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Auckland

Addiction - Who is in Charge? - Concurrent Workshop Repeated

Saturday, 22 June 2013

Start 11:00am

Duration: 55mins

Skellerup

Start 12:05pm

Duration: 55mins

Skellerup



General Practice Conference & Medical Exhibition

20-23 June 2013 | Energy Events Centre | Rotorua

ADDICTION WHO IS IN CHARGE?

Graham Gulbrandsen,

FRNZCGP, FACHAM

General Practitioner, Kingsland

Rotorua GPCME 22 June 2013

- What is going on in the addicted brain?
 - current concepts
- This understanding may help us work more effectively with our addicted patients

Outline: Addiction, Who Is In Charge?

- Genetics
- Neurons & neurotransmission
- Dopamine theory of addiction
- 'Diabolical learning'
- Action of drugs on the brain
- Recovery
- MODA Section 24
- Case histories
- Do you have questions, comments, cases?

PROFESSIONAL APPROACH

Non-judgemental

‘maintain high standard of human rights’

Empathic

Addiction

Compulsive behaviour

Outside substance users personal consciousness

50% heritable

Most have psychiatric comorbidities

Chronic relapsing disorder

Different therapies → similar outcomes

Change takes time.



Australasian Professional Society on Alcohol and other Drugs Scientific Conference 2012

Melbourne Convention and Exhibition Centre

CONFERENCE HANDBOOK




AP SAD
The Australasian Professional Society
on Alcohol and other Drugs

SCIENTIFIC
CONFERENCE
18 - 21 November
Melbourne, Australia
www.apsadconference.com.au **2012**



MiA2013

MEDICINE IN ADDICTION CONFERENCE
Friday 15 – Sunday 17 March 2013

*SMC Conference and Function Centre
66 Goulburn Street Sydney*

www.ranzcp.org/mia2013



The Royal
Australian &
New Zealand
College of
Psychiatrists

Section of Addiction Psychiatry



RACGP



The Royal Australasian
College of Physicians

MEMOIRS
OF AN
ADDICTED
BRAIN

A NEUROSCIENTIST EXAMINES
HIS FORMER LIFE ON DRUGS

MARC LEWIS

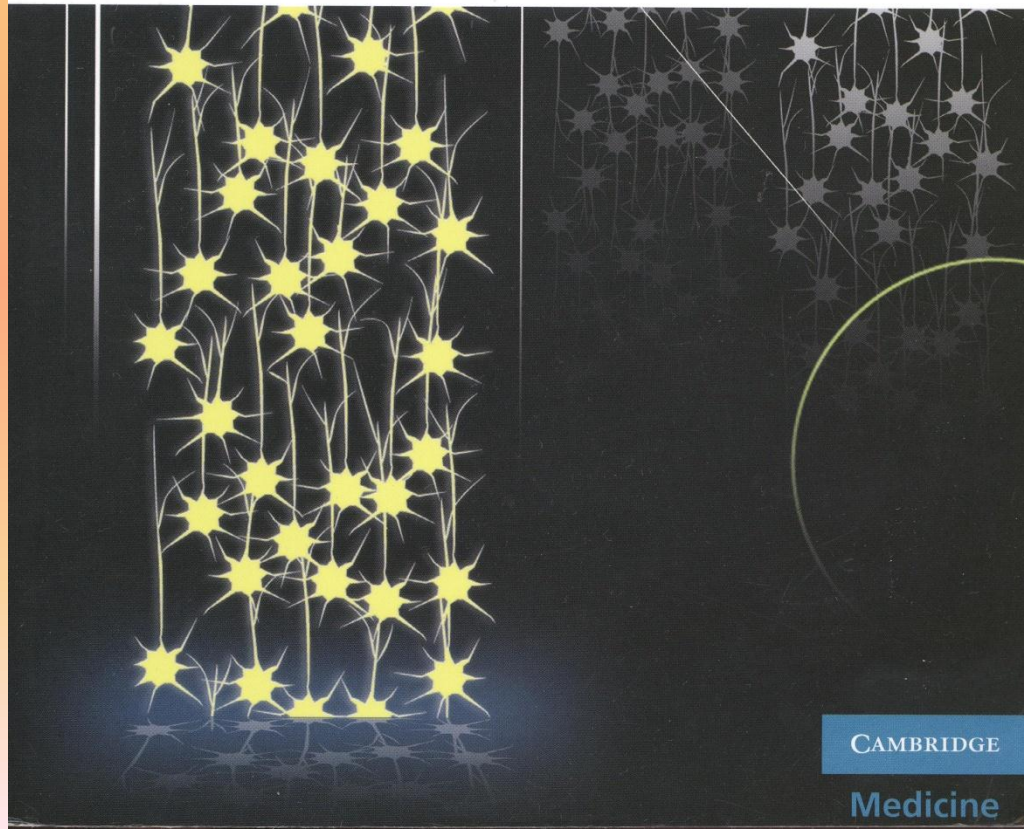
'Engrossing and vividly written ... Accessible to all.' GABOR MATÉ, MD

Third Edition

Stahl's Essential Psychopharmacology

Neuroscientific Basis and Practical Applications

Stephen M. Stahl

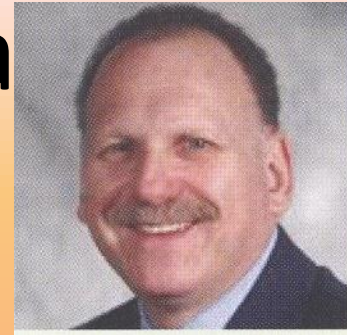


CAMBRIDGE

Medicine

Genetics of Alcohol Dependence

Henry Kranzler, Addiction Psychiatrist, University of Pennsylvania



- Alcohol dependence half genetic, half environmental
- Chromosome 4 has 2+ regions assoc w heavy drinking, eg aldehyde dehydrogenase coding & GABA receptors
- Naltrexone works better in those with Asp40 allele – may be able to target use of naltrexone, eg to Asians.

Cannabis & the Brain

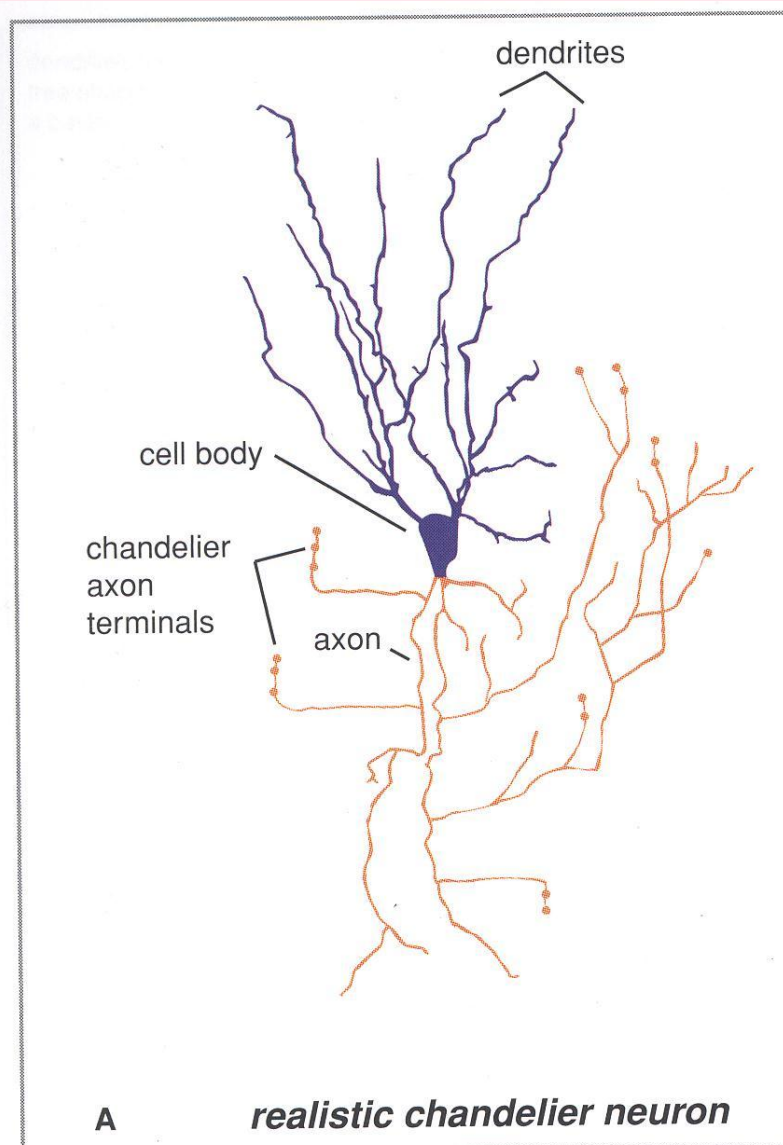
Assoc Prof Nadia Solowij

Psychologist, NSW



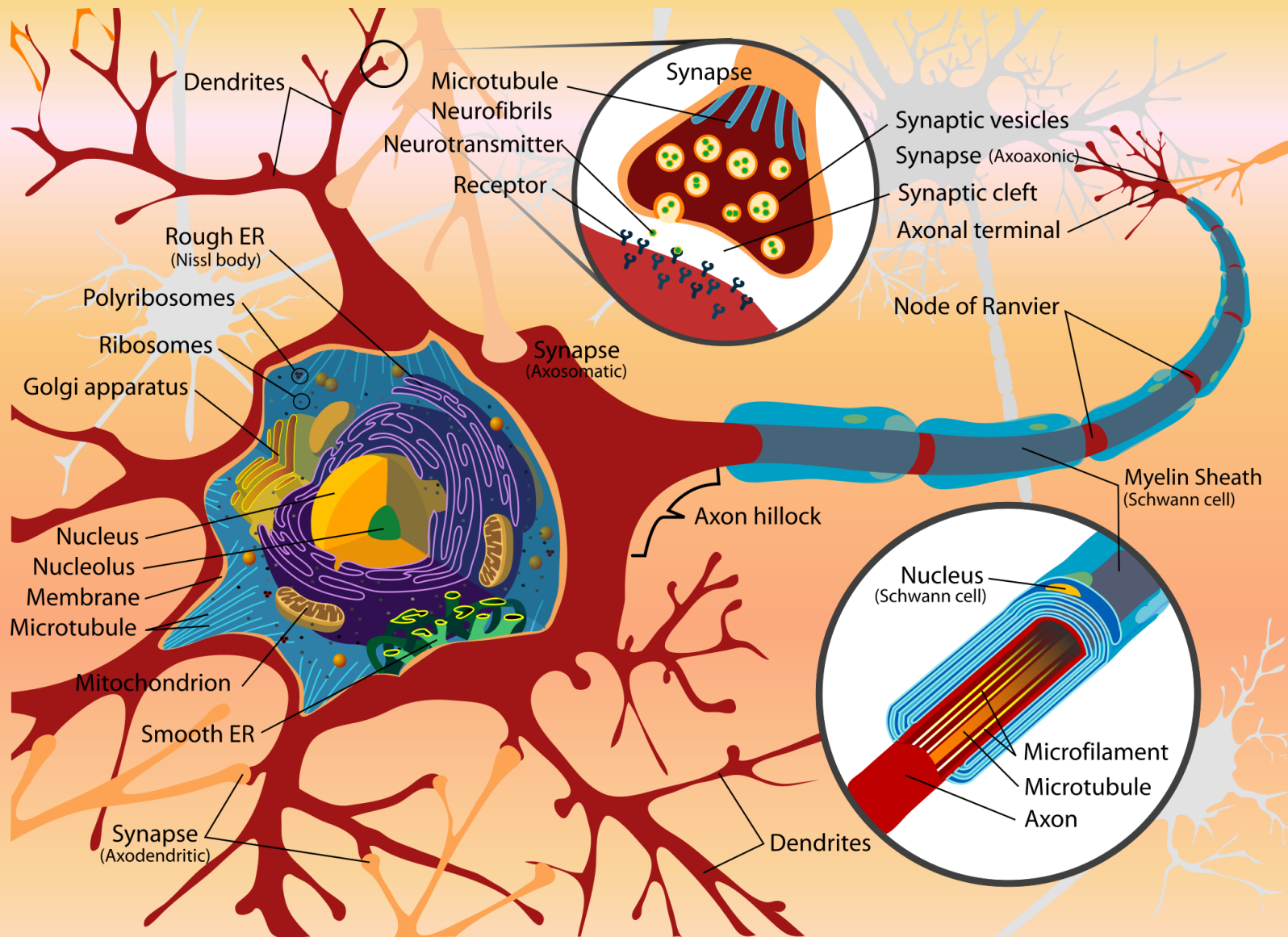
- Most people have COMT gene that protects from schizophrenia
- Cannabis may double the risk in those without
- Adolescent brain more sensitive to cannabis use: impaired memory, attention, executive functions associated with reduced prefrontal DA
- Recovery on quitting is likely but not proven.

Neurons



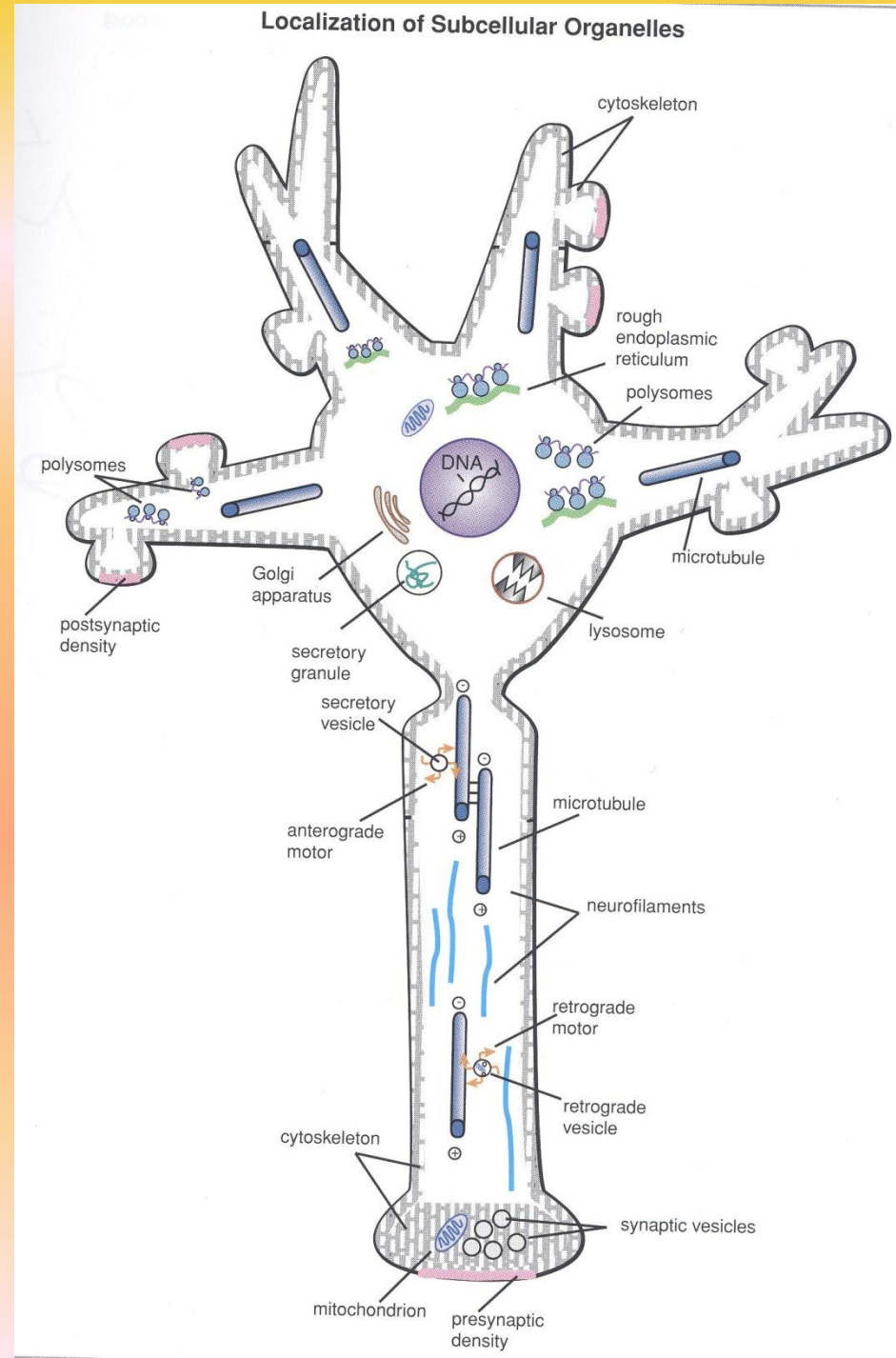
- Chandelier
- Pyramidal cell
- Basket cell
- Double bouquet cell
- Spiny
- Purkinje cell
- Up to 10,000 synapses for some neurons

[Stahl]



- Our brains form a trillion neurons
- Pruned down to 100 billion by apoptosis in adults, ie lose 90%!
- In adolescence half of all synaptic connections are selectively eliminated, leaving 100 trillion synapses

[Stahl]



- Once youve learned to ride a bike, you never forget
- Learning to play violin, or any complex task changes your brain permanently
- ‘The brain changes with addiction.’
- ‘Brains of recovered addicts still show a sharp spike in activity when pictures of paraphernalia are flashed on a screen.’
- ‘Fear and anxiety accelerate learning...’

'Neurons that fire together wire together' – Stahl p44

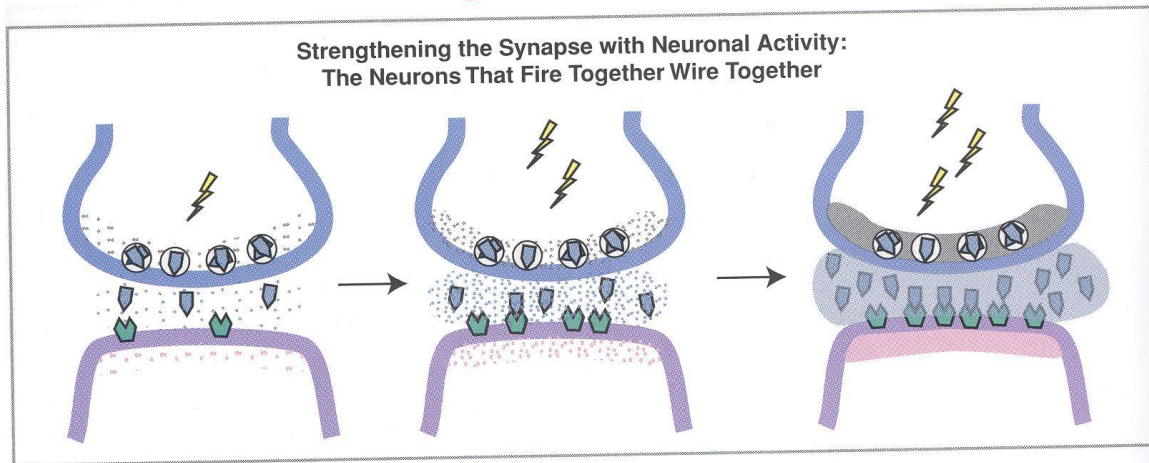


FIGURE 2-28 Strengthening the synapse. Functional synapses experience ongoing revision in response to changing conditions and the amount of use of a synapse by the neurons it connects. As depicted here, increased neurotransmitter release can alter the number of pre- and postsynaptic receptors expressed at a synapse (middle) as well as the richness of pre- and postsynaptic densities (right).

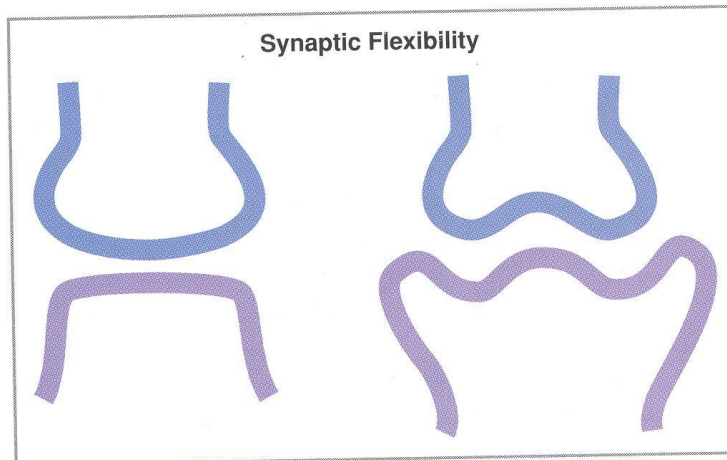


FIGURE 2-29 Synaptic flexibility. Increased utilization of a synapse can lead to adaptations on a structural level. As shown here, the surface area of both pre- and postsynaptic faces can increase to accommodate a greater number and array of receptors.

Synaptic
protein
scaffolding

'Synapses
used are
synapses
strengthened'
[Lewis]

Neuroplasticity

'Synaptic
sculpting'
[Lewis]

Neurotransmitters in the Brain

[Stahl, p52]

‘Classic Neurotransmitters’

1. Serotonin
2. Noradrenaline
3. Dopamine
4. Acetylcholine
5. Glutamate
6. GABA

TABLE 3-1 Neurotransmitters in brain

Amines	Aspartic acid (aspartate)
Serotonin	Gamma-hydroxy-butyrate
Dopamine	d-serine
Norepinephrine/noradrenaline	Gut hormones
Epinephrine/adrenaline	Cholecystokinin (CCK)
Acetylcholine	Gastrin
Tyramine	Motilin
Octopamine	Pancreatic polypeptide
Phenylethylamine	Secretin
Tryptamine	Vasoactive intestinal peptide (VIP)
Melatonin	Opioid peptides
Histamine	Dynorphin
Agmatine	Beta-endorphin
Pituitary peptides	Met-enkephalin
Corticotrophin (ACTH)	Leu-enkephalin
Growth hormone (GH)	Kyotorphin
Lipotrophin	Nociceptin (orphanin FQ)
Alpha-melanocyte-stimulating hormone (alpha-MSH)	Miscellaneous peptides
Oxytocin	Bombesin
Vasopressin	Bradykinin
Thyroid stimulating hormone (TSH)	Carnosine
Prolactin	Calcitonin G related peptide
Circulating hormones	CART (cocaine and amphetamine related transcript)
Angiogenesis	Neuropeptide Y
Calcitonin	Neurotensin
Glucagon	Delta sleep factor
Insulin	Galanin
Leptin	Orexin/hypocretin
Atrial natriuretic factor	Melanocyte concentration hormone
Estrogens	Gases
Androgens	Nitric oxide (NO)
Progestins	Carbon monoxide (CO)
Thyroid hormones	Lipid neurotransmitter
Cortisol	Anandamide
Hypothalamic releasing hormones	Neurokinins/tachykinins
Corticotrophin-releasing hormone (CRH)	Substance P
Gonadotropin releasing hormone (GnRH)	Neurokinin A
Luteinizing hormone releasing hormone (LHRH)	Neurokinin B
Somatostatin	Purines
Thyrotropin releasing hormone (TRH)	ATP (adenosine triphosphate)
Growth hormone releasing hormone (GHRH)	ADP (adenosine diphosphate)
Amino acids	AMP (adenosine monophosphate)
Gamma-aminobutyric acid (GABA)	Adenosine
Glycine	
Glutamic acid (glutamate)	

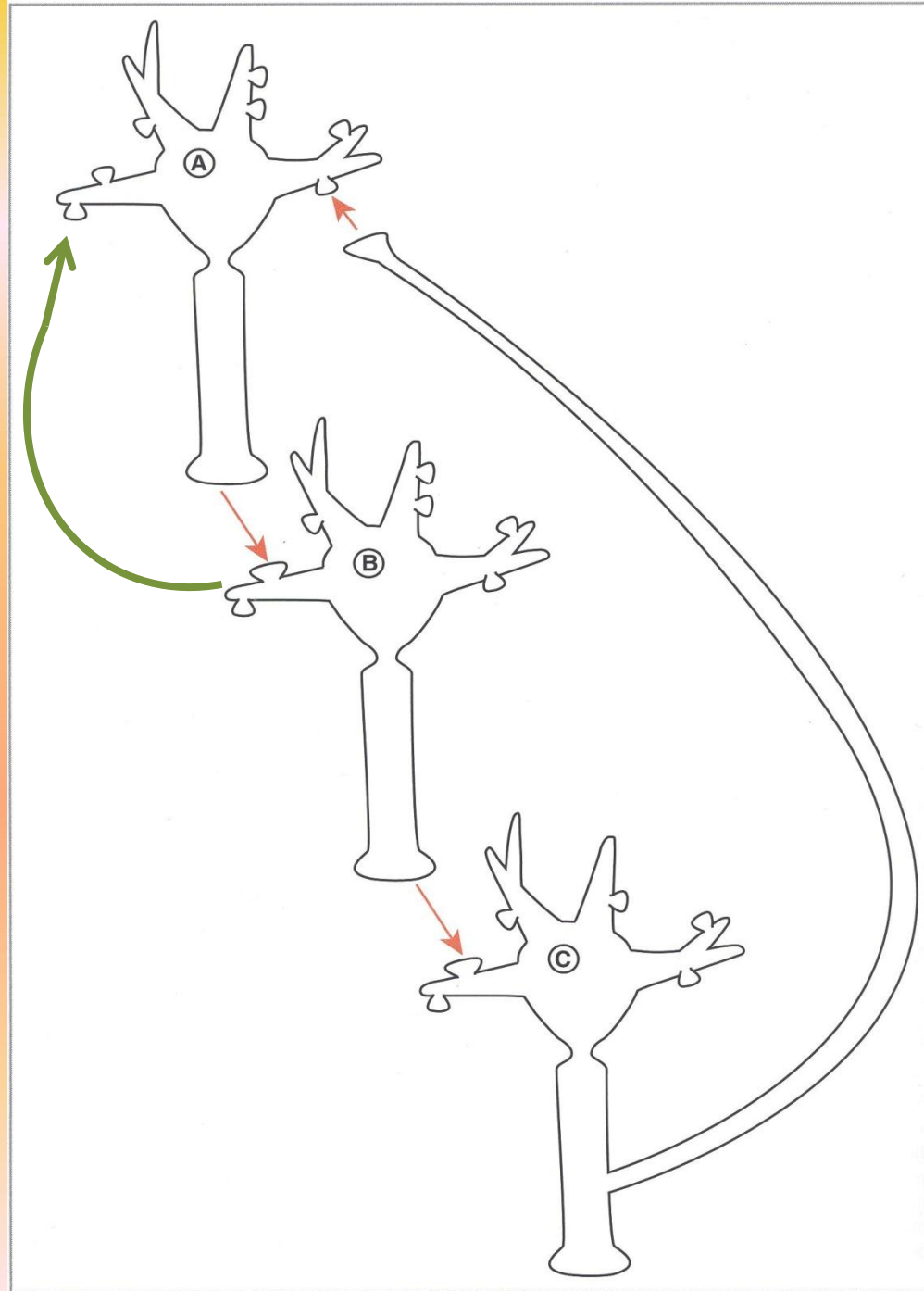
- GABA inhibits
- Glutamate excites
- - the brain's zeros and ones

[Lewis, p24]

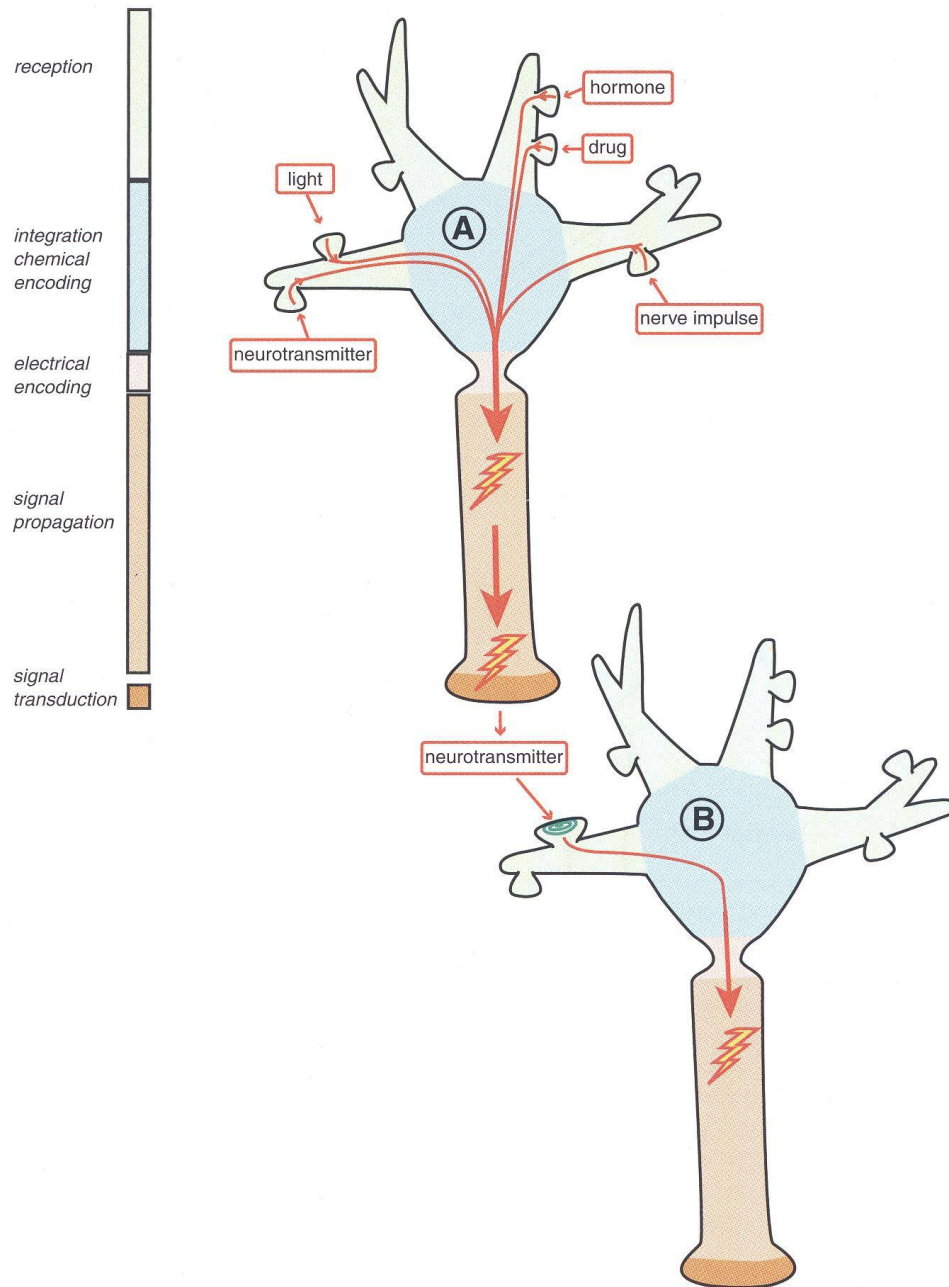
Brain circuits

- Schematic
- There may also be short feedback loops eg retrograde neurotransmission eg **anandamide**, NO & nerve growth factors

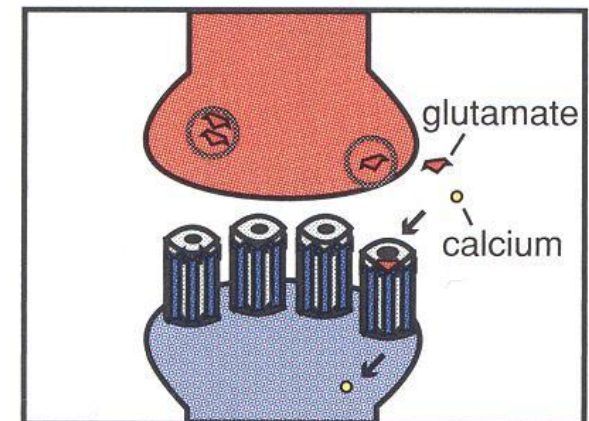
[Modified from Stahl, p56]



Classic Synaptic Neurotransmission: Fast Communication

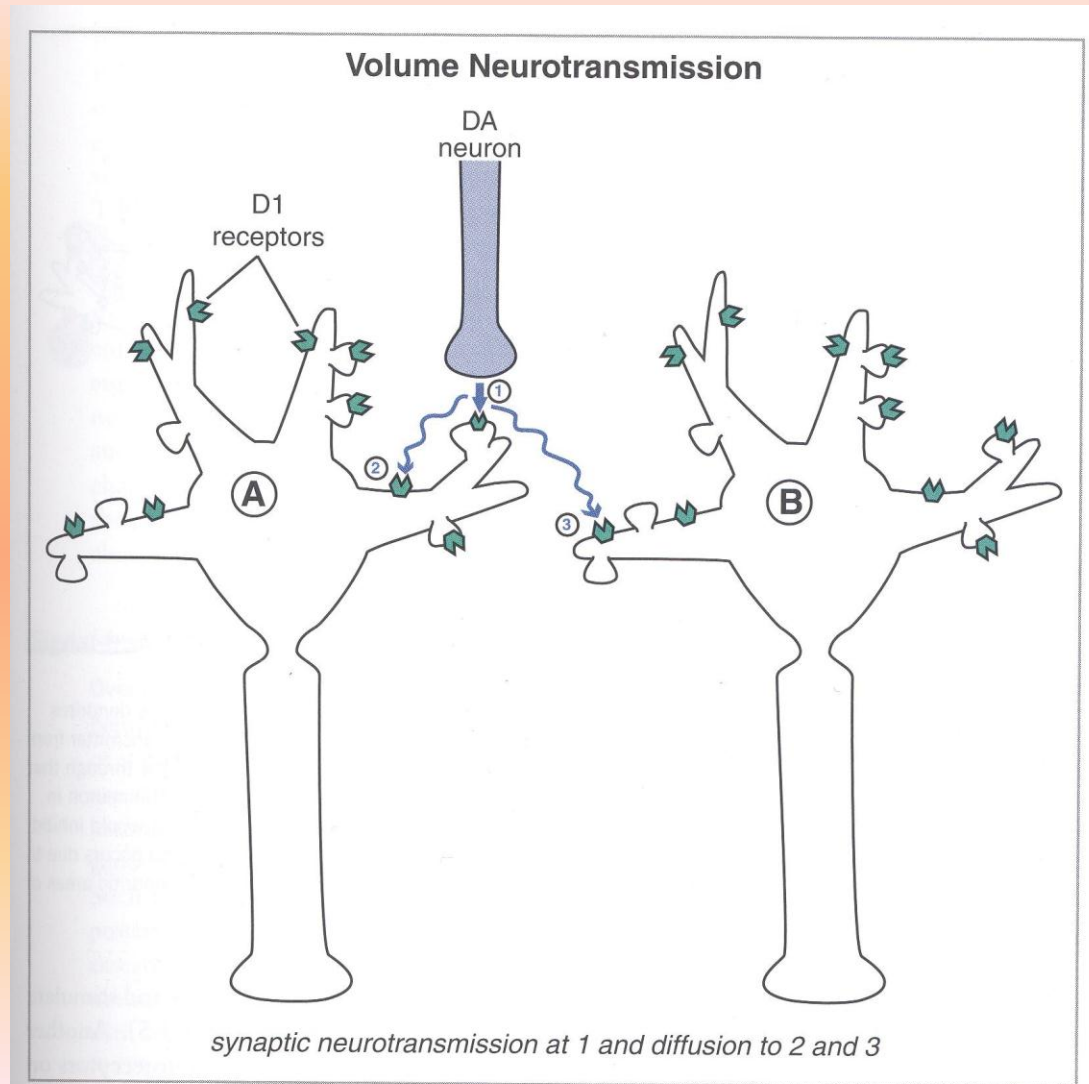


[Stahl, p55, p47]

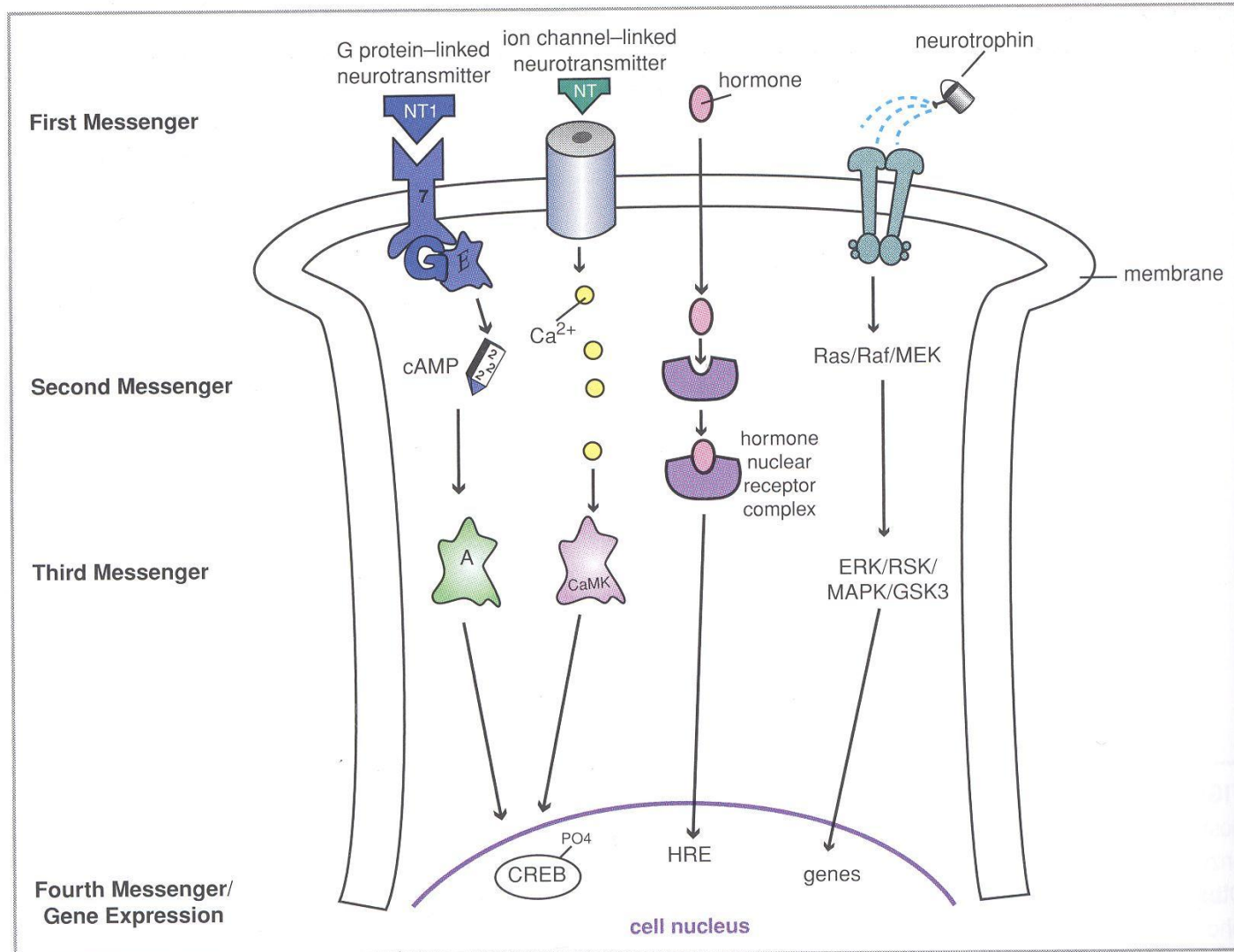


Glutamate opens the ion channel,
allowing calcium to enter the cell.

Volume neurotransmission, eg DA in prefrontal cortex [Stahl, p59]



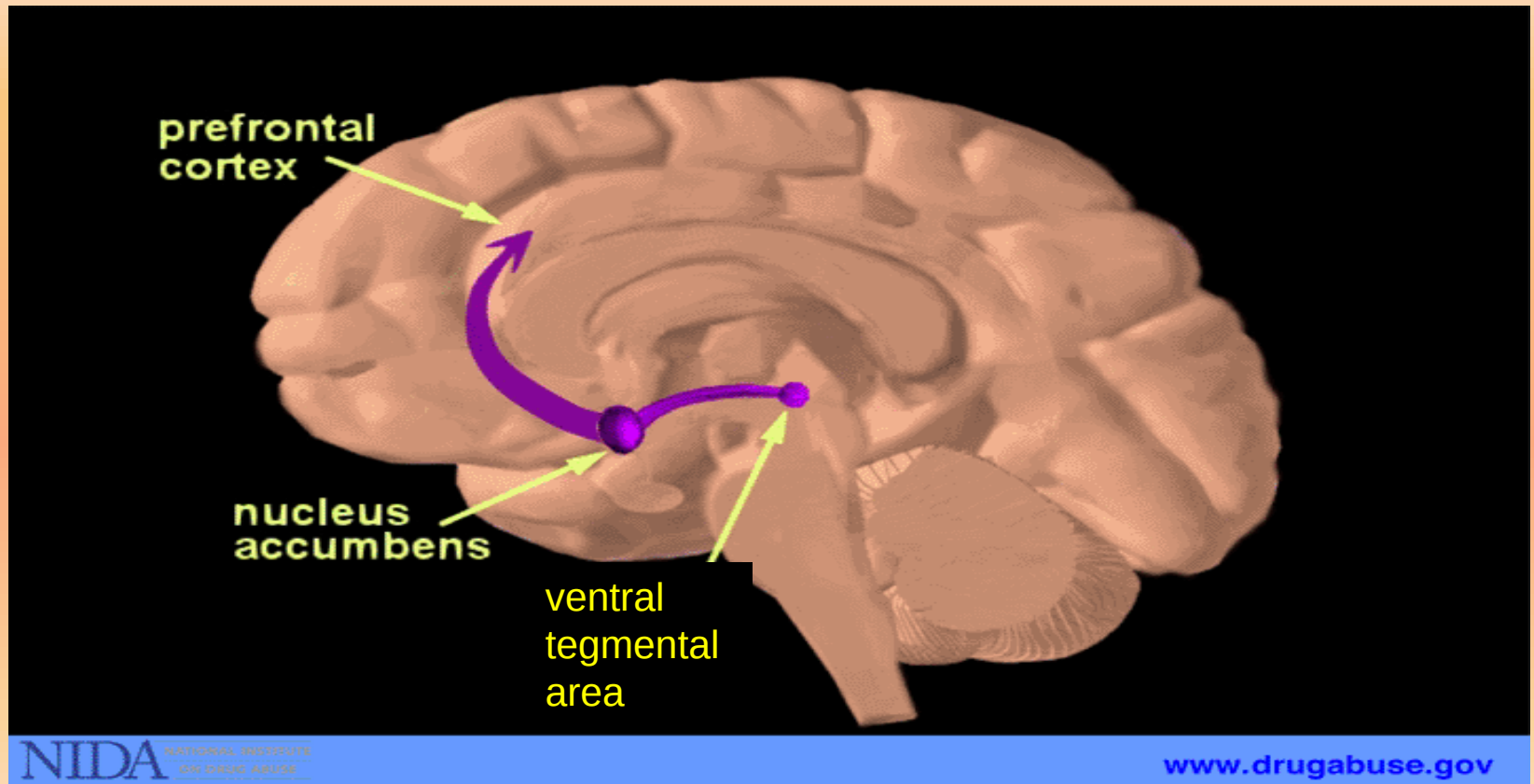
Receptor activation opens ion channels AND activates genes in nucleus of neuron



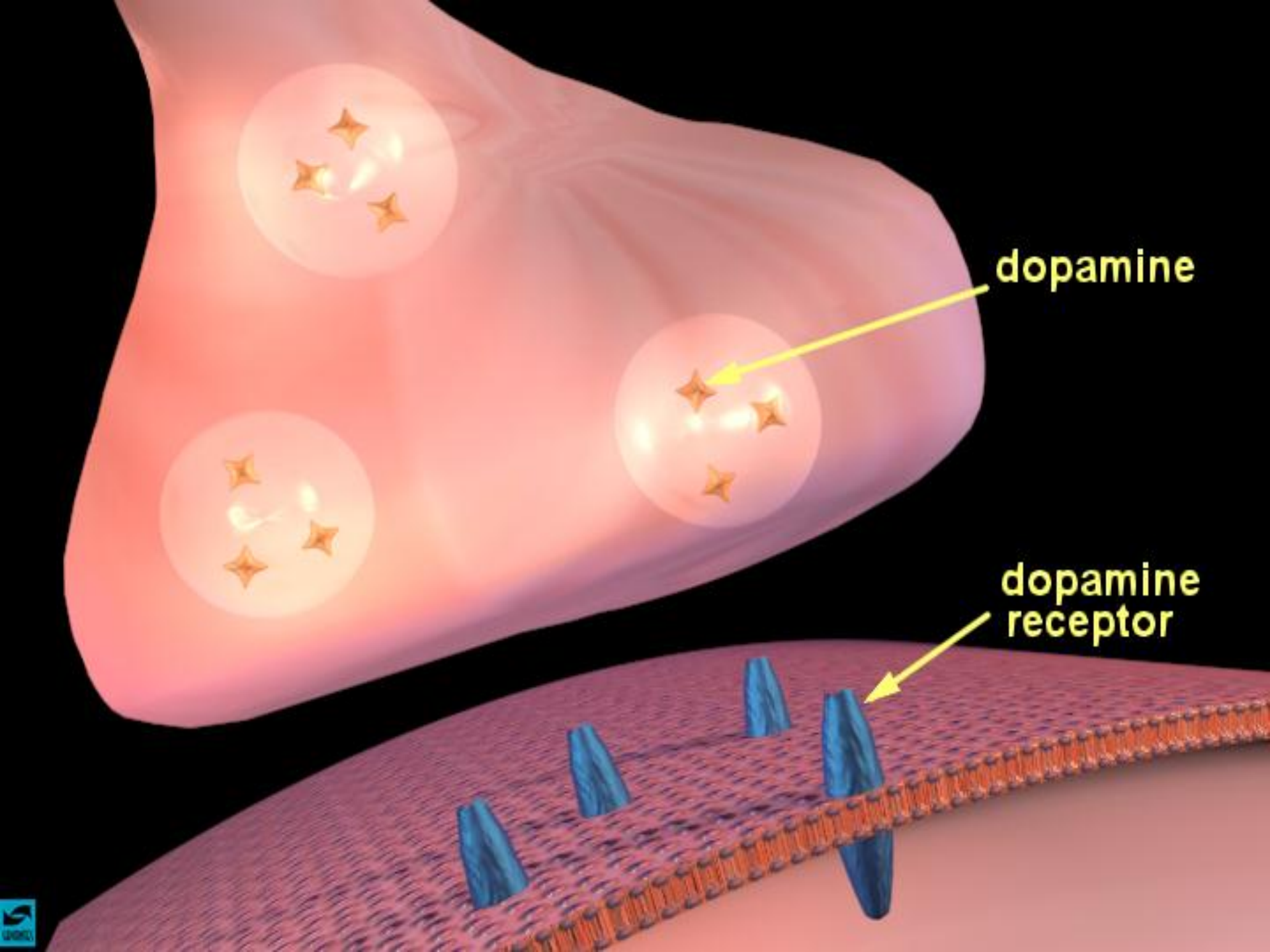
[Stahl,
p66]

Dopamine Theory of Addiction, the final common pathway

The Reward Pathway

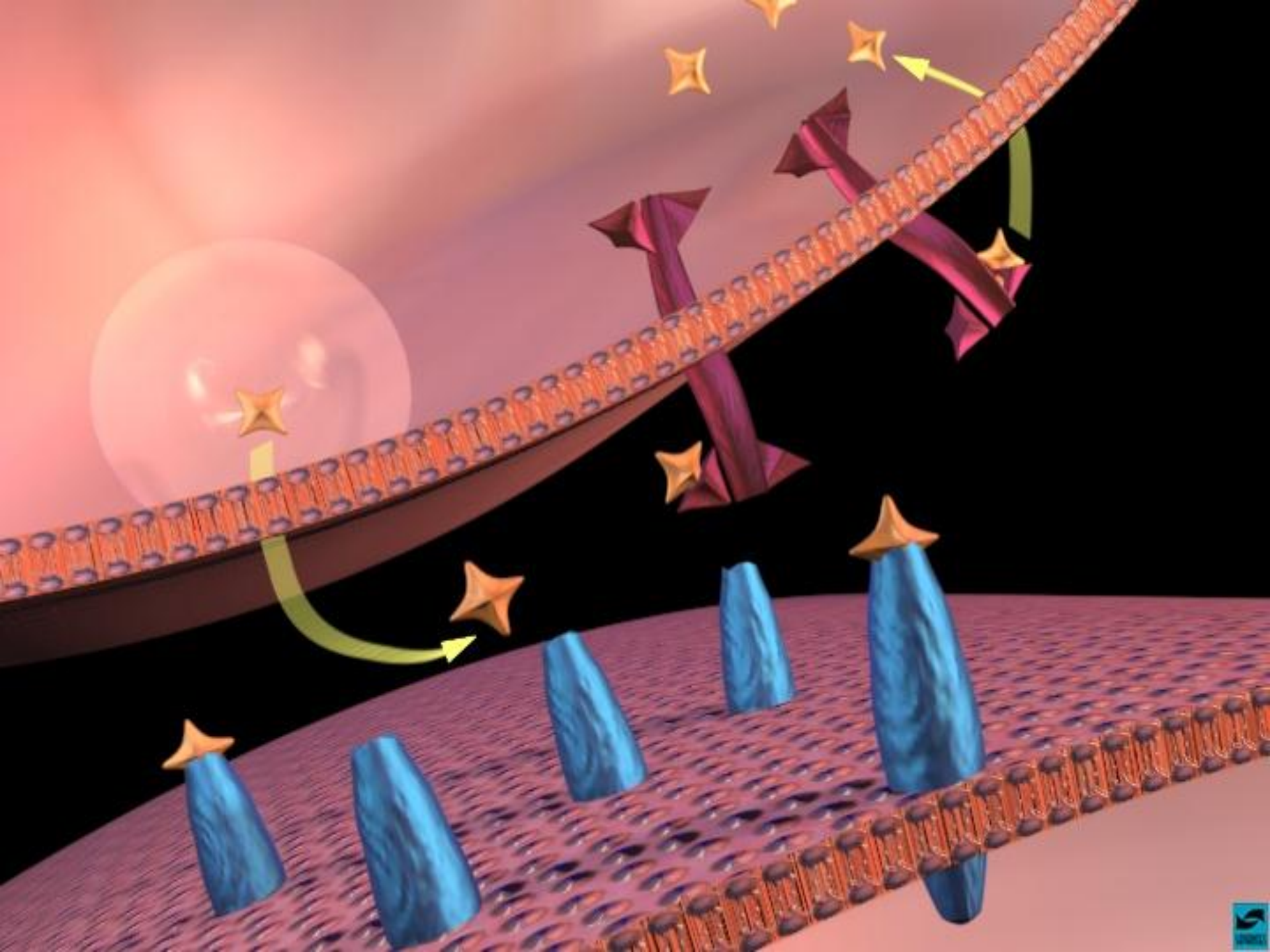


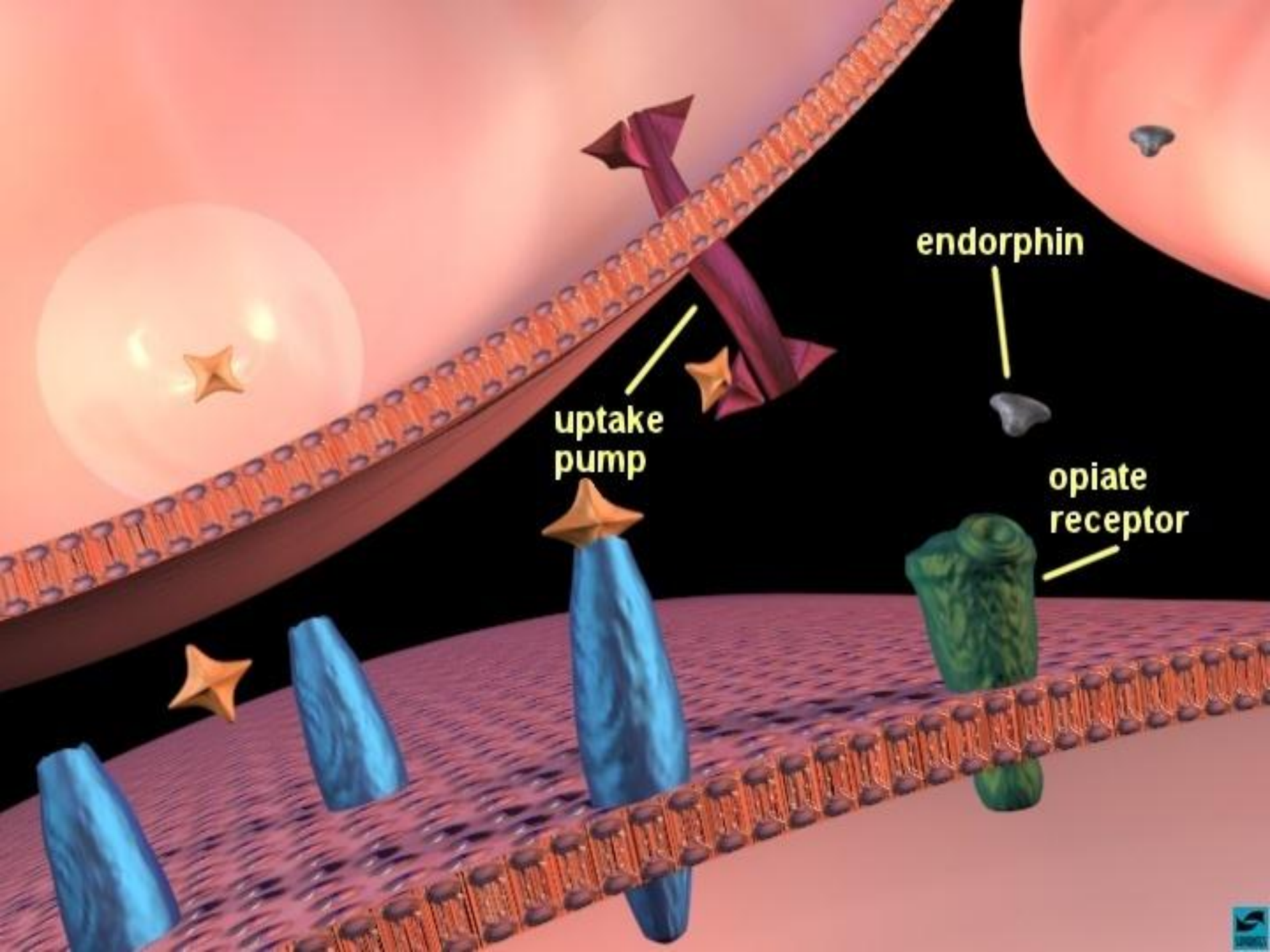
Adjacent ventral pallidum may be another 'hedonic hotspot'



dopamine

dopamine
receptor

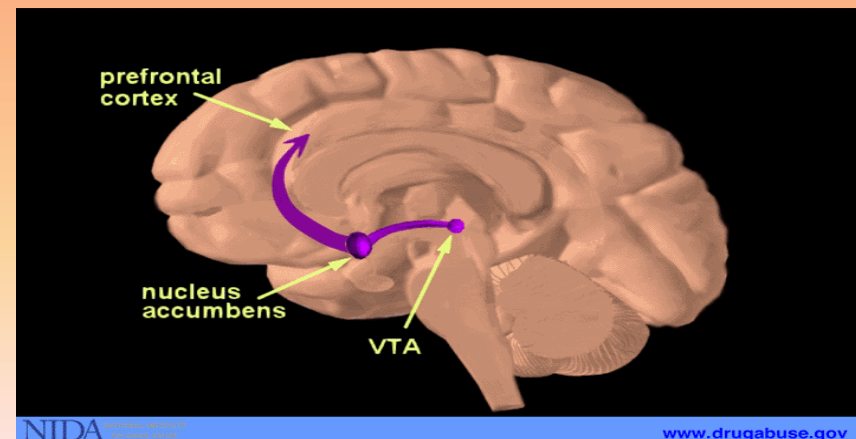




- ‘In the presence of the same old reward time after time, dopamine levels go down!’ [Lewis]
- Tolerance – more substance needed to achieve pleasure.

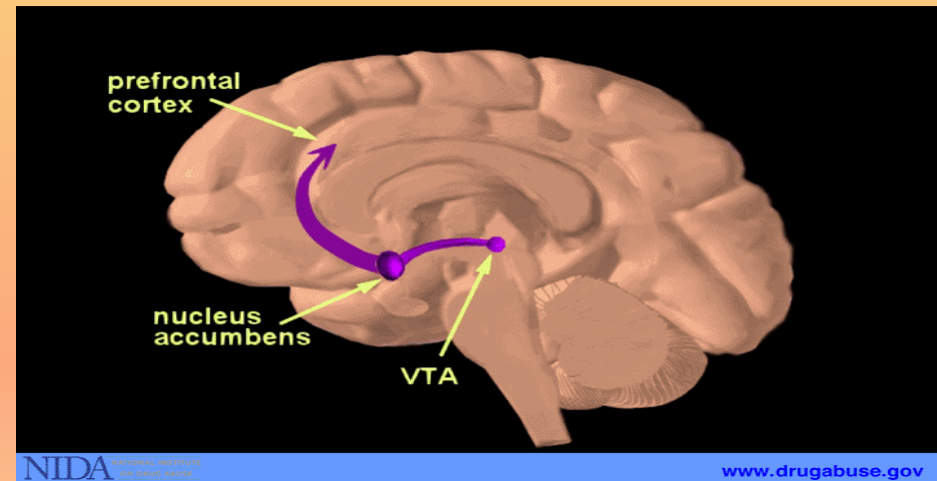
'Reactive reward system' - Stahl

- If projections to primitive brain: VTA & Amygdala, dominate:
- Impulsivity, **COMPULSIVELY WANTING MORE**
- Learned drug-seeking behaviour
- Responding to drug-related cues
- Instant gratification.



'Reflective reward system' - Stahl

- Circuits between Nucleus Accumbens and Prefrontal Cortex, **LIKING THE SUBSTANCE**
- PFC: analysing, will-power, decisions based on
 - 'Neurodevelopment
 - Genetics
 - Experience
 - Peer pressure
 - Learning social rules
 - Suppressing current pleasure for more valuable future gain... Delayed gratification.
 - Value of education, career, family etc.



‘Diabolical Learning’ – Stahl, p229

- Seen in mental health, chronic pain & addiction
- the short-term rewards of substance abuse reinforce addiction circuits
- Repeated use of ‘sick circuits’ reinforces them (reactive reward system)
- this reduces ‘healthy circuits’ (reflective reward system) – disuse atrophy, ‘use it or lose it’
- neural plasticity makes changes for good and bad: ‘virtuous’ learning vs ‘diabolical’ learning’.

‘The good news here is that these ideas are consistent with the notion that a clinician may not only be merciful in reducing symptoms for here-and-now relief but in doing so aggressively, completely, and persistently over time – also “save” the patient’s brain and prevent the development of very difficult symptoms, where the learning in the circuit may be difficult to reverse, or where loss of neurons may be impossible to reverse.’

SPECIFIC ACTIONS OF SOME DRUGS

Alcohol

- Enhances inhibitory GABA
- → reduces excitatory effects of glutamate
- ‘information flow is now sluggish, with big signals still getting through while small signals fade into static’
- ‘mental anaesthesia’ to life’s worries

[Lewis, p25]

Reduce your long-term health risks



No more than...

2

STANDARD DRINKS

3

STANDARD DRINKS

Daily

and no more
than 10 a week

and no more
than 15 a week

And

at least 2 alcohol-free days per week

Reduce your risk of injury



No more than...

4

STANDARD DRINKS

5

STANDARD DRINKS

On any single occasion

Pregnant women



No alcohol

0

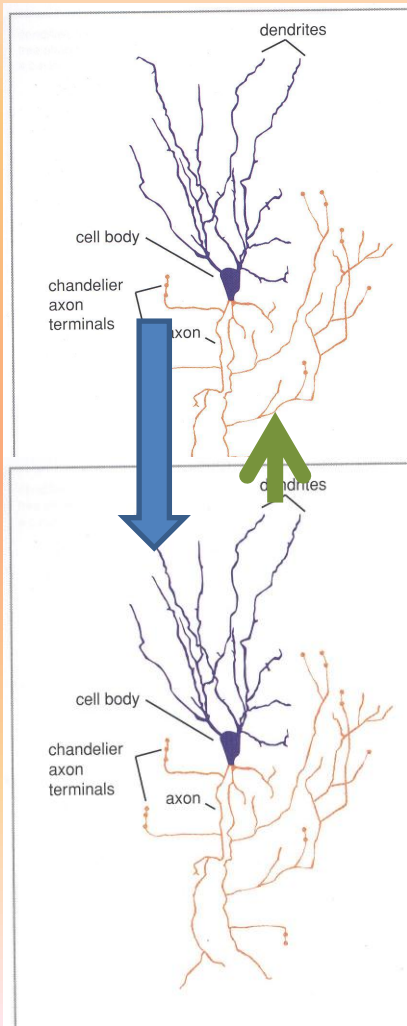
STANDARD DRINKS

There is no
known safe level
of alcohol use at
any stage of
pregnancy

NZ Low Risk
Alcohol Guidelines
2012

Cannabis

- Anandamide decreases refractory firing time, increasing neuronal responsiveness



neocortical system matures most during adolescence, and it's at this time that they 'amplify[ing] their tendency to do things, to imbue their plans with more confidence than they deserve...

...and this kind of thinking bears an uncanny resemblance to the delusional profundity of a marijuana high.'

'Teenagers are insane' [Nigel Latta]

...and stimulant properties. [Stahl]

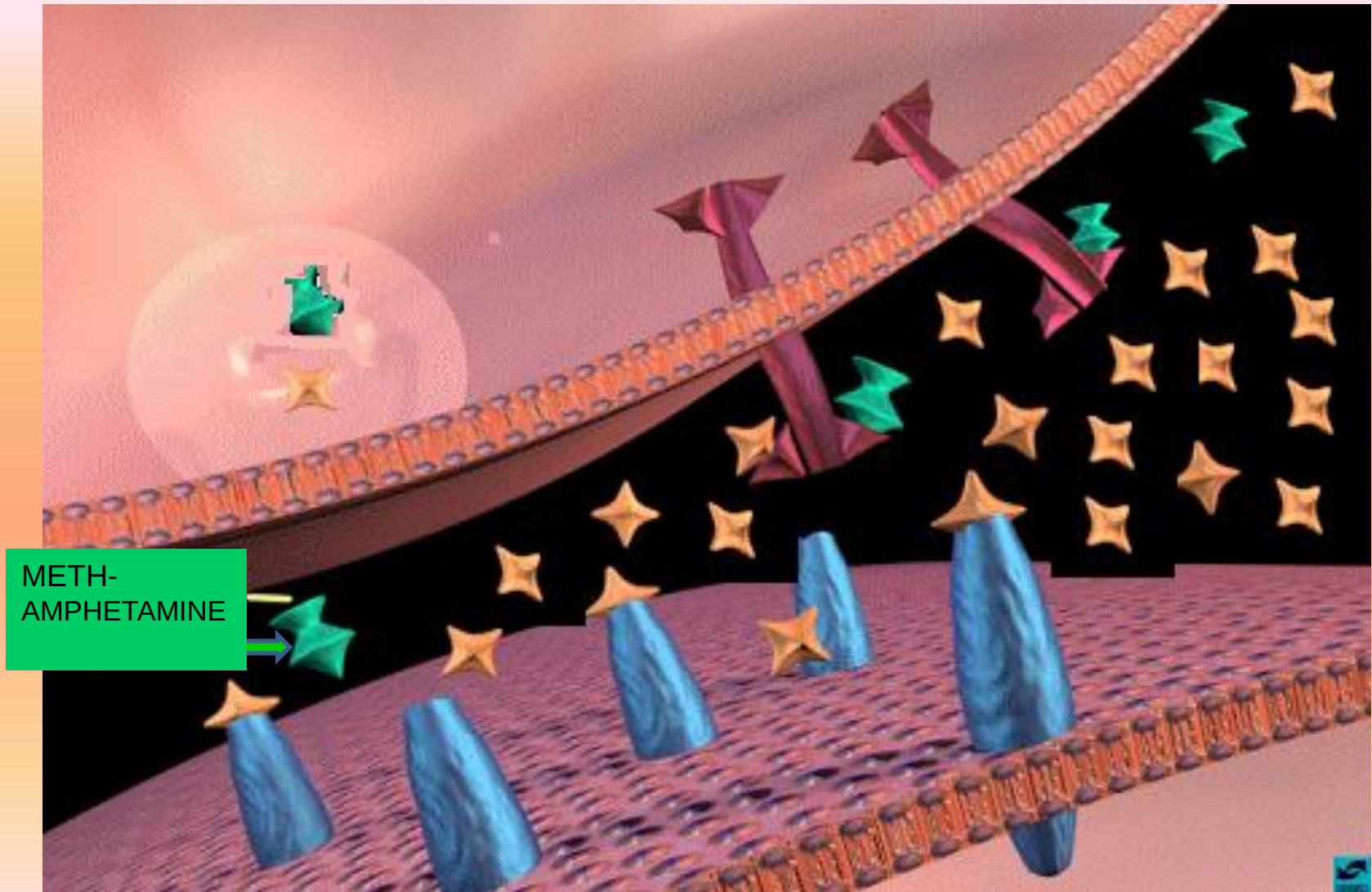
Serotonin, a neuromodulator

- Serotonin regulates information flow thru the brain by inhibiting some neurons firing. ‘...it soothes neurons that might otherwise fire too often, too quickly.’
- Depression & anxiety; ‘...brain becomes too active. Which is most of the time if you feel the world is dark and threatening. Extra serotonin [from SSRIs] makes the thinking process more relaxed....’ [Lewis, p81]

LSD

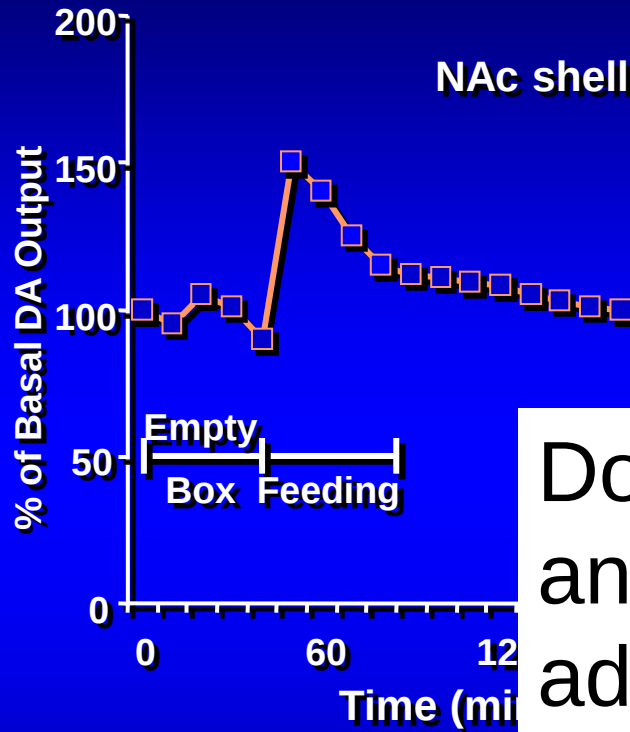
- Hallucinogens act at serotonin receptors, blocking the effects of serotonin
- ‘...the serotonin system... gets dynamited by LSD.’ [Lewis, p80]
- ‘Acid opens everything up, so that even the tiny details of perception mushroom, layer by layer, an elaborate mandala. The world *out there* becomes a galaxy of sparkling connections because there are no serotonin filters modifying the stream of input.’ [Lewis]

Amphetamines, stimulants



Natural Rewards Elevate Dopamine

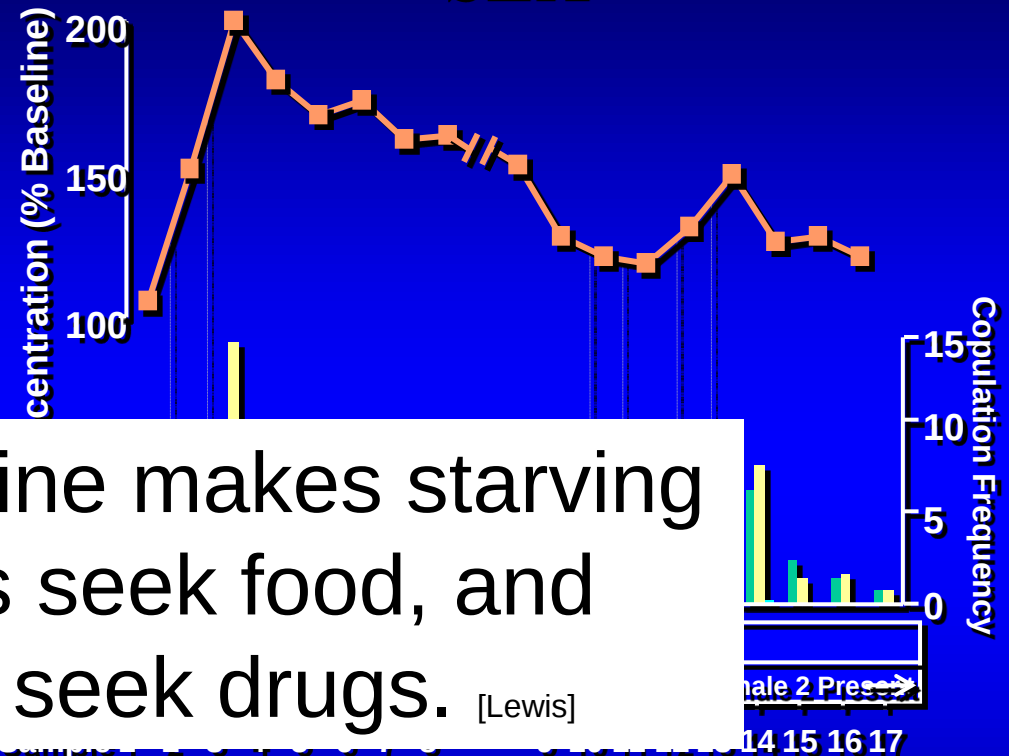
FOOD



Source: Di Chiara et al.

Levels

SEX

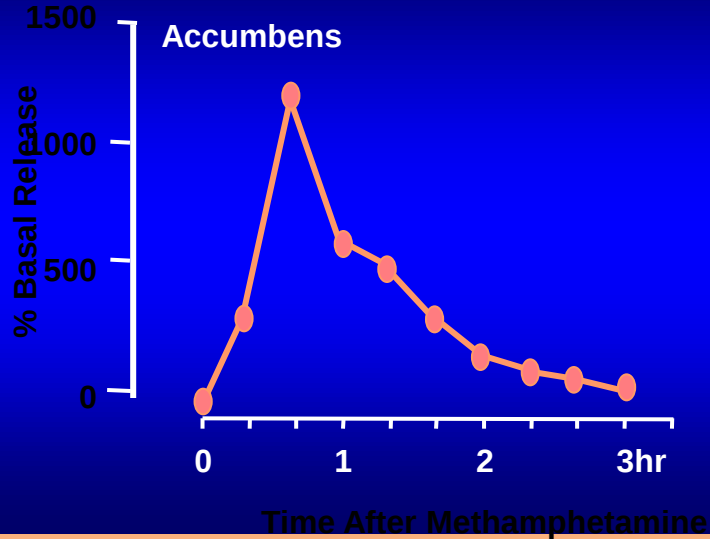


Source: Fiorino and Phillips

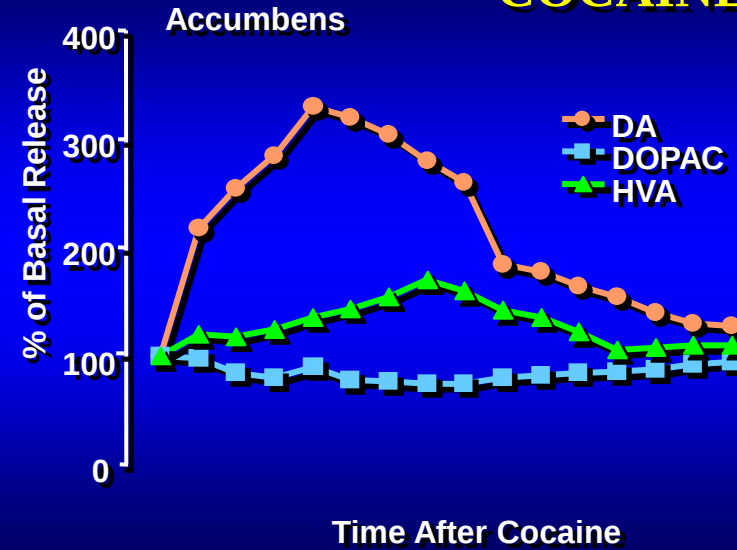
Dopamine makes starving animals seek food, and addicts seek drugs. [Lewis]

Effects of Drugs on Dopamine Release

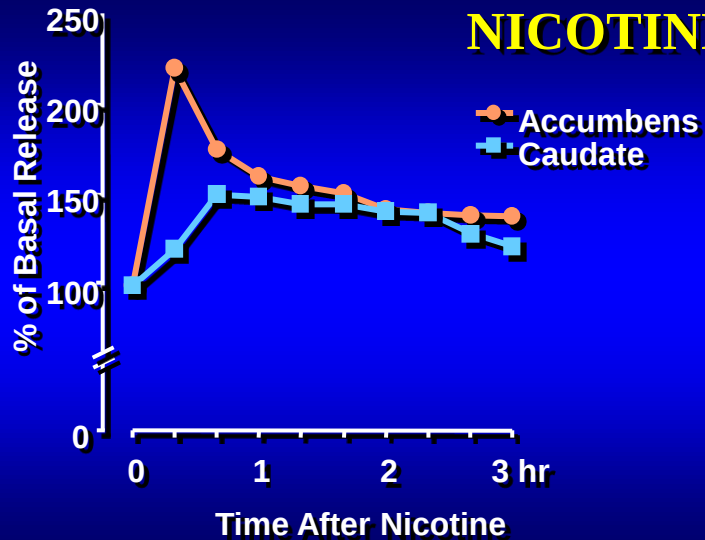
METHAMPHETAMINE



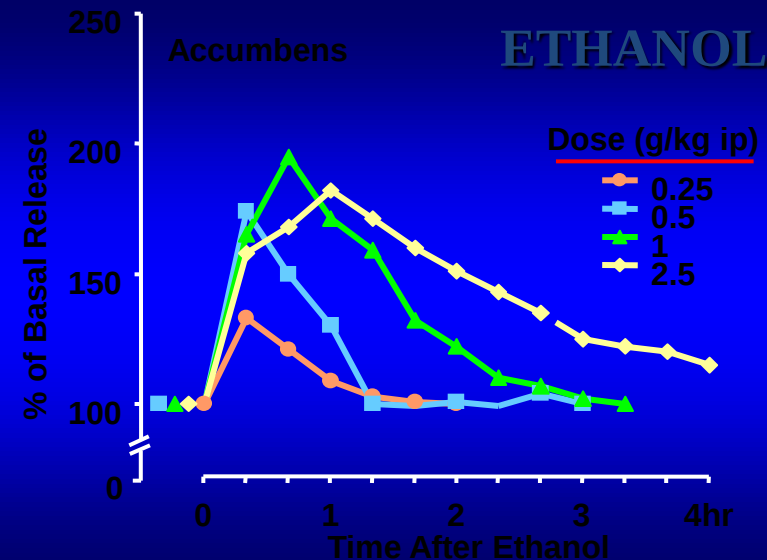
COCAINE

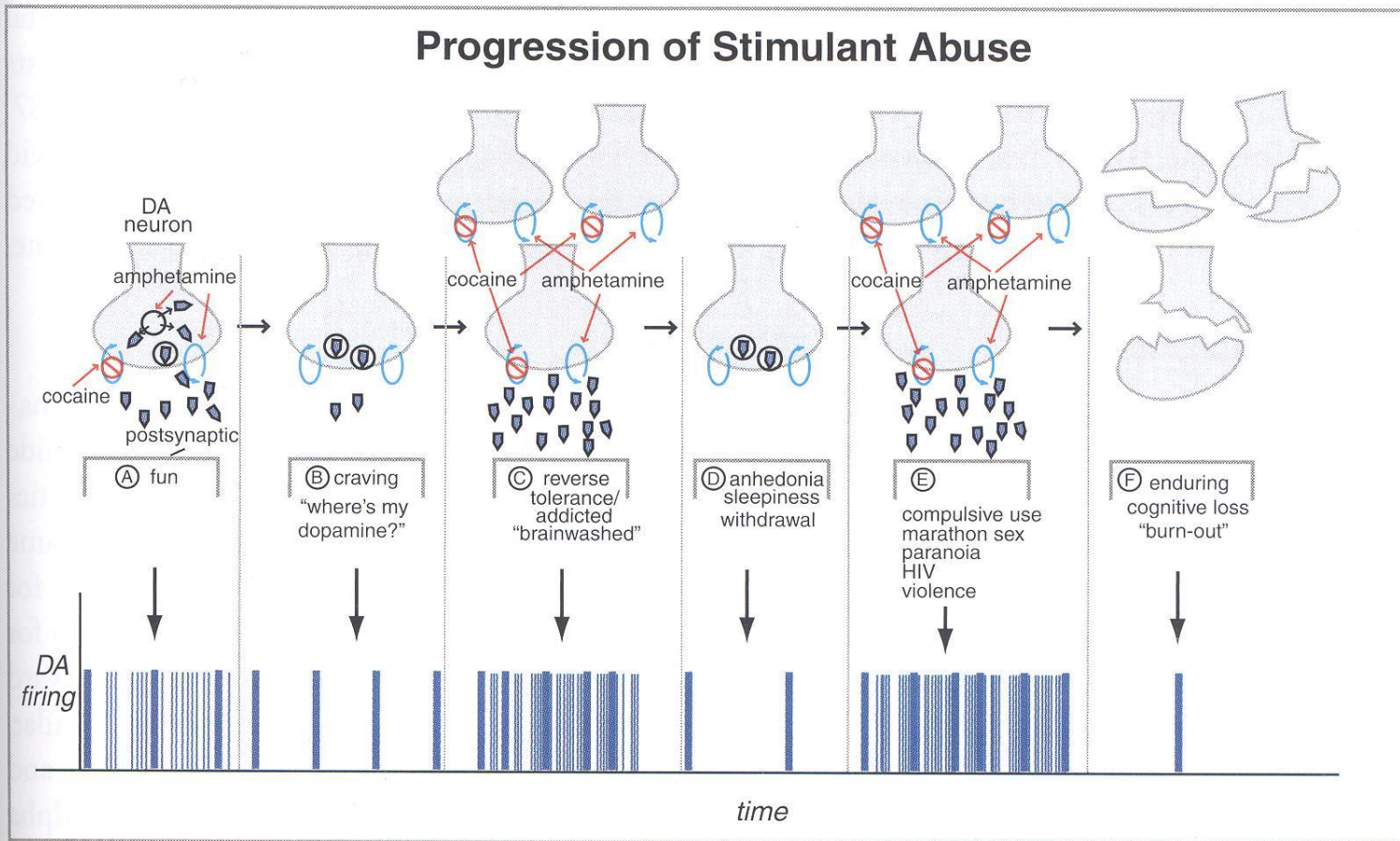


NICOTINE



ETHANOL





**'...the higher
the high,
the lower
the low...'**

FIGURE 19-36A, B, C, D, E, and F Progression of stimulant abuse. (A) First doses of stimulants such as amphetamine or cocaine cause pleasurable phasic dopamine firing. (B) With chronic use, reward conditioning causes craving between stimulant doses and only residual tonic dopamine firing with lack of pleasurable phasic dopamine firing. (C) In this addicted state, higher and higher doses of stimulants are needed in order to achieve the pleasurable highs of phasic dopamine firing. (D) Unfortunately, the higher the high, the lower the low, and between stimulant doses the individual experiences not only the absence of a high but also withdrawal symptoms such as sleepiness and anhedonia. (E) The effort to combat withdrawal can lead to compulsive use and impulsive, dangerous behaviors in order to secure the stimulant. (F) Finally, there may be enduring if not irreversible changes in dopamine neurons, including long-lasting depletions of dopamine levels and axonal degeneration, a state that clinically and pathologically is appropriately called "burn-out."

Stimulant Self Management

Would you want to stop using something that gave: euphoria, increased energy & mental alertness, wakefulness, weight loss & increased libido???

- Non-dependent experimental or recreational use – majority of users
- Expense
- Tolerance
- Dysphoria, paranoia, the Crash, withdrawal
- Loss of relationships, family, job etc

Opioids

- Inhibit firing of neurons activated by pain or stress
- Opioid receptors found all thru spinal cord and brain; highest density in cortex where we consciously 'feel' pain
- They suppress corticotrophin-releasing factor
- Opioids → 'ahhhhhh' ... 'the stuff of mother love multiplied a thousandfold' [Lewis], euphoria or rush followed by 'profound sense of tranquillity' then drowsiness or 'nodding'. [Stahl, p977, p979]

COGNITIVE PERFORMANCE IN OST, ABSTINENT OPIOID USERS AND NON OPIOID USERS

Prof Shane Darke, NDARC, Australia



- Methadone and buprenorphine may both be associated with cognitive impairments across a range of cognitive domains: disinhibition, poor problem solving, slow processing, poor learning
- We must manage these patients differently
- They may not be deliberately difficult!

COGNITIVE PERFORMANCE IN OST

continued

CONFOUNDERS

What was the premorbid IQ?

Lifestyle of opioid users puts them at risk of cognitive impairment: od's, accidents incl head injuries, assaults, abuse & trauma from childhood, other drug use eg alcohol.

Nicotine, for example

- Prefrontal cortex says, 'No, dont have that cigarette.' (Reflective reward system)
- Amygdala says, 'But I want it now.' (Reactive reward system)
- Ongoing conflict uses lots of glucose energy
- PFC gets tired of controlling the impulse, 'ego depletion'
- '...like a muscle. Try holding your arm out at your side for half an hour...it gets harder and harder...' like resisting temptation [Lewis, p246]

- Smoker gives in
- Dopamine surge on anticipating the cigarette
- DA surge on smoking it
- BUT, by the end of a 'standard cigarette' nicotinic receptors shut down, desensitise
- In about 45 minutes they resensitise → craving, withdrawal due to low DA
- → another cigarette, 20 per day, actually! [Stahl]

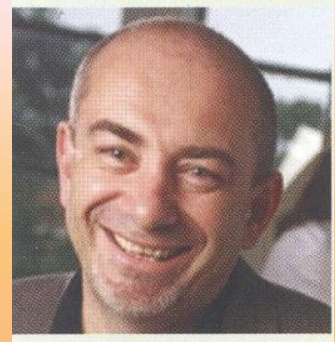
Varenicline (champix) blocks craving

‘Many of these patients are prescribed varenicline for only 12 weeks, which might be far too short a period of time for maximal effectiveness...’

Stahl, p965

NEUROBIOLOGY OF DECISION-MAKING

Prof Bernard Balleine, Behavioural Neuroscience & Addictive Disorders Lab, NSW



- **‘Decision loop’** for highly processed, goal directed decisions
- **‘Habit loop’** to exploit our discoveries eg when driving ‘automatically’
- If one loop is down, the other takes over
- Decision loop failure seen in psychosis, OCD, depression, addiction
- Habit loop failure seen in ADHD, addiction

NEUROBIOLOGY OF DECISION-MAKING

continued

- Loops affected by being young, old, brain injury, degeneration
- **Damaged decision loops match DSM criteria for dependence:** insensitive to negative feedback
- DA agonists may help decision making.

Behaviour change, or not...

- Why are we here?
- At this conference?
- How many great ideas do you have?
- How many changes do you make to your practice?
- How many of those changes last?
- Usual behaviour is highly ingrained in learning and memory circuits
- Shift from usual behaviour takes time & repetition.

RECOVERY

Don't give up, shift happens!

- ‘...the kinds of drugs we seek stand in for the kinds of needs that have gone unfulfilled.’ [Lewis, p302]
 - Loss of belonging – opioids
 - Loss of power – methamphetamine
- With ‘... the support of an environment, or a relationship, or a philosophy, religion, or narrative sufficient to take up some of the strain... don't give up. The brain loses a great deal of flexibility with addiction, but it doesn't lose it all.’ [Lewis, pp304, 306.]

‘Research suggests that targeted stimulation of the brain’s prefrontal cortex is a promising treatment for addiction’ [National Institute on Drug Abuse]

What can we do???

- Non-judgemental understanding
- Offer positive support
- Involve family/whanau
- Refer to your local Alcohol & Drugs Service
- Recommend long-term rehab to literally reprogram the brain
- Treat mental health issues, psychotherapy
- Medication as appropriate.

MODA

SECTION 24 – THE RULES

Treatment of people dependent on controlled drugs (see Section 24 of The Misuse of Drugs Act 1975)

Section 24(1) states that “...every medical practitioner commits an offence against this Act....who prescribes, administers or supplies any controlled drug for or to any person, whom the practitioner has reason to believe is dependent (on that or any other controlled drug) in the course, or for the purpose of treatment of dependency **except....**

....**except** if the medical practitioner is acting with the permission in writing, given in relation to that particular person by an authorised medical practitioner.”
S24(2)(d).

Only gazetted specialist services (e.g. Alcohol & Drug Services), gazetted GP's and Authorised GP's can prescribe for people dependent on controlled drugs.
See S24(2)(a)(b)(c)

Classification of Controlled Drugs

- Class A drugs pose a very high risk of harm
- Class B drugs pose a high risk of harm
- Class C drugs pose a moderate risk of harm

- Class A: eg. heroin; methamphetamine
- Class B1: eg. morphine; opium; cannabis
oil
- Class B2: eg. methylphenidate;
amphetamine
- Class B3: eg. fentanyl; pethidine

- C1:eg. cannabis plant; Catha edulis plant (Khat)
- C2:eg. codeine; dihydrocodeine
- C3:eg. Pholcodine
- C4:eg. buprenorphine; barbiturates (no longer prescribed)
- C5:eg. benzodiazepines; phenobarbitone; ephedrine; pseudoephedrine
- C6:eg. codeine/paracetamol; (mixtures of class C drugs with other substances)

CASE HISTORIES

Bruce, 38, liquor outlet manager amphetamine dependence

HISTORY

Late 2012: seen w ex-partner

Referred by CADS, and will be doing their
program

Alcohol

- heavy drinking as part of his job, over 20 years
- less in recent years.

Methamphetamine, 6 years, no other stimulants
or other drugs

- helped him reduce alcohol

- eased depression

- had more days using than not, never IDU

- last meth use was a week ago. He is being
offered free drugs by 'friends'

- difficulty sleeping

- waking feeling flat

- irritable

- not motivated.

Depression

- when marriage split
- went thru a breakdown
- saw a private psychiatrist
- tried fluoxetine, quetiapine
- no recent meds prescribed
- his ex- gave him amitriptyline 75mg: good nights sleep, getting into a routine, dry mouth
- while he is sick his insurance covers him
- thoughts of death, has wondered if it is worth living, being a burden to others, but safe.

- Kessler 10 score 40 = high risk of anxiety/depression

PLAN

- Continue CADS program, increase exercise, work part-time
- Rx: Amitriptyline 25mg Tab - 1 - 3 FOR SLEEP
- Review in 1 week.

- Seen a week later
 - Attended CADS once
 - Made excuses to visit a 'drug buddy' to say he had stopped P, and used once with this friend
 - Mind is clearer
 - Sleeping better
 - Coffee increased to 7 daily
 - Reduced libido off P
-
- Reduced P use to once in 2 weeks cf most days past 6 years.

- Wants to feel less depressed, but 'actually reasonably happy with myself'
- 'looked' at John Kerwins Journal
- Not suicidal
- Agrees to increase amitrip from 75 to 125mg nocte

2 weeks later

- Seen with his ex-
- Used P once in 4 weeks
- Spending more time w his kids
- Missed 2 CADS group sessions, one w the flu, the other out of guilt from missing the 1st one
- Amitrip 125mg nocte
- See in 2 weeks.

3 weeks later

- Completed CADS starter course
- Will do the next program
- Head clearer, joy in lifes simple pleasures
- Weight 112 → 120kg off P
- A few beers, cannabis twice, no more P
- See in 4 weeks: no show....

Now???

- Feb – Mar 2013: 8 wk Bridge program
- Stayed alcohol- & drug-free
- Increased exercise
- Attends AA meetings & psychotherapy
- Reports 'great mental health'
- Reunited w his ex
- Excited she is pregnant!

Trevor, 29, labourer synthetic drug dependence

Dec 2008: cannabis daily after work, no other drugs, never IDU

- Motivational chat

May 2009: methamphetamine every weekend

Oct 2010: seen w mother

- On bail for cooking P, possession firearms
- Cannabis daily
- No tobacco or alcohol
- Poor sleep, afraid of being attacked
- Not suicidal
- Talks to friends
- Kessler 10: 32 => moderate risk anxiety/depression
- Declines SSRI or referral to CADS
- For Sickness Benefit.

December 2010

- Cannabis daily 'to cope'
- Alcohol 3 days a week
- No other drugs
- Car was stolen
- Depressed
- Kessler 10 gone from 32 to 36
- Declines SSRI, 'dont want to turn into a zombie'
- Will try melatonin, but not CADS.

March 2011

- Court hearings, more charges
- No money
- Social isolation, friends are stoners
- Some house painting, kitchen hand
- Looks depressed, K10 = 32

Plan: Sickness Benefit, but wont go to CADS.

July 2012

- Seen at ED: anxiety on stopping cannabis
- Given zopiclone 15mg, advised to see GP.

October 2012

- K2 or Illusion on waking, all day and thru night
- Stops 12 hours max
- Working full time
- Started synthetic drugs to pass drug tests at work
- Methamphetamine twice a month
- Smoking cigarettes

Plan: recommend CADS, citalopram 20mg, zopiclone x 10.

Now???

- Moved to another town
- June 2013: final court case due late 2013
- Never went to CADS
- Acupuncturist told him K2 was destroying him
- Stopped K2
- Gone back to normal cannabis, daily
- Works as plumber
- Cannabis at work, but feels safe because job mainly involves lying on the ground!

4 Take Home Points:

1. Non-judgemental, harm-minimisation approach as many won't achieve abstinence
2. Brief advice & counselling are effective, but require patience
3. Manage mental illness
4. Refer to addiction services or rehabilitation centres; 'shift happens', but may need time & support.

Your cases,
questions,
comments....

Acknowledgements

- Stahl's Essential Psychopharmacology. Neuroscientific Basis and Practical Applications. 3rd Edition, Cambridge, 2008. Stephen Stahl.
- Memoirs of an Addicted Brain. A Neuroscientist Examines his Former Life on Drugs. Scribe, 2008. Marc Lewis.
- www.drugabuse.gov [National Institute on Drug Abuse]
- & You, my audience – thanks for attending.

