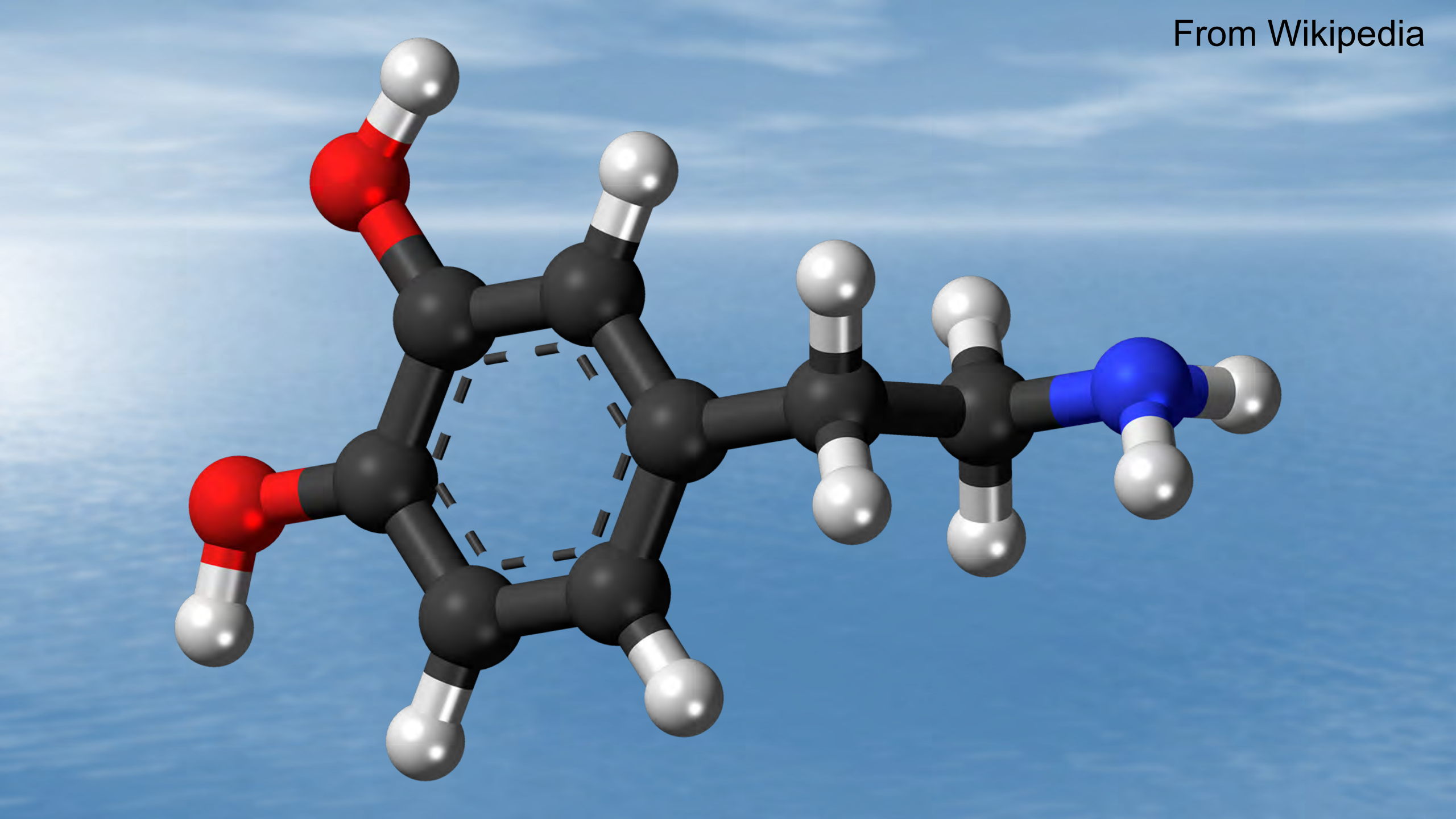
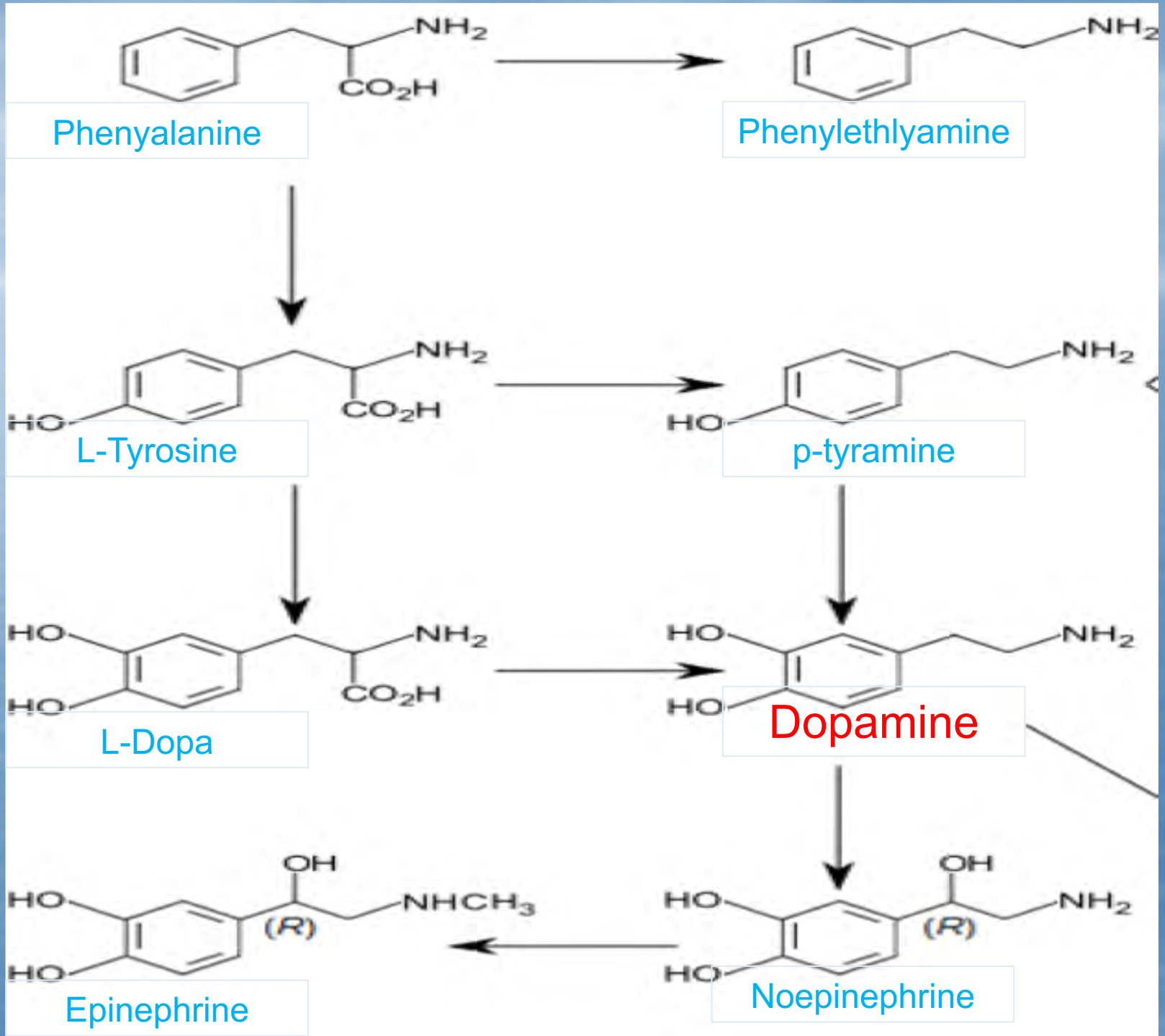
DISEASE MODEL OF ADDICTION

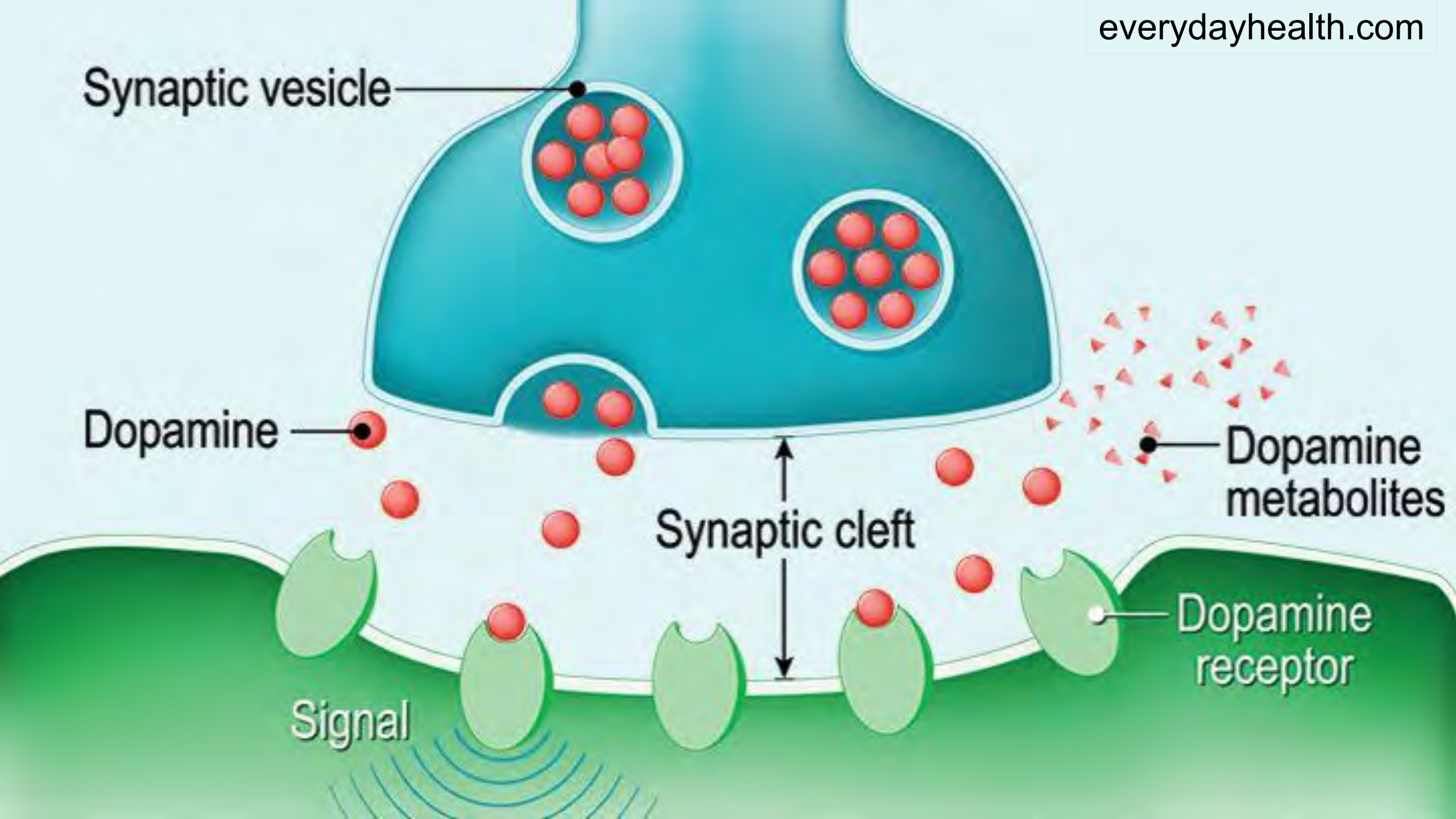
Brian Pinkston, MD, MPH
Associate Professor
Director, Aerospace Medicine Center
University of Texas Medical Branch


103

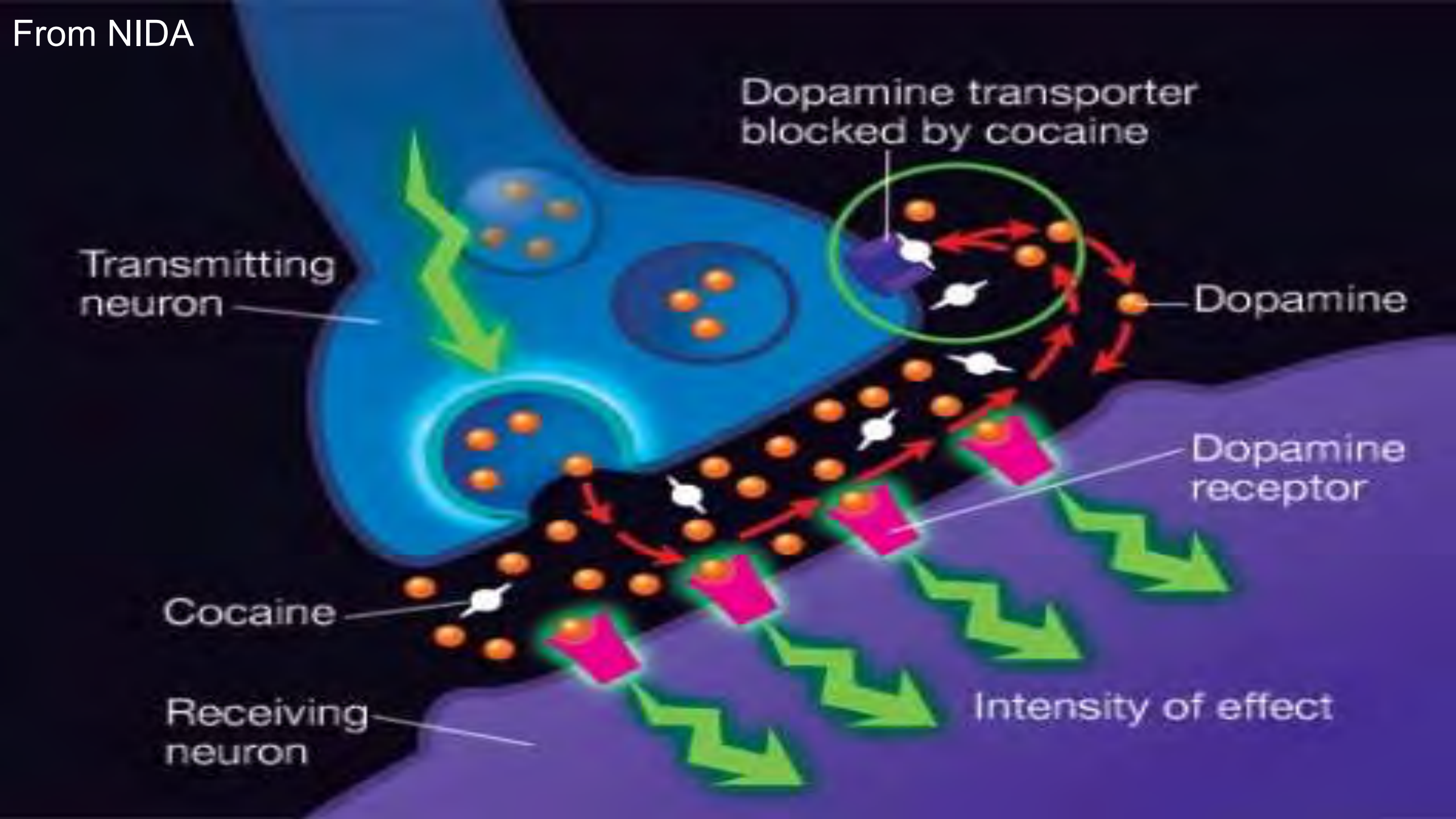

From Wikipedia

From Wikipedia




everydayhealth.com
Synaptic vesicle
Dopamine
Dopamine metabolites
Synaptic cleft
Dopamine receptor
Signal

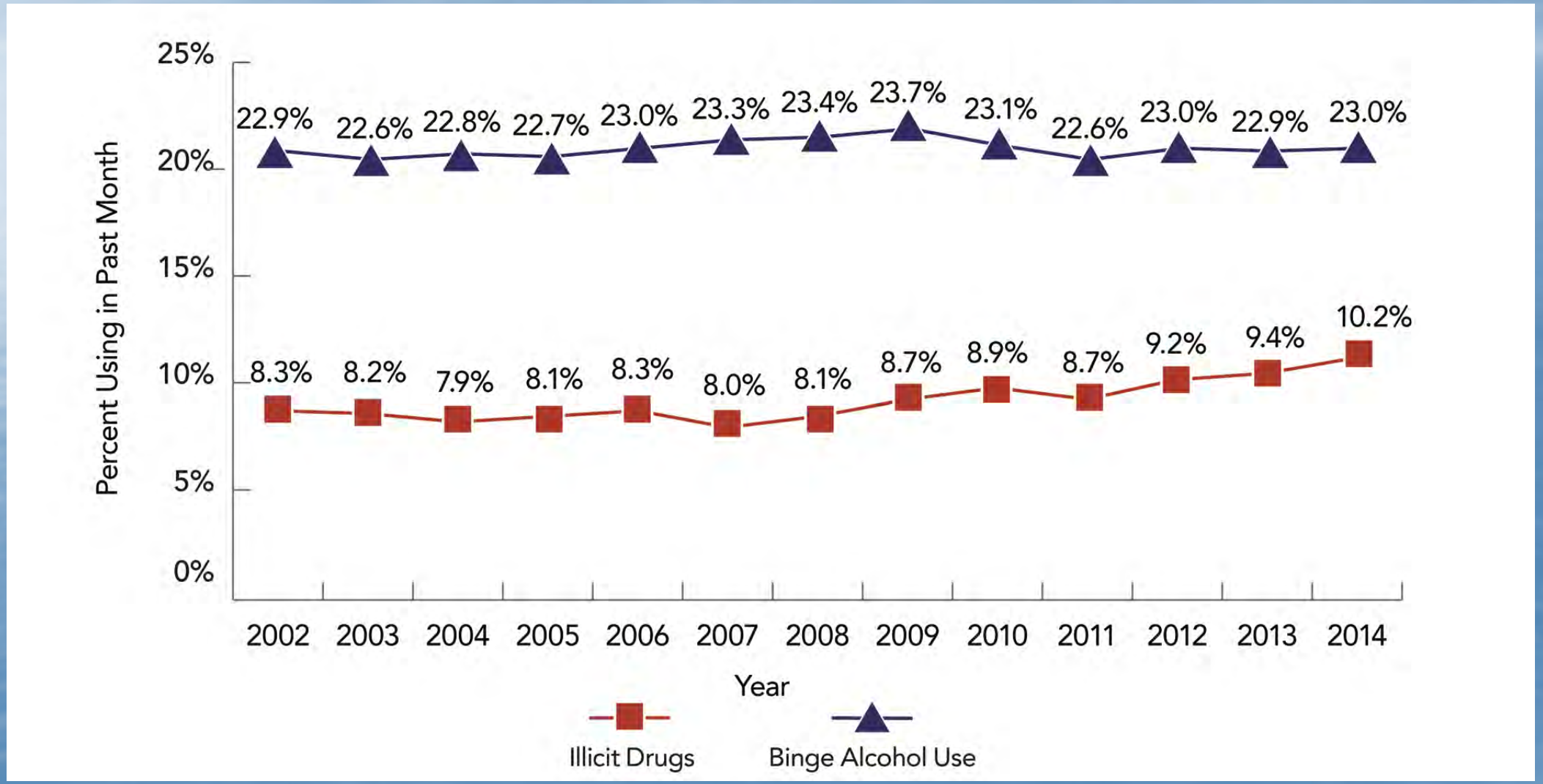
From NIDA


Dopamine transporter
blocked by cocaine
Transmitting
neuron
Dopamine
Dopamine
receptor
Cocaine
Receiving
neuron
Intensity of effect

2014 SUBSTANCE USE, PAST YEAR INITIATION OF SUBSTANCE USE, AND MET DIAGNOSTIC CRITERIA FOR A SUBSTANCE USE DISORDER IN THE PAST YEAR AMONG PERSONS AGED 12 YEARS OR OLDER) # IN MILLIONS

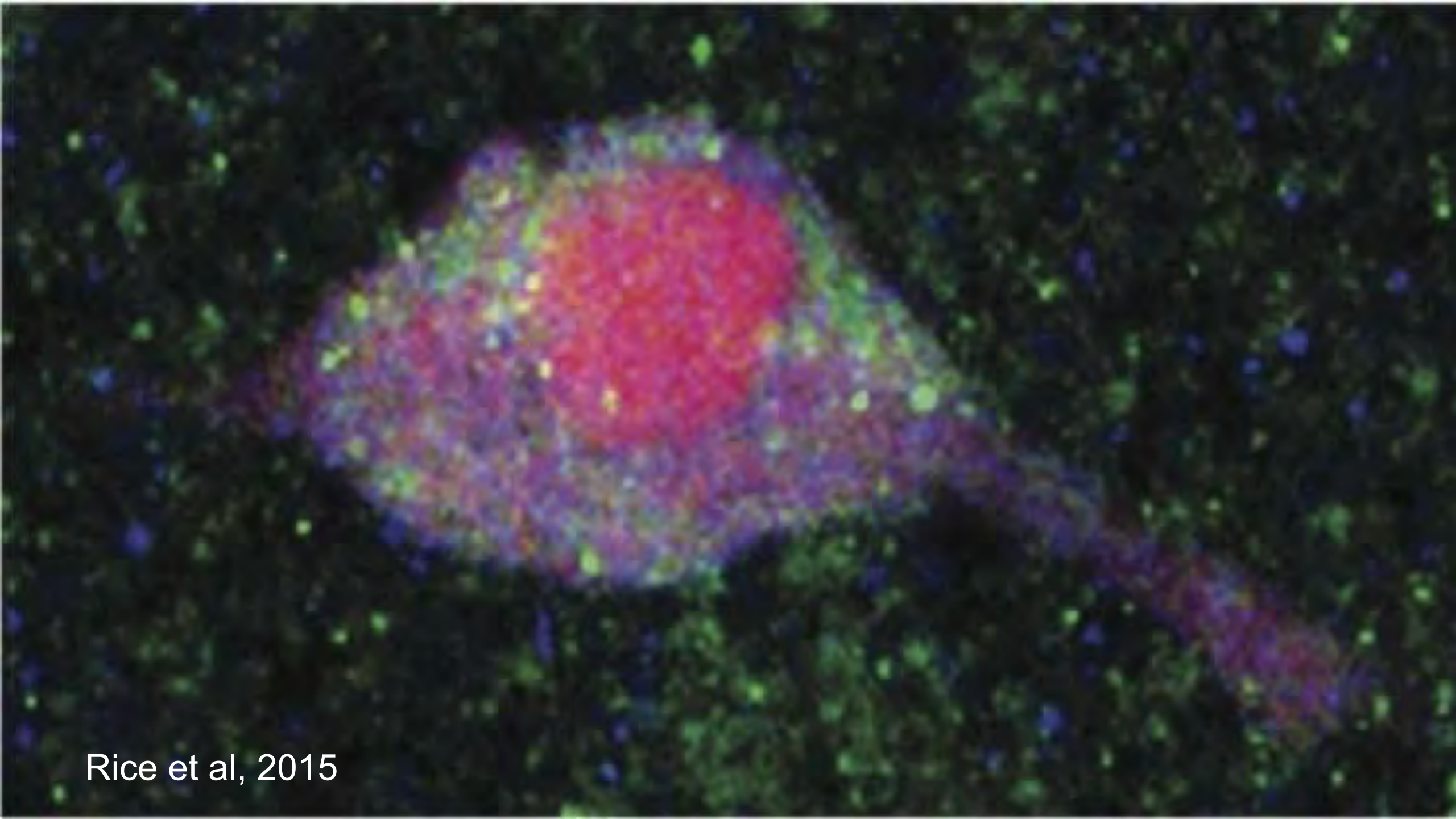
Substance	Past Year Use or Misuse[v]		Past Year Initiation Among Total Population[vi]		Met Diagnostic Criteria for a Substance Use Disorder[vi,vii]	
	#	%	#	%	#	%
Alcohol	175.8	65.7	4.8	1.8	15.7	5.9
Drinking Pattern						
Binge Drinking[i]	66.7	24.9	da	da	da	da
Heavy Drinking[i]	17.3	6.5	da	da	da	da
Any Illicit Drug[ii]	47.7	17.8	nr	nr	7.7	2.9
Cocaine/Crack	36.0	1.8	1.0	0.4	0.9	0.3
Heroin	0.8	0.3	0.1	0.1	0.6	0.2
Hallucinogens	4.7	1.8	1.2	0.4	0.3	0.1
Marijuana[iii]	36.0	13.5	2.6	1.0	4.0	1.5
Inhalants	1.8	0.7	0.6	0.2	0.1	0.0
Misuse of Psychotherapeutics[iv]	18.9	7.1	nr	nr	2.7	1.0
Pain Relievers	12.5	4.7	2.1	0.8	2.0	0.8
Tranquilizers	6.1	2.3	1.4	0.5	0.7	0.3
Stimulants	5.3	2.0	1.3	0.5	0.4	0.2
Sedatives	1.5	0.6	0.4	0.2	0.2	0.1
Alcohol or Any Illicit Drugs[ii]	182.3	68.1	nr	nr	20.8	7.8
Alcohol and Any Illicit Drugs[ii]	41.3	15.4	nr	nr	2.7	1.0

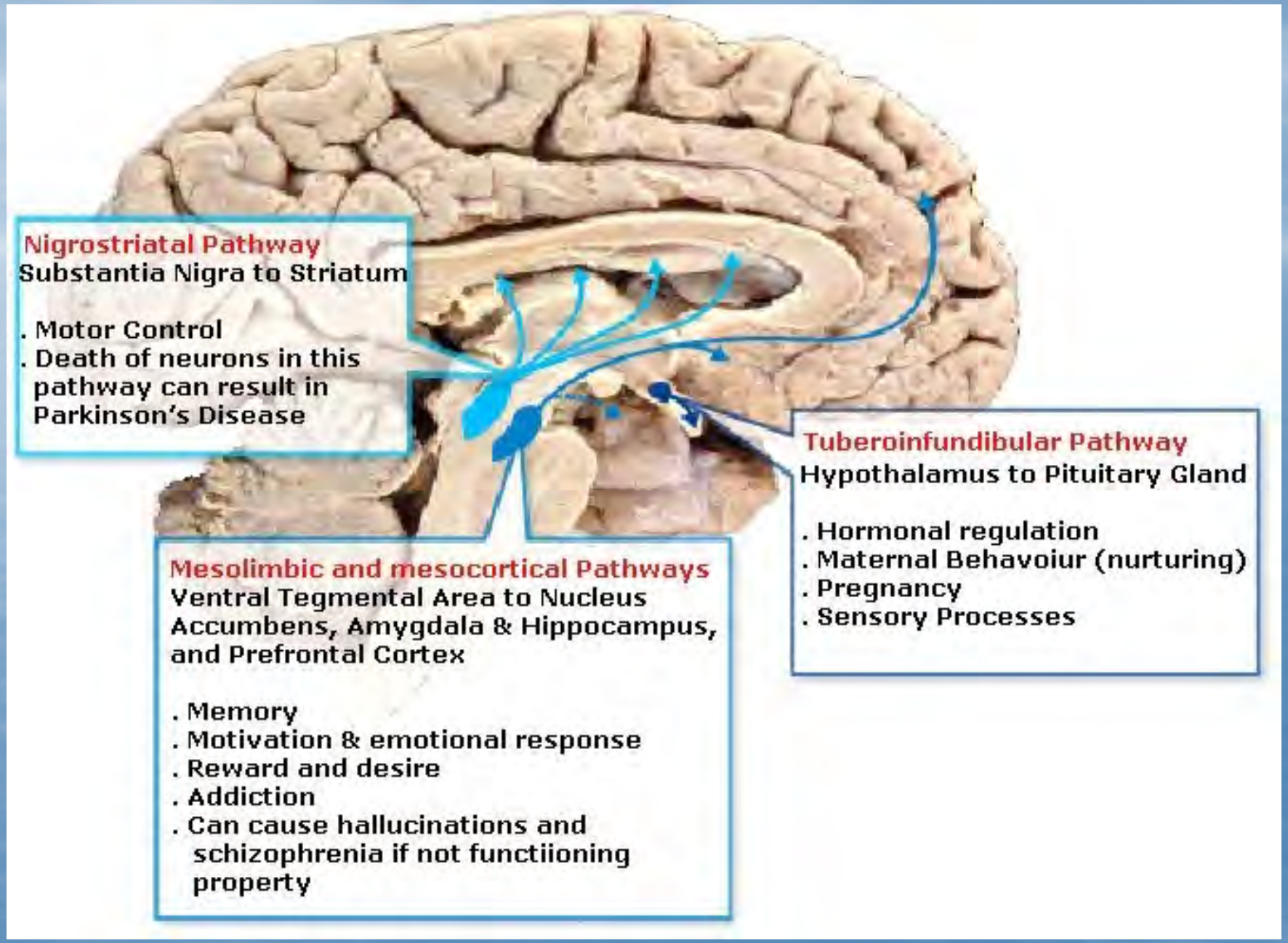
PAST MONTH RATES OF SUBSTANCE USE AMONG PEOPLE AGED 12 OR OLDER:PERCENTAGES, 2002-2014, 2014
NATIONAL SURVEY ON DRUG USE AND HEALTH (NSDUH)



Type 1 Diabetes

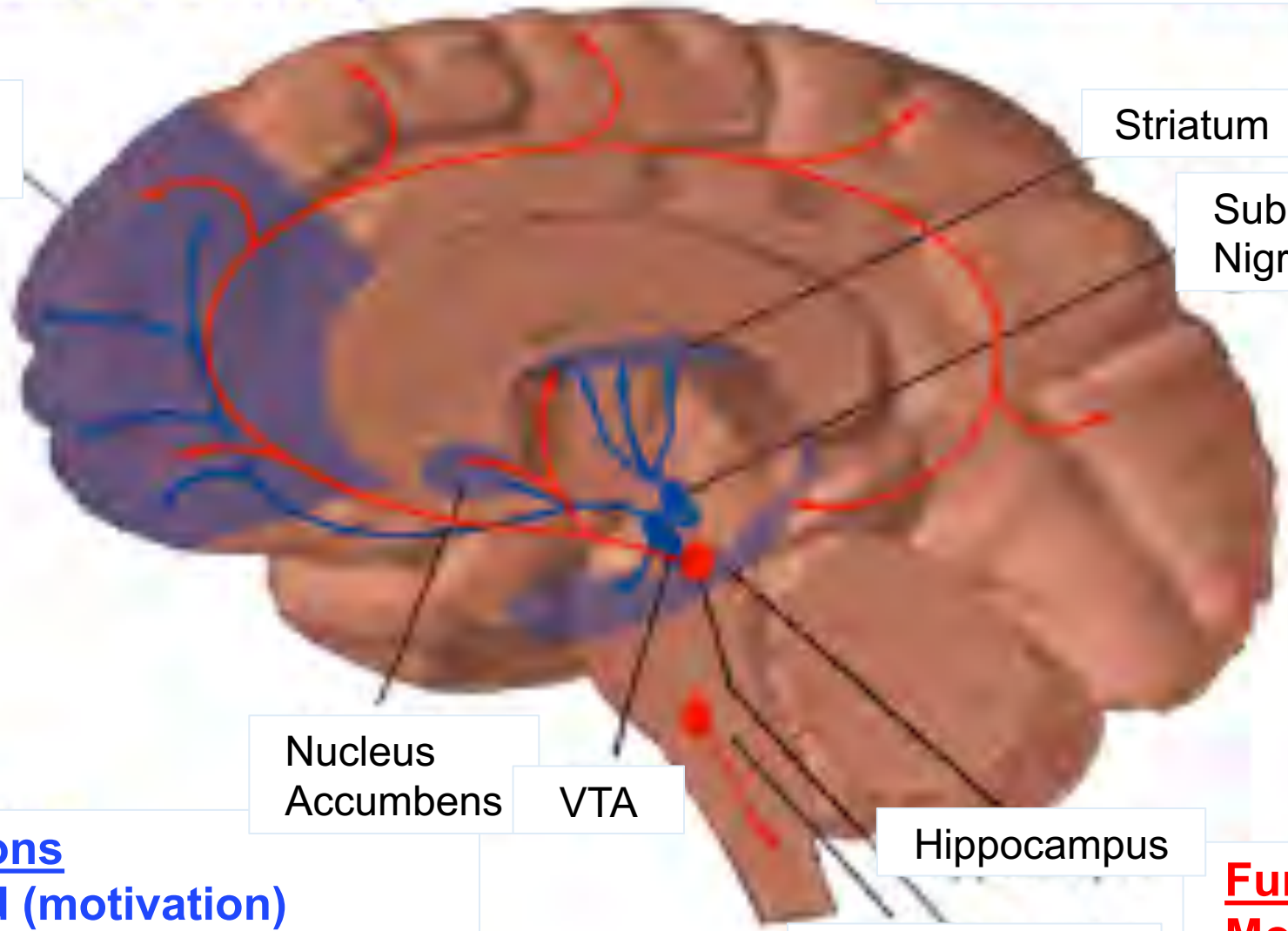
Type 2 Diabetes


Rice et al, 2015


Nigrostriatal Pathway
Substantia Nigra to Striatum
. Motor Control
. Death of neurons in this pathway can result in Parkinson's Disease
Tuberoinfundibular Pathway
Hypothalamus to Pituitary Gland
. Hormonal regulation
. Maternal Behavoiur (nurturing)
. Pregnancy
. Sensory Processes
Mesolimbic and mesocortical Pathways
Ventral Tegmental Area to Nucleus Accumbens, Amygdala & Hippocampus, and Prefrontal Cortex
. Memory
. Motivation & emotional response
. Reward and desire
. Addiction
. Can cause hallucinations and schizophrenia if not functiioning property

Dopamine Pathways

Serotonin Pathways

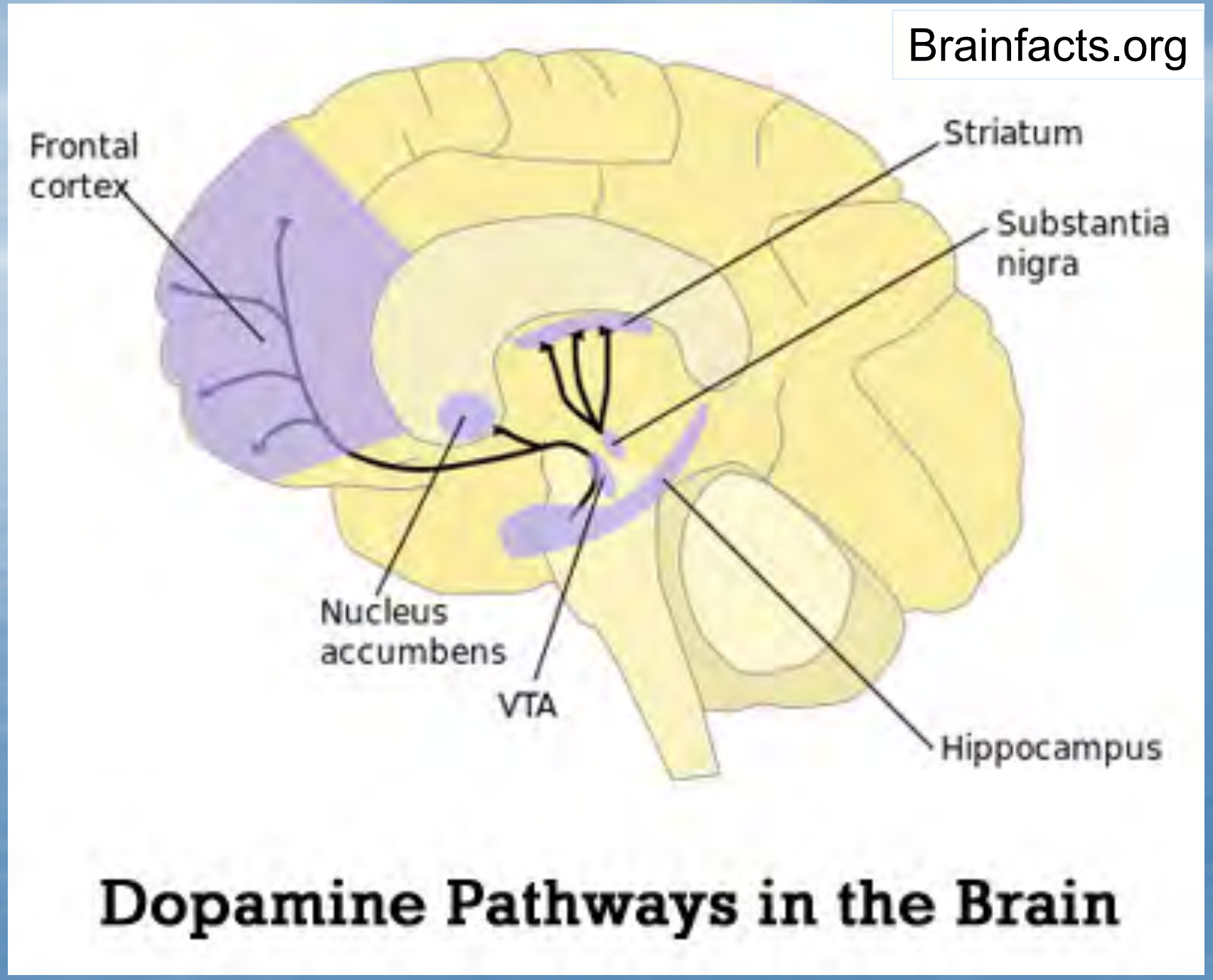


Functions

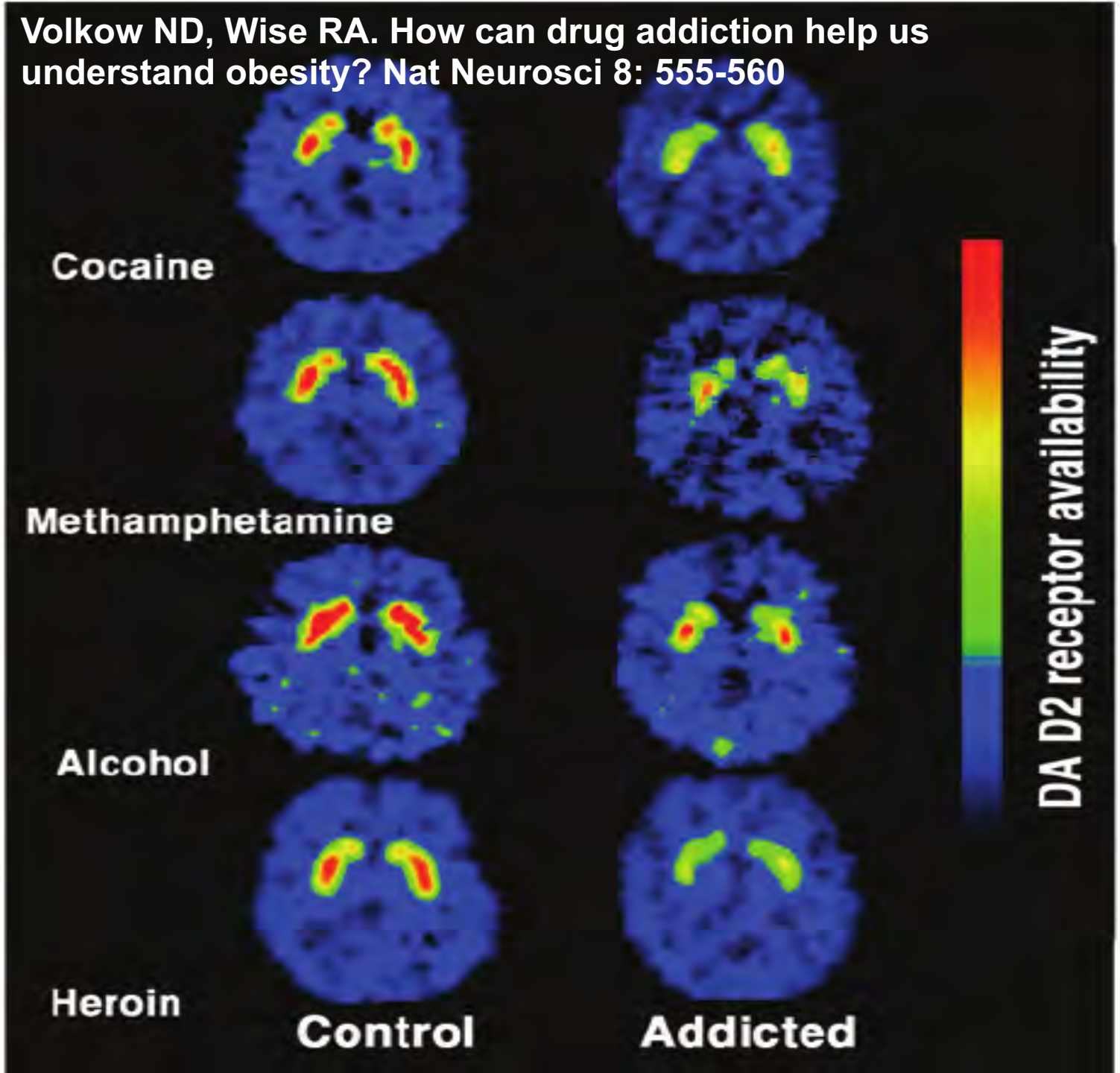
Reward (motivation)
Pleasure, Euphoria
Motor Function (fine tuning)
Compulsion
Perserveration

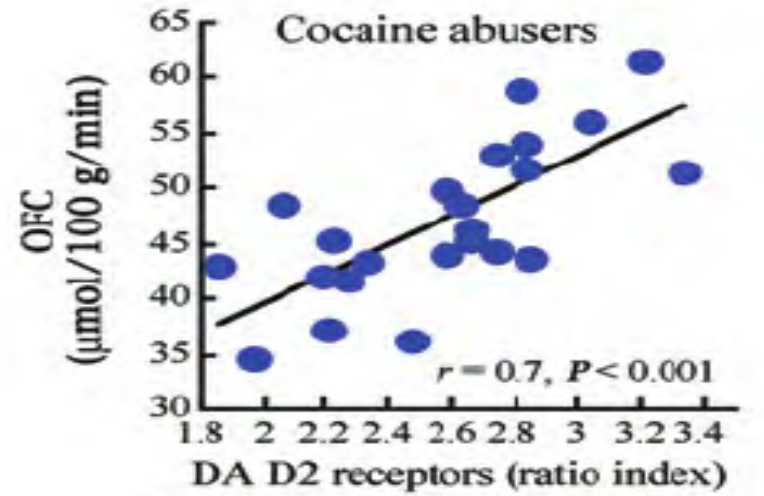
Functions

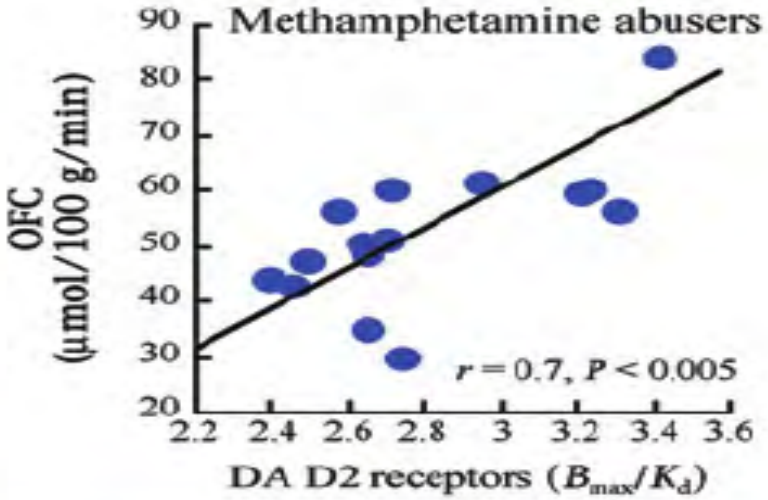
Mood
Memory
Sleep
Cognitiion

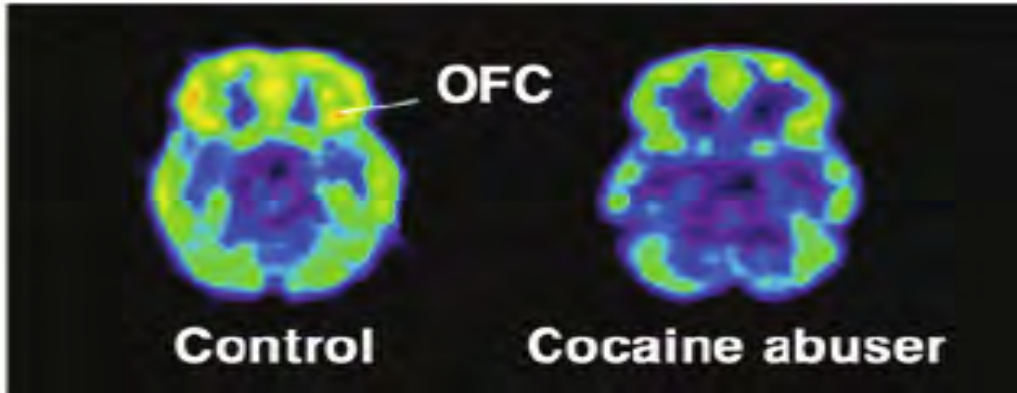

Brainfacts.org
Frontal cortex
Striatum
Substantia nigra
Nucleus accumbens
VTA
Hippocampus
Dopamine Pathways in the Brain

Volkow ND, Wise RA. How can drug addiction help us understand obesity? Nat Neurosci 8: 555-560

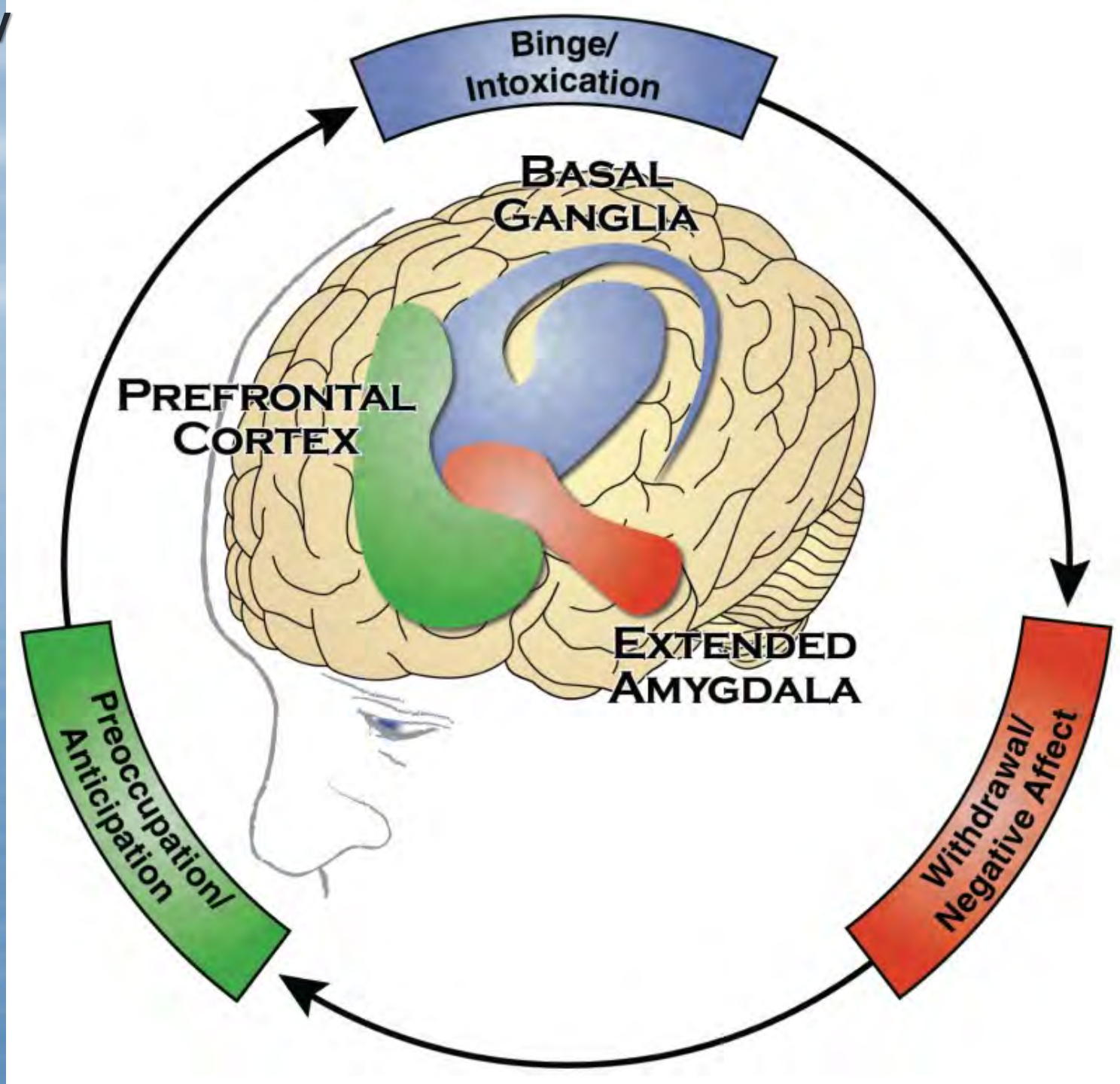








NCBI.NLM.NIH.GOV



US SURGEON GENERAL FINDINGS (2016)

“Well-supported scientific evidence shows that disruptions in three areas of the brain are particularly important in the onset, development, and maintenance of substance use disorders: the basal ganglia, the extended amygdala, and the prefrontal cortex. “

US SURGEON GENERAL (2016)
VS.
BIG BOOK (1939)

These disruptions (are):

(1) enable substance-associated cues to trigger substance seeking (i.e., they increase incentive salience); Cunning

(2) reduce sensitivity of brain systems involved in the experience of pleasure or reward, and heighten activation of brain stress systems; Baffling

and

(3) reduce functioning of brain executive control systems, which are involved in the ability to make decisions and regulate one's actions, emotions, and impulses.

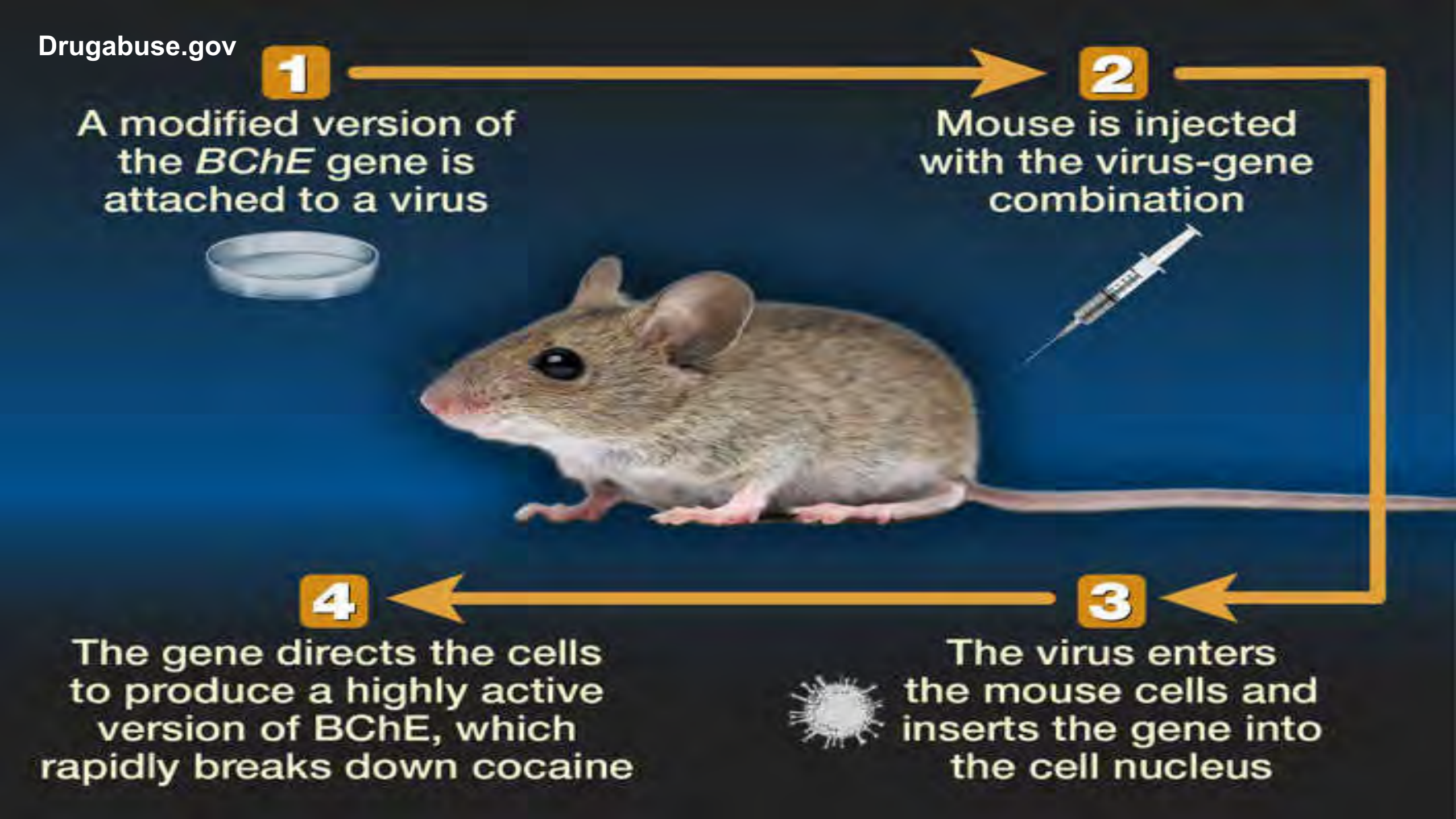
Powerful

CHARACTERISTICS OF ADDICTION (2016)

- Impulsivity
- Positive Reinforcement
- Negative Reinforcement
- Compulsivity

HENCE, STEP 1 – POWERLESSNESS AND NEED FOR HIGHER POWER

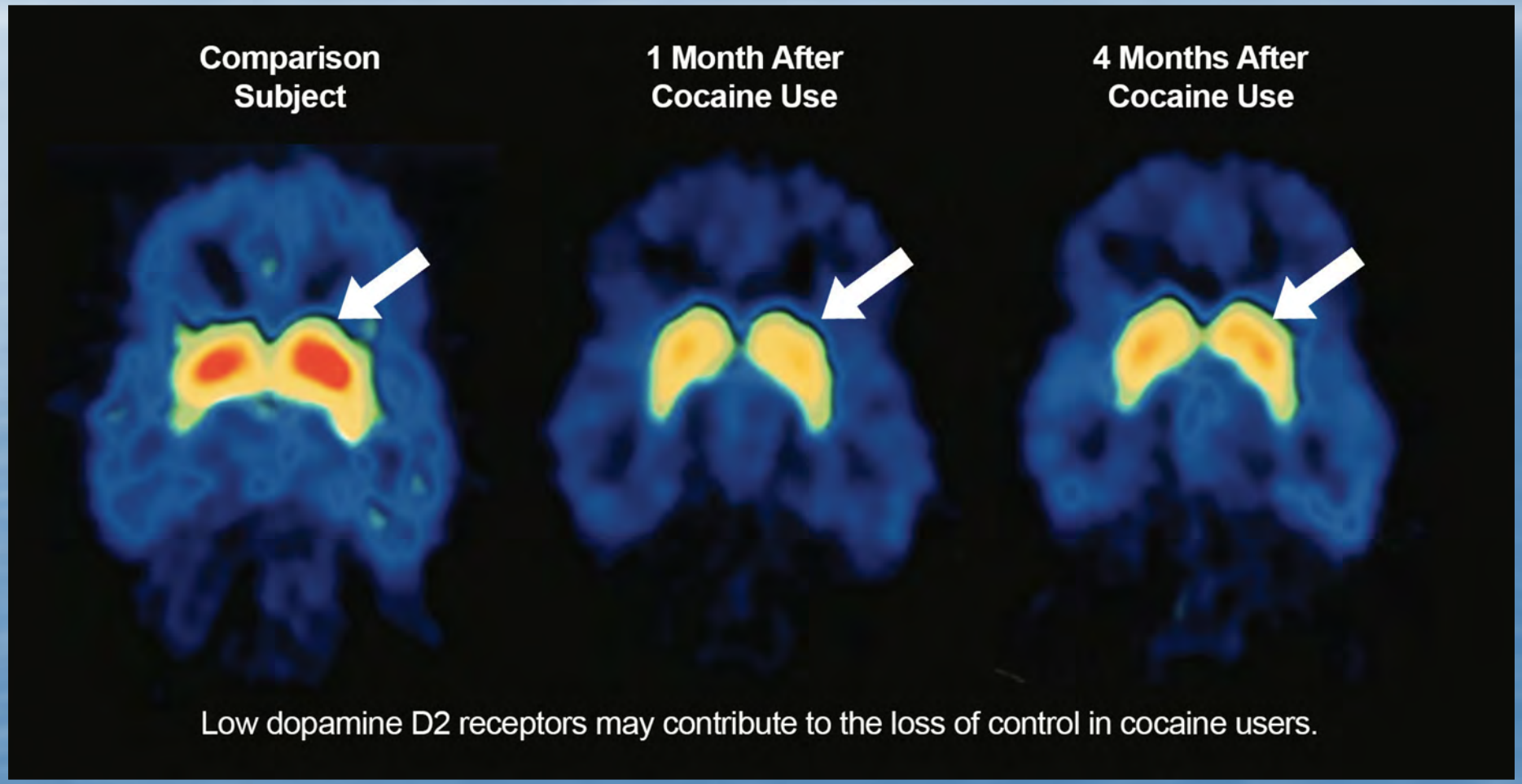
Drugabuse.gov



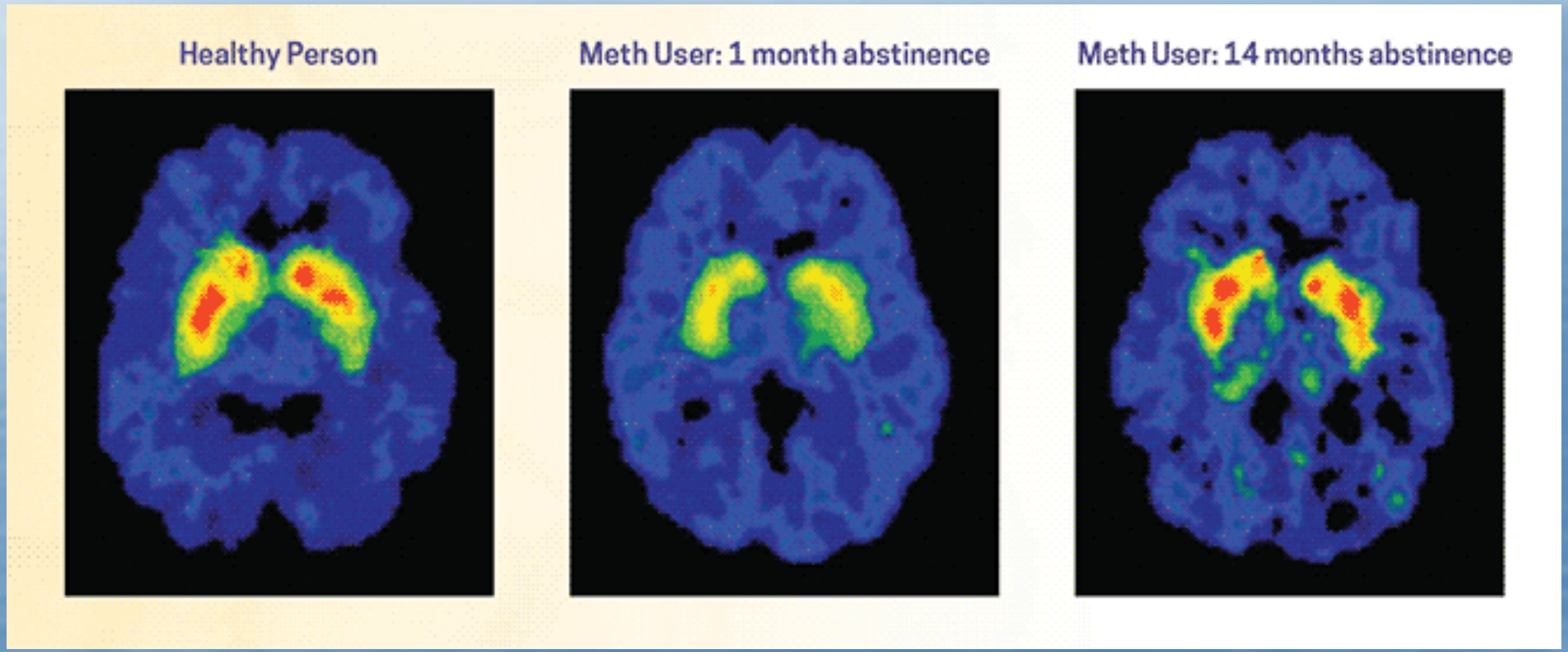
IN THE MEANTIME…

- **Cognitive-behavioral therapy** seeks to help patients recognize, avoid, and cope with the situations in which they're most likely to use drugs.
- **Contingency management** uses positive reinforcement such as providing rewards or privileges for remaining drugfree, for attending and participating in counseling sessions, or for taking treatment medications as prescribed.
- **Motivational enhancement therapy** uses strategies to make the most of people's readiness to change their behavior and enter treatment.
- **Family therapy** helps people (especially young people) with drug use problems, as well as their families, address influences on drug use patterns and improve overall family functioning.
- CHANGING NEURAL PATHWAYS
- Recently heard quote from Austin TX:
- ” The more I miss meetings, the more I miss drinking”

TIME-RELATED DECREASE IN DOPAMINE RELEASED IN THE BRAIN OF A COCAINE USER



TIME-RELATED INCREASE IN DOPAMINE TRANSPORTERS



CNS Vital Signs Clinical Report	Test Date: March 31, 2012 08:49:04
Subject ID: [redacted]	Administrator: William Lambos
Language: English (United States)	Age: 13
Total Test Time: 48:12 (min:secs)	Test Date GMT: March 31, 2012 13:49:08

Patient Profile	Percentile Range				> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range				> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Subject Score	Standard Score	Percentile	Valid Score**	Above	Average	Low Average	Low	Very Low
Neurocognitive Index (NCI)	NA	64	1	No					X
Composite Memory	71	46	1	Yes					X
Verbal Memory	39	53	1	Yes					X
Visual Memory	32	58	1	Yes					X
Psychomotor Speed	129	84	14	Yes			X		
Reaction Time*	1058	48	1	No					X
Complex Attention*	37	71	3	No				X	
Cognitive Flexibility	-5	70	2	No				X	
Processing Speed	42	92	30	Yes		X			
Executive Function	-1	72	3	No				X	
Social Acuity	1	65	1	Yes					X
Reasoning	-5	71	3	No				X	
Sustained Attention	19	92	30	Yes		X			
Working Memory	6	93	32	Yes		X			

DOPAMINE AGONISTS (STIMULATORS)

- LEVODOPA – TREATS PARKINSON'S MOVEMENT DISORDER
- METHYLPHENIDATE and others – ADHD
- PRAMIPEXOLE – TREATS RESTLESS LEG SYNDROME
- PROMAZINE – TREATS AGITATION/RESTLESSNESS

DOPAMINE ANTAGONISTS (INHIBITORS)

- RESPIRIDINE, THIORIDAZINE, FLUPHENAZINE – TREAT PSYCHOSIS
- PIMOZIDE – TREATS TICS IN TOURETTE'S SYNDROME
- ZIPRASIDONE – TREATS BIPOLAR I
- PROMAZINE – TREATS AGITATION/RESTLESSNESS

MEDICATIONS TO TREAT ADDICTION

- Naltrexone (Vivitrol).
- Buprenorphine (Probuphine, Suboxone).
- Disulfiram (Antabuse).
- Acamprosate (Campral)
- Modafinil (Provigil).
- Mirtazapine (Remeron).
- Bupropion (Wellbutrin, Zyban).
- Gabapentin (Neurontin).
- Vigabatrin (Sabril).
- Baclofen (Lioresal).
- Topiramate (Topamax).

MEDICATIONS TO TREAT ADDICTION

- **Opioid**
  - Methadone
  - Buprenorphine
  - Extended-release naltrexone
  - Lofexidine
- **Nicotine**
  - Nicotine replacement therapies (available as a patch, inhaler, or gum)
  - Bupropion
  - Varenicline
- **Alcohol**
  - Naltrexone
  - Disulfiram
  - Acamprosate