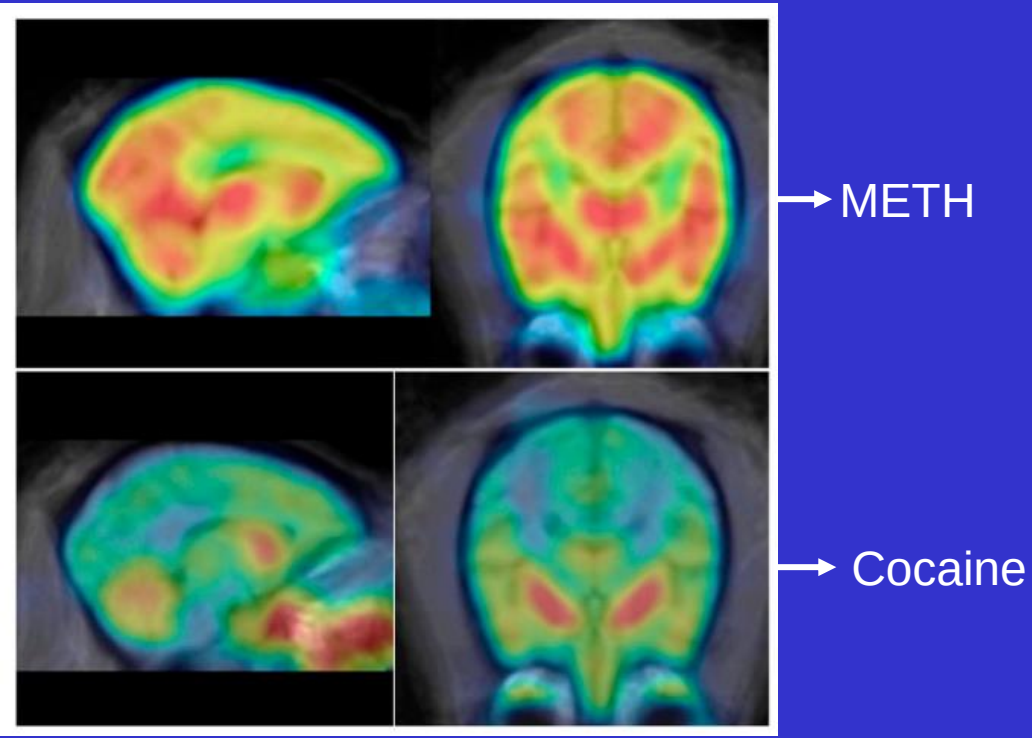
- The purest form of methamphetamine, clear crystals of d-methamphetamine hydrochloride.
- Increased energy, excitement, euphoria that can lead to violence
- Smoked or injected with effects far superior and more durable than other routes of intake and other amphetamines

Consequences

- Anxiety, depression, insomnia
- Inability of social relations
- Paranoia, hallucinations, psychotic behavior with murderous and suicidal thoughts

Table. Summary of Methamphetamine Pharmacokinetics by Administration Route[10]

	Bioavailability	Dose	T ½ (hr)	Time peak effect
Intravenous	100%	30 mg	9	< 15 min
Smoking	67%	30 mg	12	20 min
Oral	67%	30 mg	9	180 min
Intranasal	79%	50 mg	11	< 15 min



Summed brain images from Baboons for 11C-d-methamphetamine (top row, from 0–90 min) and 11C-l-(2)-cocaine (bottom row, from 0–54 min) in same animal. 11C distribution is widespread over cortical and subcortical brain regions for 11C-d-methamphetamine but is highly localized in striatum for 11C-(2)-cocaine.

Fowler et al., 2007

Criteria of the DMS-V for the diagnosis of:
addiction
withdrawal
intoxication

Stimulantants use disorder

Stimulant Intoxication

Diagnostic Criteria

A. Recent use of an amphetamine-type substance, cocaine, or other stimulant.

B. Clinically significant problematic behavioral or psychological changes (e.g., euphoria or affective blunting; changes in sociability; hypervigilance; interpersonal sensitivity; anxiety, tension, or anger; stereotyped behaviors; impaired judgment) that developed during, or shortly after, use of a stimulant.

C. Two (or more) of the following signs or symptoms, developing during, or shortly after, stimulant use:

1. Tachycardia or bradycardia.
2. Pupillary dilation.
3. Elevated or lowered blood pressure.
4. Perspiration or chills.
5. Nausea or vomiting.
6. Evidence of weight loss.
7. Psychomotor agitation or retardation.
8. Muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias.
9. Confusion, seizures, dyskinesias, dystonias, or coma.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance.

Specify **the specific intoxicant** (i.e., amphetamine-type substance, cocaine, or other stimulant).

Specify if:

With perceptual disturbances: This specifier may be noted when hallucinations with intact reality testing or auditory, visual, or tactile illusions occur in the absence of a delirium.

Diagnostic Criteria

A. Cessation of (or reduction in) prolonged amphetamine-type substance, cocaine, or other stimulant use.

B. Dysphoric mood and two (or more) of the following physiological changes, developing within a few hours to several days after Criterion A:

   1. Fatigue.
   2. Vivid, unpleasant dreams.
   3. Insomnia or hypersomnia.
   4. Increased appetite.
   5. Psychomotor retardation or agitation.

C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Specify **the specific substance that causes the withdrawal syndrome** (i.e., amphetamine-type substance, cocaine, or other stimulant).

Diagnostic Features

The essential feature of stimulant withdrawal is the presence of a characteristic withdrawal syndrome that develops within a few hours to several days after the cessation of (or marked reduction in) stimulant use (generally high dose) that has been prolonged (Criterion A). The withdrawal syndrome is characterized by the development of dysphoric mood accompanied by two or more of the following physiological changes: fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite, and psychomotor retardation or agitation (Criterion B). Bradycardia is often present and is a reliable measure of stimulant withdrawal.

Anhedonia and drug craving can often be present but are not part of the diagnostic criteria. These symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (Criterion C). The symptoms must not be attributable to another medical condition and are not better explained by another mental disorder (Criterion D).

THERAPY

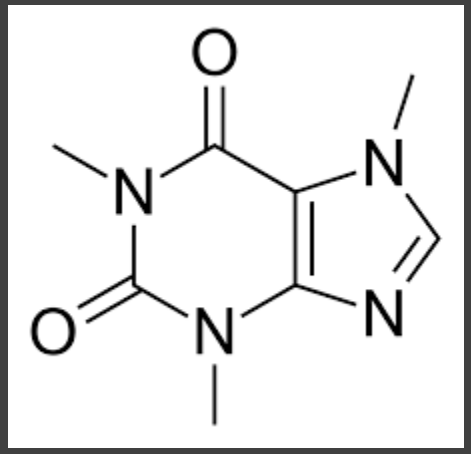
- Methylphenidate (reduces craving, does not affect compulsion)
- Modafinil (reduces cocaine intake)
- Slow release methamphetamine (reduces cocaine use)
- Antidepressants (reduce cocaine consumption, but no craving)
- Dopamine receptor antagonists (not effective)
- Vaccination


Coca-Cola
CLASSIC
12-12 OZ CANS (144 FL OZ) 12-355 mL CANS (4.26 L)


EST. 1706
TWININGS
TEAMEN TO CONNOISSEURS
FOR OVER 275 YEARS
ENGLISH BREAKFAST
TEA
NET WEIGHT 113g
Full bodied Ceylon and Indian teas skilfully blended to produce a real English brew
BLENDED BY
R. TWINING AND COMPANY LIMITED
LONDON ENGLAND WC2R 1AP

Caffeine

CAFFEINE

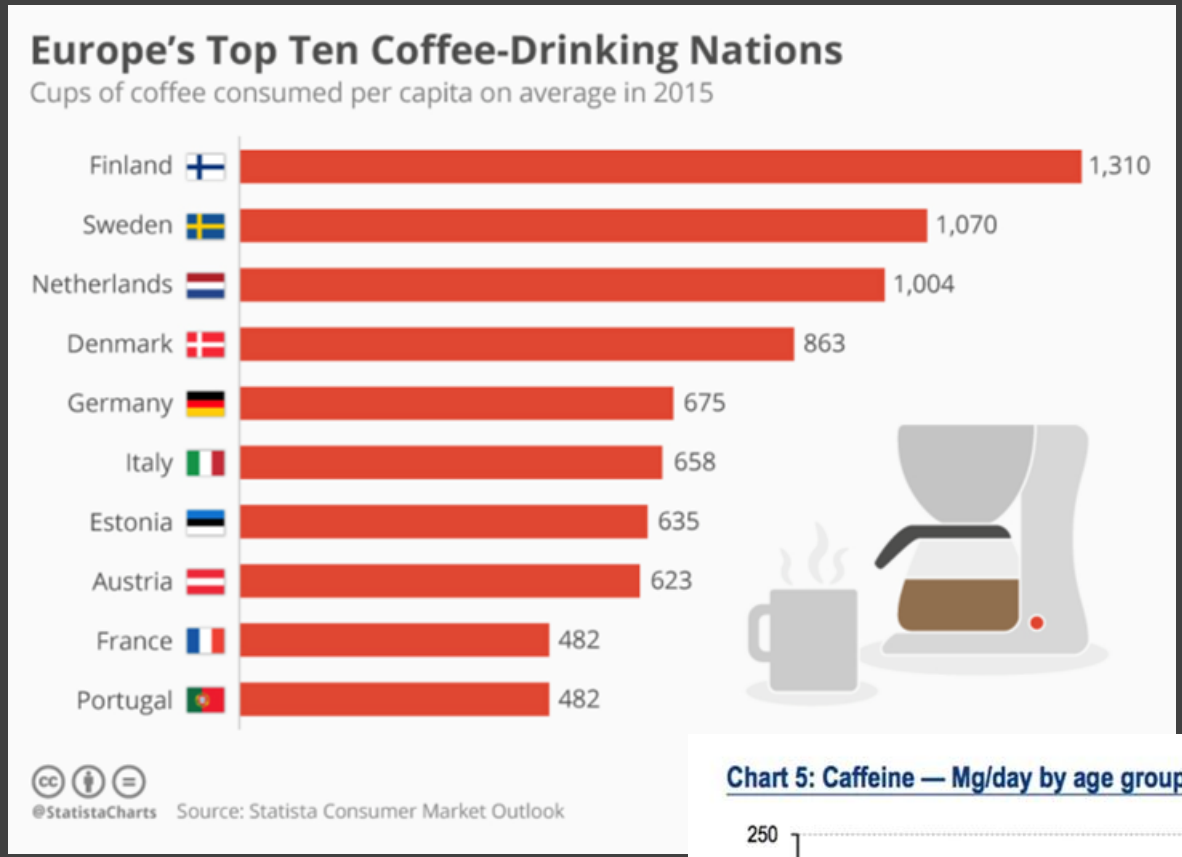


1 cup (60-100 mg caffeine) (5 μM)

1-10 cups antagonism adenosine receptors A_1/A_{2A} receptors

10-20 cups: inhibition cAMP and phosphodiesterase (100 μM); release of Ca^{2+} (1 mM)

CAFFEINE (thè, cola, cocoa)
THEOPHYILLINE (thè)
THEOBROMINE (cocoa)


Europe's Top Ten Coffee-Drinking Nations
Cups of coffee consumed per capita on average in 2015
Finland 1,310
Sweden 1,070
Netherlands 1,004
Denmark 863
Germany 675
Italy 658
Estonia 635
Austria 623
France 482
Portugal 482
@StatistaCharts
Source: Statista Consumer Market Outlook

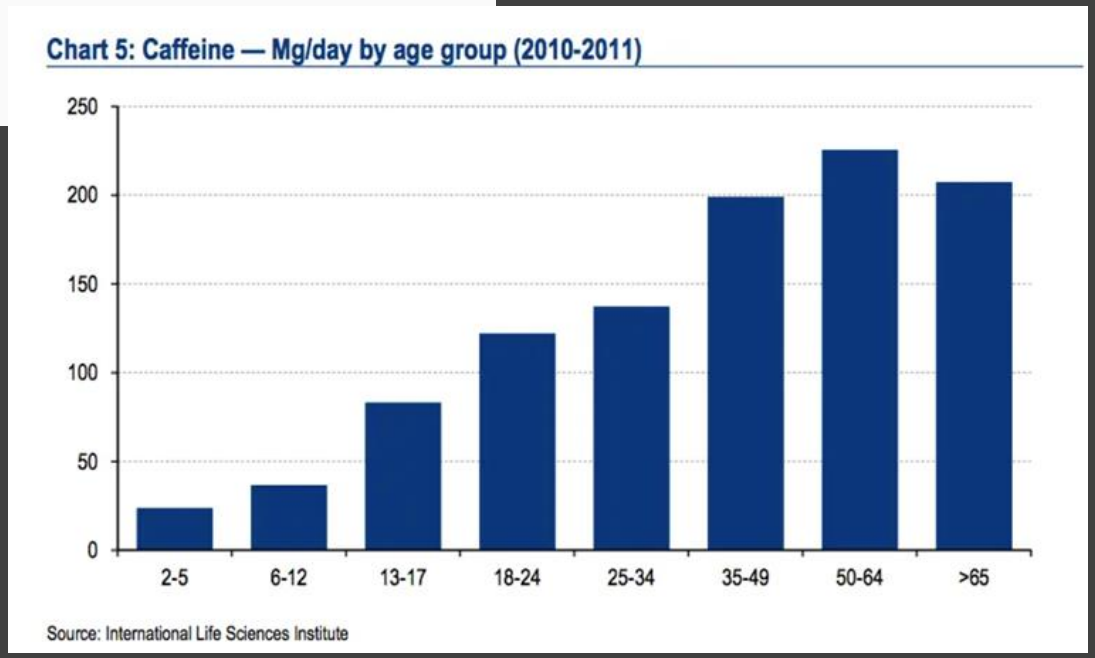


Chart 5: Caffeine — Mg/day by age group (2010-2011)
250
200
150
100
50
0
2-5
6-12
13-17
18-24
25-34
35-49
50-64
>65
Source: International Life Sciences Institute

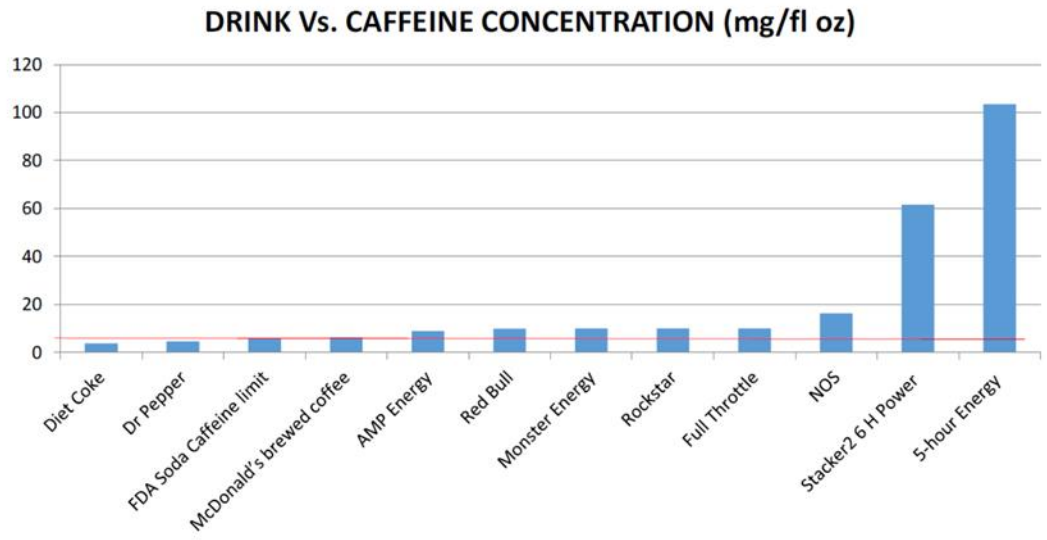
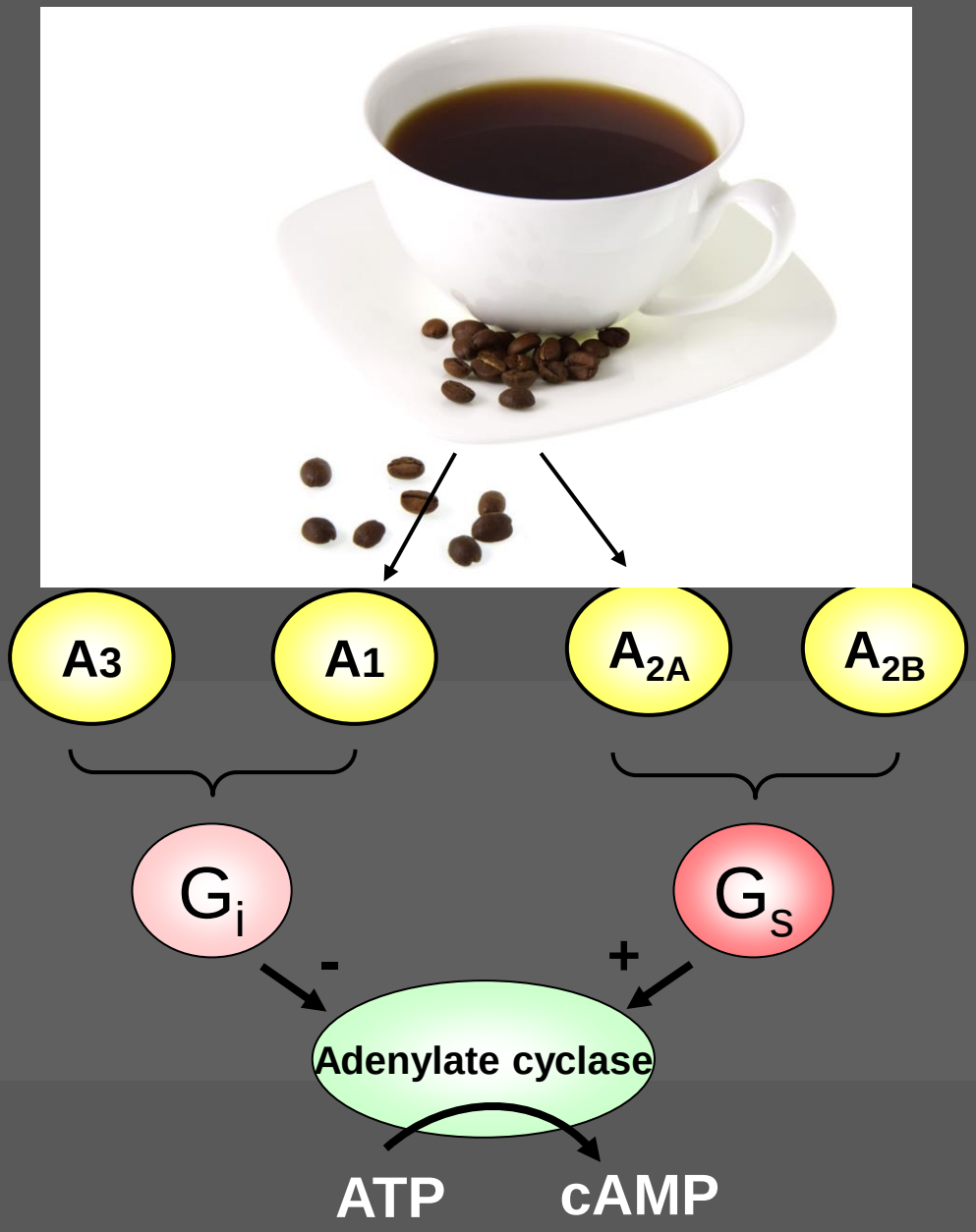


Figure 1: Various drinks in their caffeine concentration. Note red horizontal line specifies the FDA imposed limit of 71 mg caffeine/12 fl oz soda.

https://cheatdaydesign.com/caffeine-in-energy-drinks/

Caffeine is an antagonist of the adenosine receptors



ADENOSINE

- **Formed either intra-extra cellularly from ATP**
- **Homeostatic modulator (sleep, pain, arousal, hypoxia/ ischemia, seizures)**
- **Neuromodulator (release, receptor interaction)**
- **Acts through specific metabotropic receptors (A_1, A_{2A}, A_{2B}, A_3)**

Methylxanthines

- Caffeine and theophylline produce psychomotor stimulant effects.
- Average caffeine consumption from beverages is about 200 mg/day.
- Main psychological effect is reduced fatigue and improved mental performance, without euphoria. Even large doses do not cause stereotyped behaviour or psychotomimetic effects.
- Methylxanthines act mainly by antagonism at purine A_2-receptors, and partly by inhibiting phosphodiesterase, thus producing effects similar to those of β-adrenoceptor agonists.
- Peripheral actions are exerted mainly on heart, smooth muscle and kidney.
- Theophylline is used clinically as a bronchodilator; caffeine is not used clinically.

↑ contractility

↑ diuresis

↑ Gastric secretion HCl

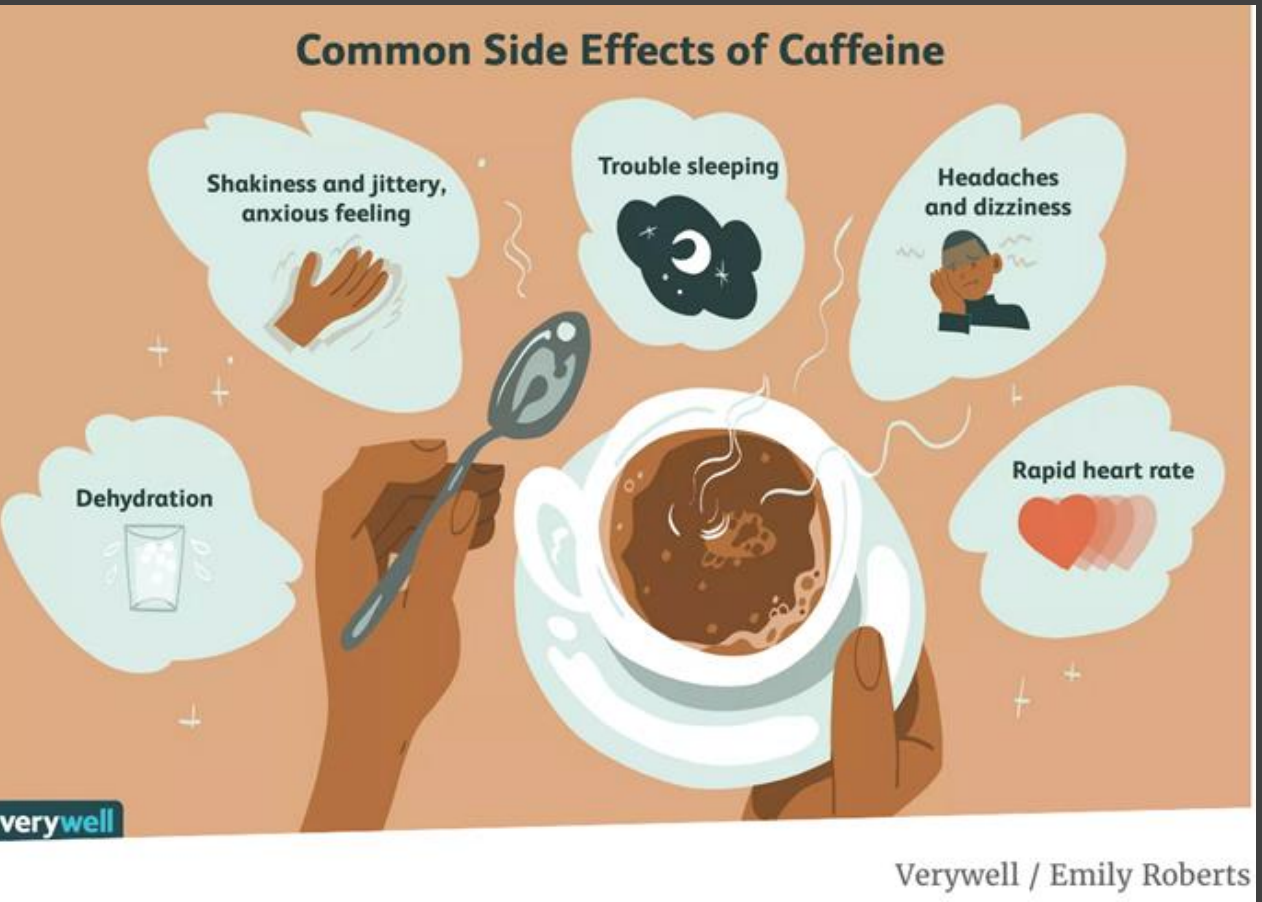
Caffeine

- **Pharmacokinetics**

CNS and all organs

Placenta, breast milk

Metabolized liver, excreted urine



High doses: cardiac arrhythmias, convulsions

Withdrawal crisis: headache, irritability

Caffeine Withdrawal

Diagnostic Criteria — 292.0 (F15.93)

A. Prolonged daily use of caffeine.

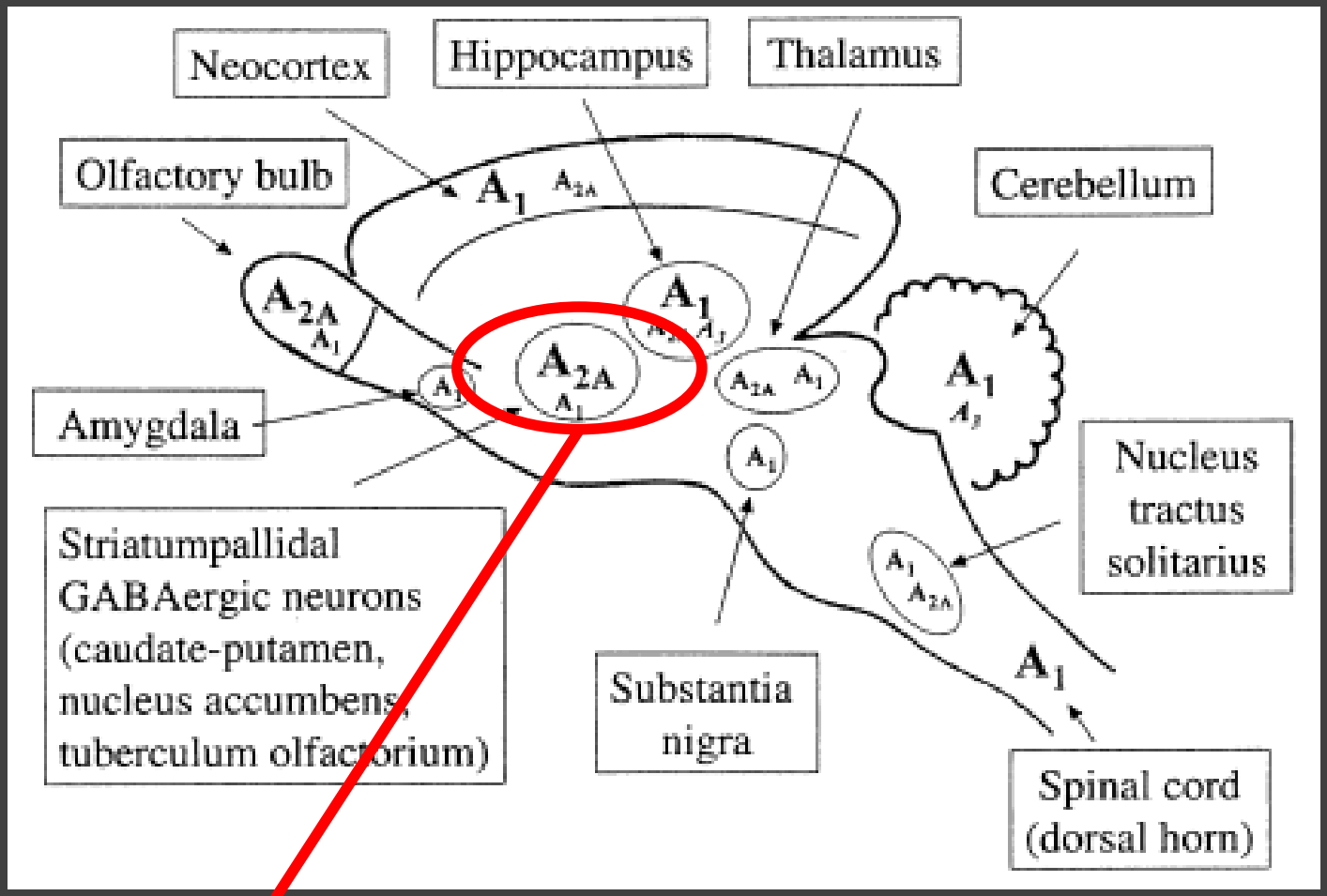
B. Abrupt cessation of or reduction in caffeine use, followed within 24 hours by three (or more) of the following signs or symptoms:

   1. Headache.
   2. Marked fatigue or drowsiness.
   3. Dysphoric mood, depressed mood, or irritability.
   4. Difficulty concentrating.
   5. Flu-like symptoms (nausea, vomiting, or muscle pain/stiffness).

C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The signs or symptoms are not associated with the physiological effects of another medical condition (e.g., migraine, viral illness) and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

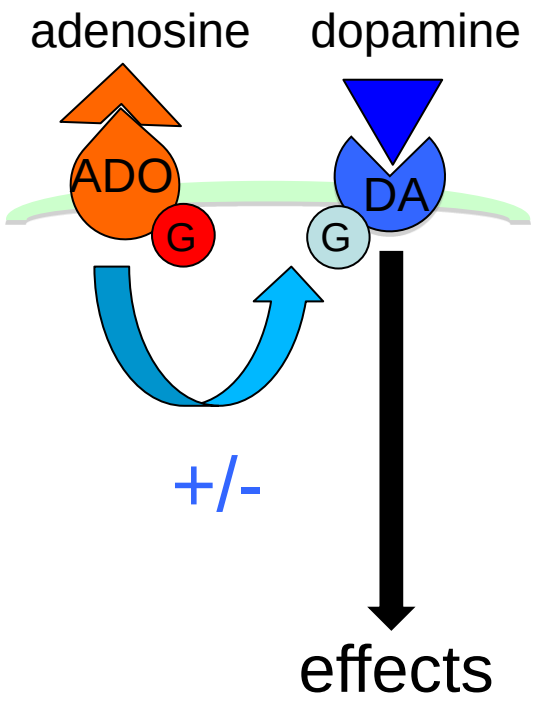
ADENOSINE RECEPTORS ARE HIGHLY ENRICHED IN DOPAMINERGIC REGIONS OF THE BRAIN



More than 95% of A_{2A} receptors are located in striatal dopamine-enriched areas

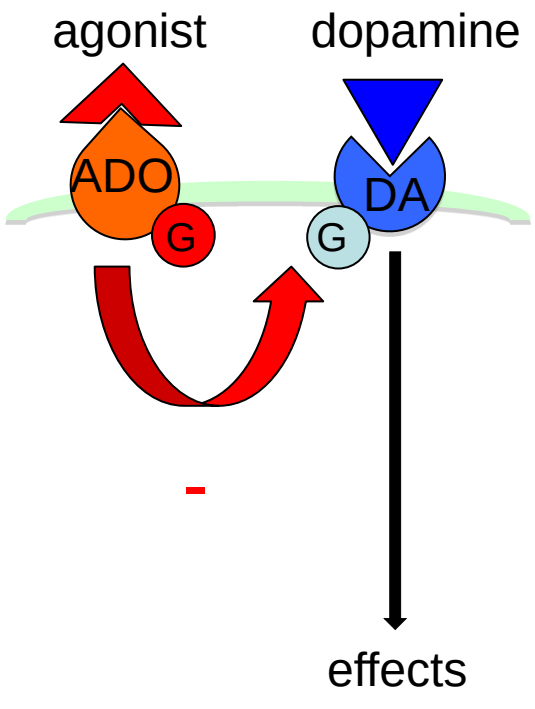
ADENOSINE AND DOPAMINE RECEPTORS INTERACT IN AN OPPOSITE WAY

A



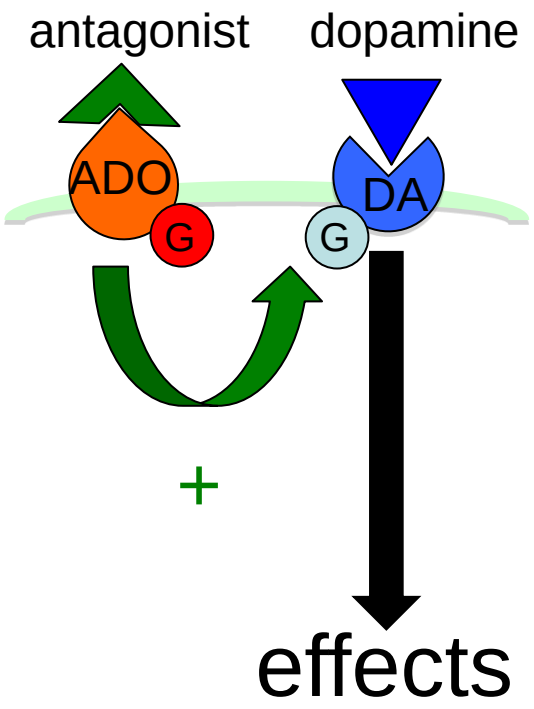
normal condition

B



stimulation of
adenosine receptors

C



blockade of
adenosine receptors

Drug Alcohol Depend. 1998 Jun-Jul;51(1-2):199-206.

Caffeine-an atypical drug of dependence

Daly JW, Fredholm BB

Caffeine has both positive effects that contribute to widespread consumption of caffeine-containing beverages and adverse unpleasant effects if doses are increased. Caffeine has weak reinforcing properties, but with little or no evidence for upward dose adjustment, possibly because of the adverse effects of higher doses. Withdrawal symptoms, although relatively limited with respect to severity, do occur, and may contribute to maintenance of caffeine consumption. Health hazards are small if any and caffeine use is not associated with incapacitation

CAFFEINE CONSUMPTION AND SUBSTANCE ABUSE

In general, caffeine is not considered a substance of abuse, but several studies have reported that caffeine consumption is often a correlate in drug abuse
(Istvan and Matarazzo, Psychol Bull, 1984; Swanson et al., Addict Behav 1994)

Studies in experimental animals and humans suggest that the effects of caffeine may share some similarities with those elicited by certain substances of abuse and that, accordingly, caffeine could function as a trigger for drug abuse