Alcohol Dependence & Its Treatment

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50 million ltrs/yr of beer to 120million ltrs/yr from 02-05 to 250 million in 2015

No.1 consumer of whisky

40% of job absenteeism

75% of emergency admissions

20% of head injuries

1/3rd of Suicides

2/3rd of Wife abuse

9% market share of Asian International brand market

525% taxation on alcohol – Max. in the world.

24% of urban per family income & 32% of rural family income

1.7ltrs/head/yr of legal alcohol

30% of fatal road accidents

MINDCRAFT

75% of the population doesn't drink

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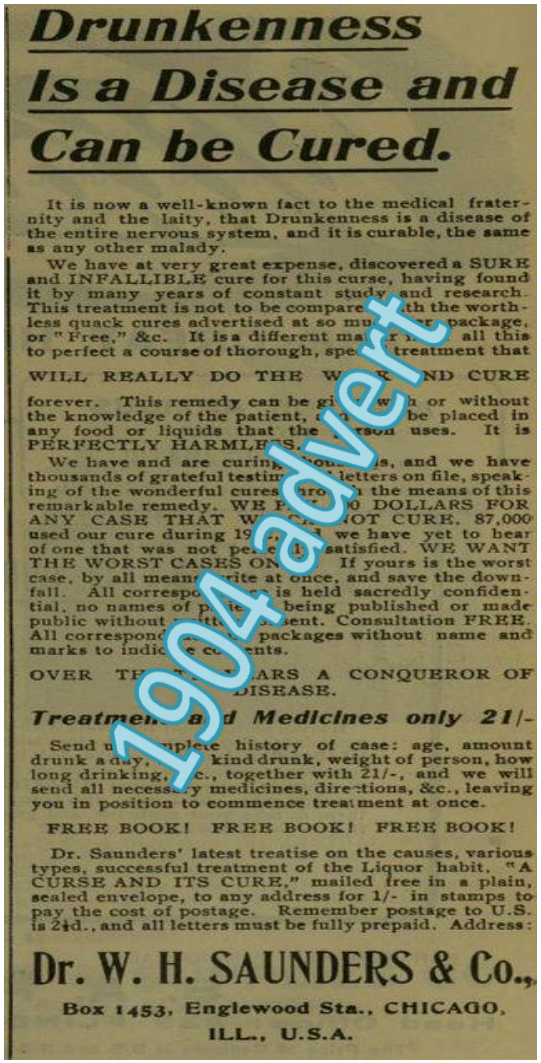
Myths about alcohol

- Excessive drinking causes alcoholism.
- Regular drinking is alcoholism
- Alcohol abuse is not a problem.
- All social menace due to alcohol is because of alcoholics
- Alcohol problem is problem of “will power”
- All alcoholics are crooks/ criminals/ and a pain in the

Alcohol Dependence

- **Impaired Control 4**:
  - Amount, duration,
  - Regularity, attempts at giving up,
  - Preoccupation with procuring, craving.
  - Relapses
- **Social Impairment 3**: unfulfilled obligations; direct attribution to substance use; unsurmountable need to get the substance
- **Risky drinking 2**: Physical/psychological probs
- **Pharmacological criteria 2**: tolerance, withdrawals

Alcoholism as a Disease



Drunkenness Is a Disease and Can be Cured.

It is now a well-known fact to the medical fraternity and the laity, that Drunkenness is a disease of the entire nervous system, and it is curable, the same as any other malady.

We have at very great expense, discovered a SURE and INFALLIBLE cure for this curse, having found it by many years of constant study and research. This treatment is not to be compare[d] with the worthless quack cures advertised at so mu[ch] per package, or "Free," &c. It is a different ma[tter] all this to perfect a course of thorough, spe[cific] treatment that

WILL REALLY DO THE W[ORK] AND CURE

forever. This remedy can be gi[ven] with or without the knowledge of the patient, [can] be placed in any food or liquids that the [per]son uses. It is PERFECTLY HARMLE[SS].

We have and are curin[g] thousands of grateful testim[onials] letters on file, speaking of the wonderful cures [wro]ught by the means of this remarkable remedy. WE F[OR]FEIT 500 DOLLARS FOR ANY CASE THAT W[E] DO NOT CURE. 87,000 used our cure during 19[03] we have yet to hear of one that was not pe[rfect]ly satisfied. WE WANT THE WORST CASES ON[E]. If yours is the worst case, by all mean[s] write at once, and save the downfall. All correspo[nd]ence is held sacredly confidential, no names of p[at]ients being published or made public without [our] written consent. Consultation FREE. All correspond[ence] in plain packages without name and marks to indic[ate] contents.

OVER TH[IRTY] YEARS A CONQUEROR OF DISEASE.

Treatment and Medicines only 21/-

Send u[s] complete history of case: age, amount drunk a day, [what] kind drunk, weight of person, how long drinking, [&c.], together with 21/-, and we will send all necessary medicines, directions, &c., leaving you in position to commence treatment at once.

FREE BOOK! FREE BOOK! FREE BOOK!

Dr. Saunders' latest treatise on the causes, various types, successful treatment of the Liquor habit, "A CURSE AND ITS CURE," mailed free in a plain, sealed envelope, to any address for 1/- in stamps to pay the cost of postage. Remember postage to U.S. is 2½d., and all letters must be fully prepaid. Address:

Dr. W. H. SAUNDERS & Co.,

Box 1453, Englewood Sta., CHICAGO, ILL., U.S.A.

1904 advert

- Thomas Trotter, a Scottish Physician
- Benjamin Rush 1745-1813- Addiction; Palsy of the will!
- Magnus Huss: Swedish Physician: 'Alcoholism' Alcoholismus Chronicus;
- Mid 19th Centaury : Disease Vs Sin continued
- Jellineck 1906 "Disease Concept of Alcoholism"
- 1933: American Association of Physicians first discussed Alcoholism as a Disease
- 1980-91 policies laid out
- 1991 AMA endorsed alcoholism as a medical disease and its treatment being part of legitimate medical practice.
- ICDs and DSMs

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DSM IV TR Terminologies

- Intoxication
- Withdrawals; severity/ complications
- Early/ Extended; Partial/full remission
- Related anxiety, psychosis, depression
- Specifiers: On aversive medication/ in protected environment.

DSM V: Substance Related and Addictive Disorders

- Substance Use Disorder and Related Disorder
- Impaired control(1-4), social impairment(5-7), risky use(8,9), pharmacological criteria(10-11).
- Caffeine SRD and not in SUD
- Mild(2-3) Mod(4-5) Sev(>6); Early R, Late R;
- Categories of substances have changed: DSM IV TR: AlcSedNCafAmphPhenInhAnxHypOpHal;
- DSM V AlcCafCanHalluInhOpSedStimTob ;
- Polysubstance dependence, intoxication or withdrawal category removed in DSM V.

Mechanism of Action

GABAa; GABAb

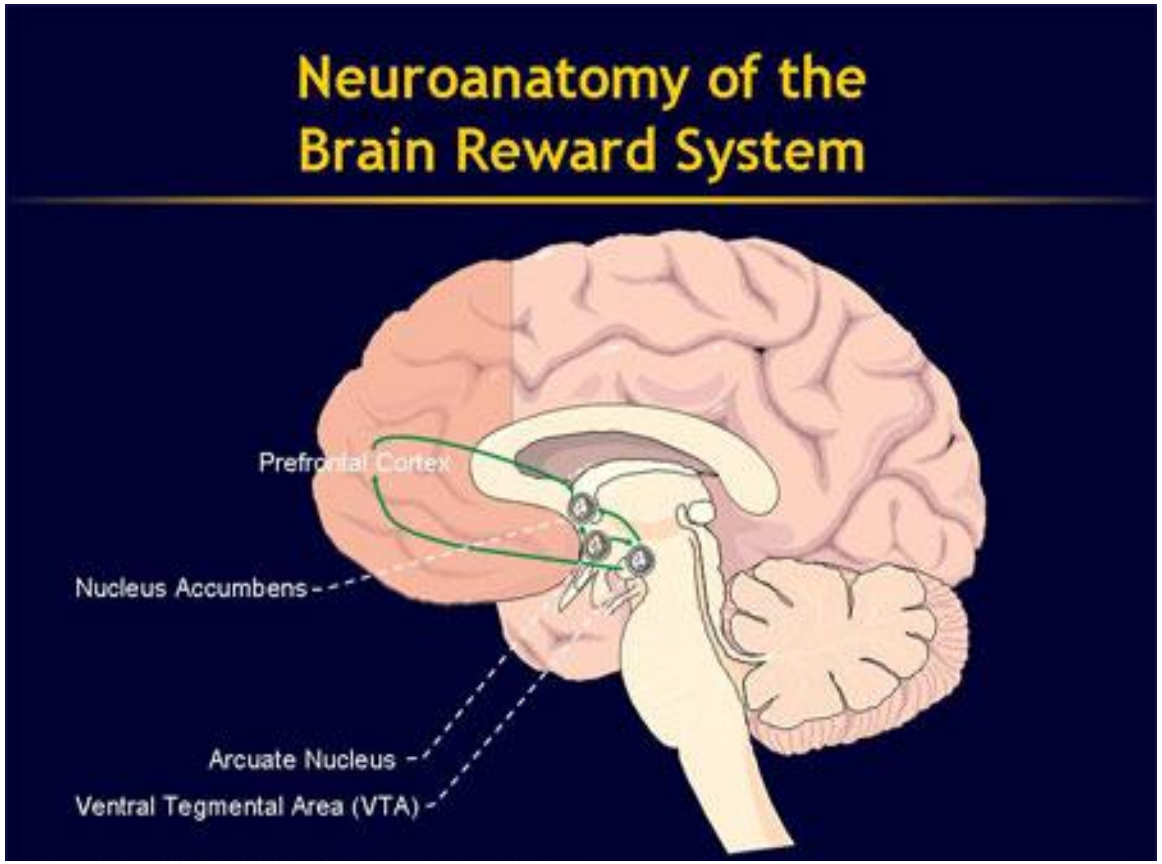
NMDA; AMPA

Mu, Delta, Kappa

D1/2/3/4

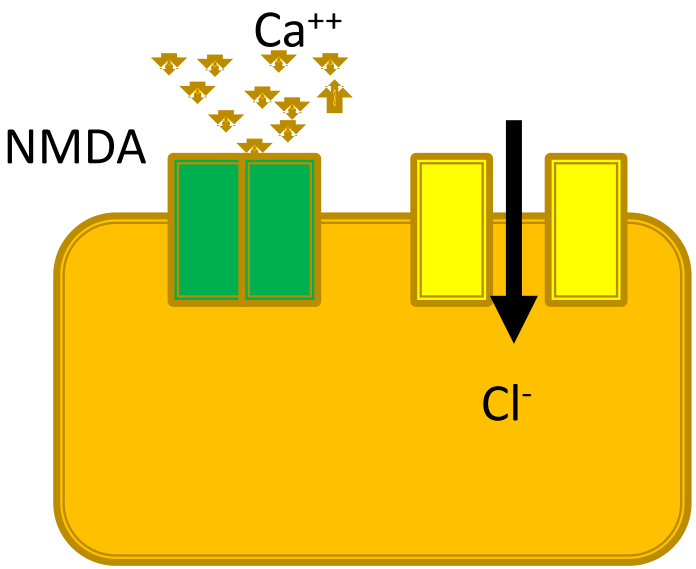
5HT3, 5HT1a

Cannabinoid

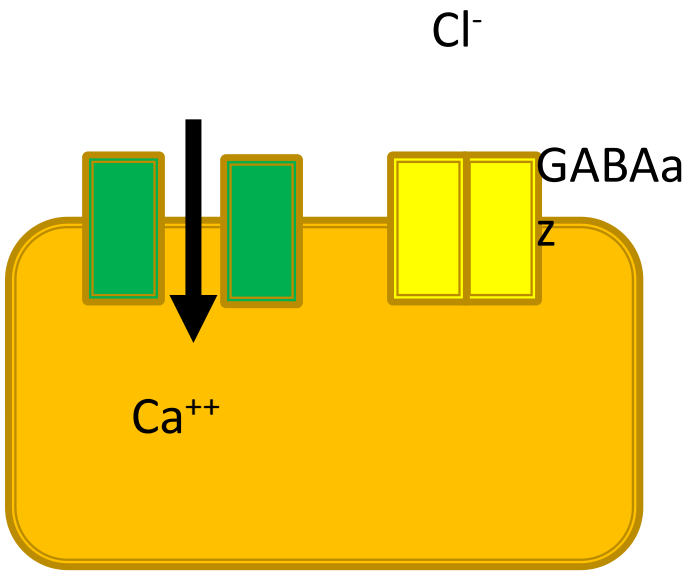


Intoxication Withdrawals

Down regulation of NMDA receptors in Intoxication and up regulation in chronic use.

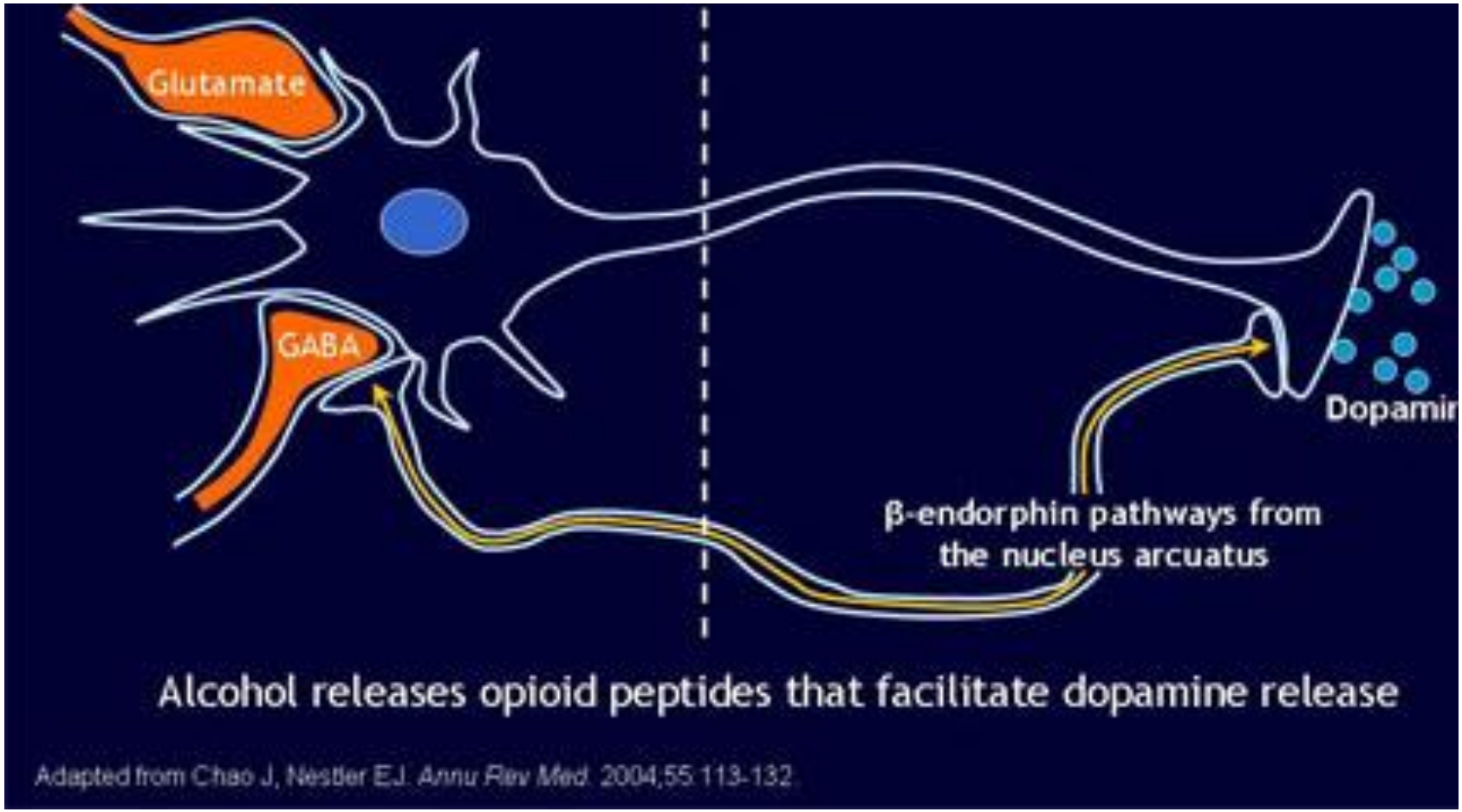


Net Inhibitory effect on the CNS

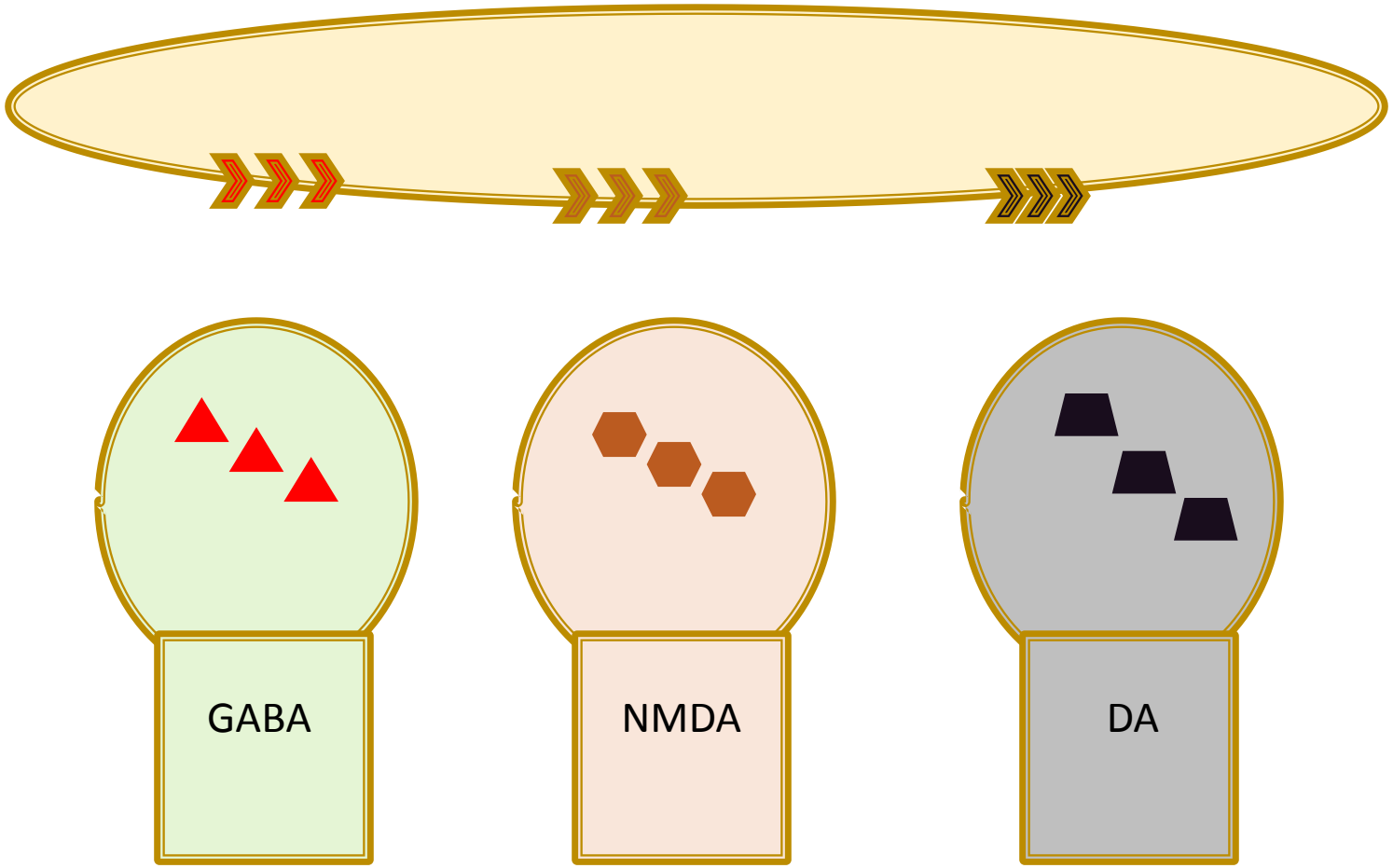


Net excitatory effect on the CNS

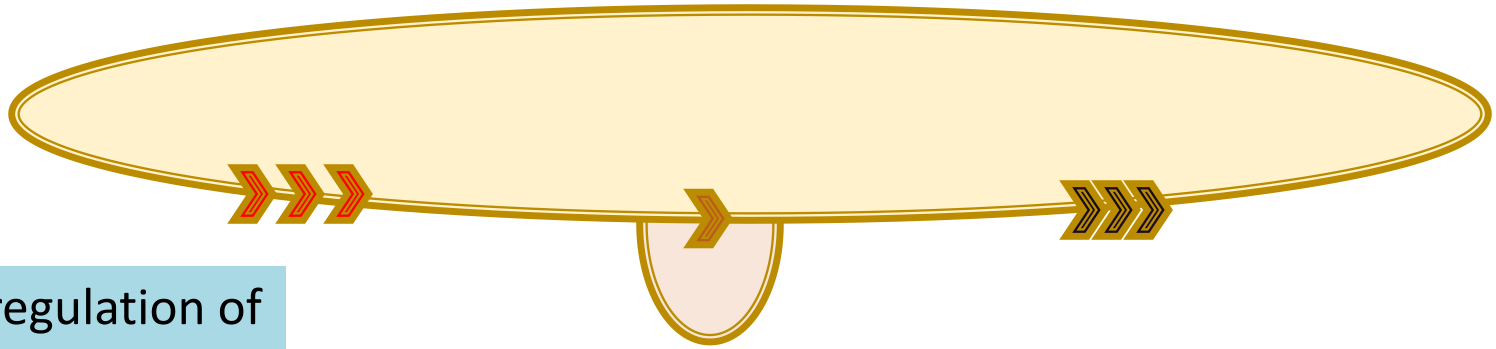
Alcohol Affects Diverse Neurotransmitter Systems



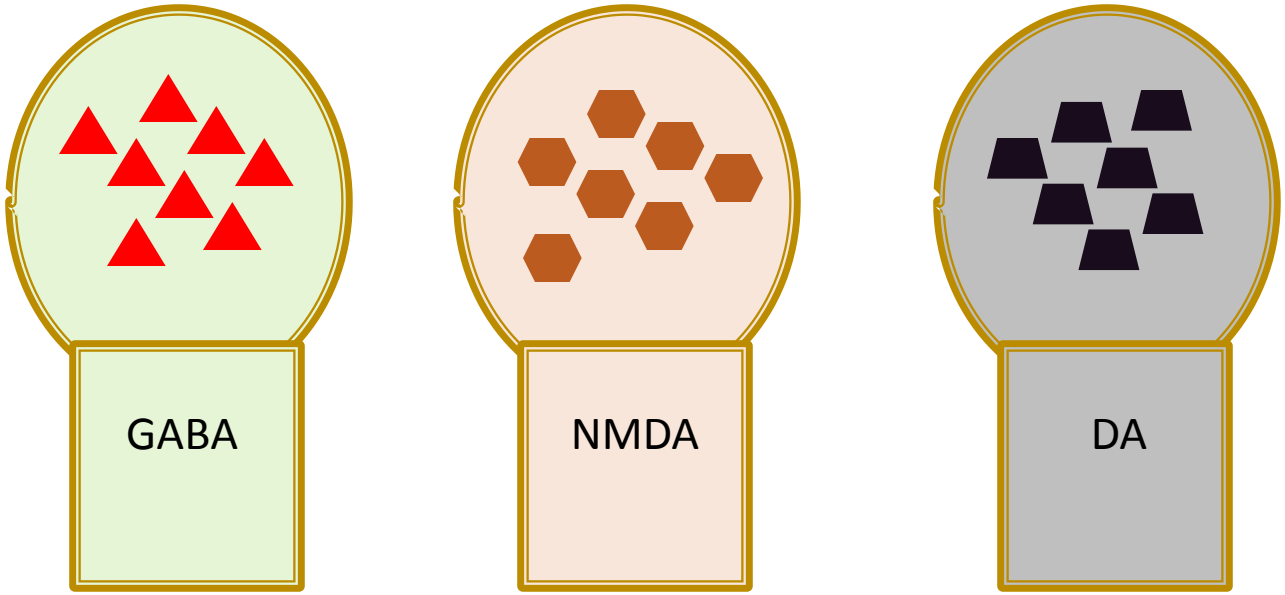
I am normal! Drama in the NA!



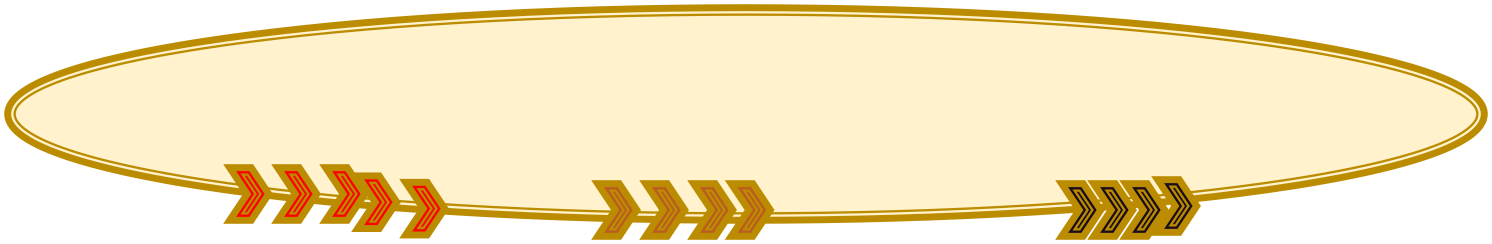
I am Intoxicated! First Act



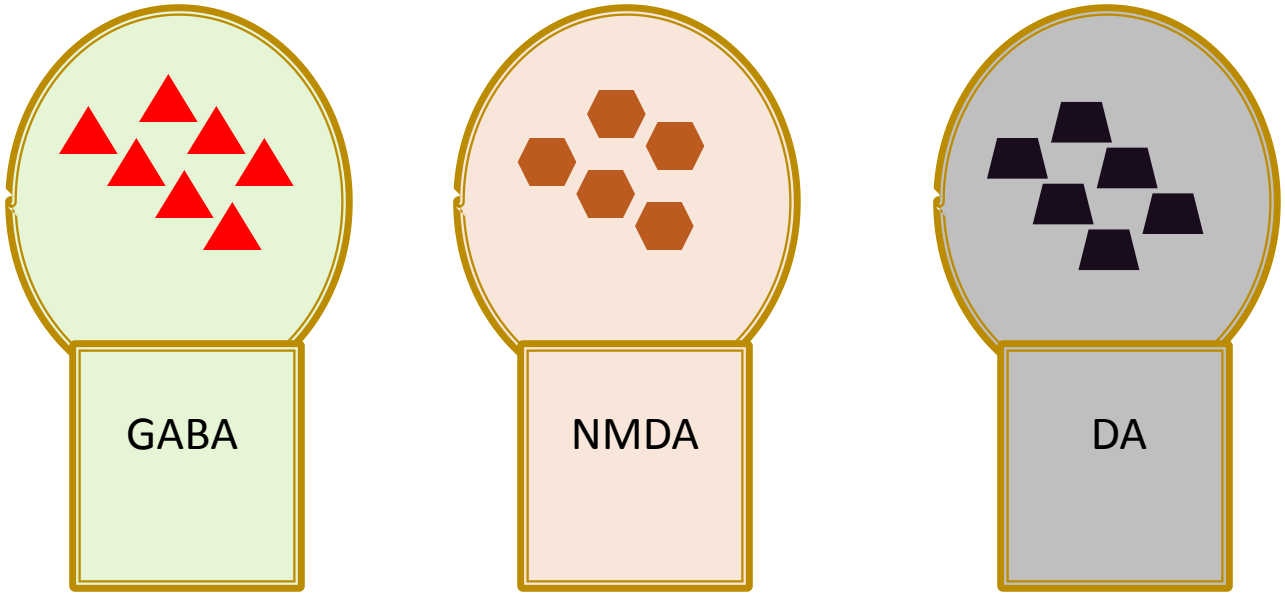
Down regulation of NMDA receptors



I am becoming dependent! Act 2

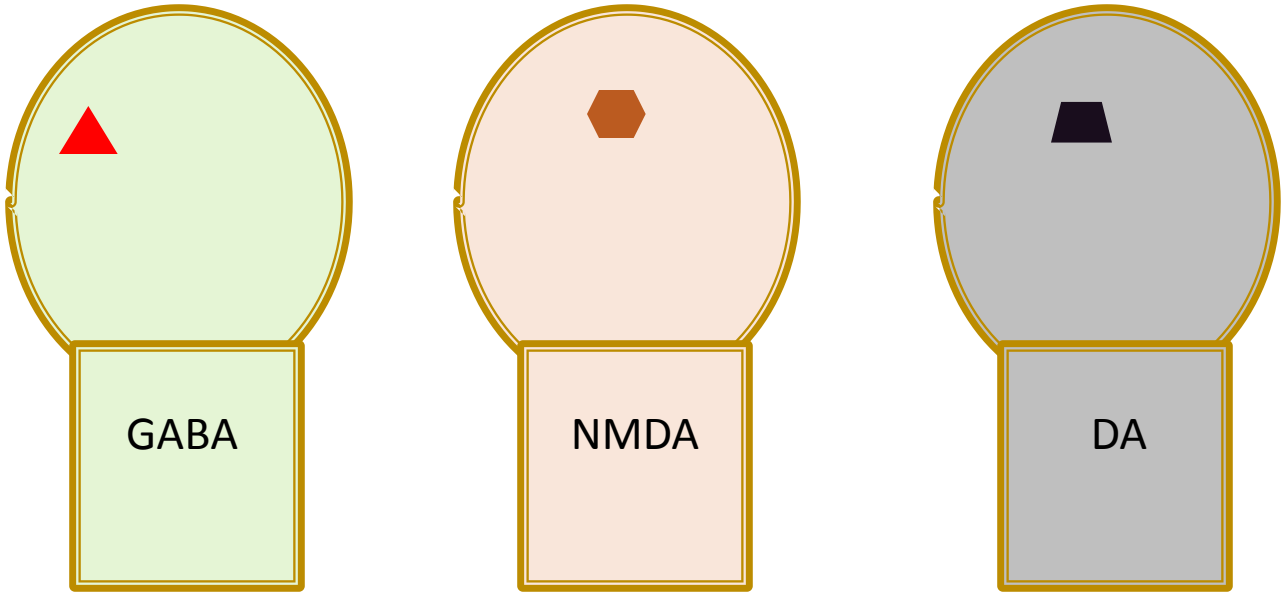


Up regulation of NMDA receptors

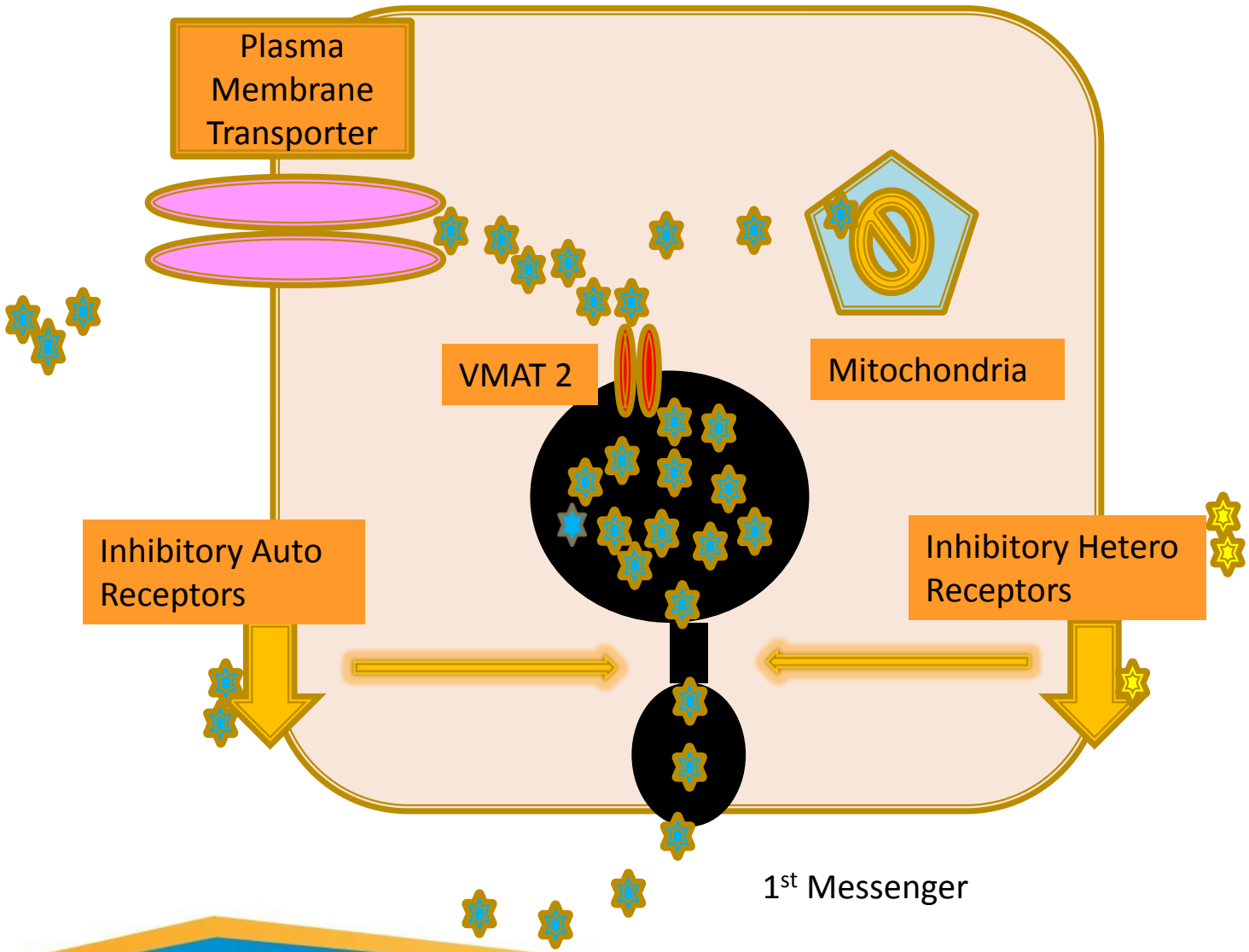


I am finally dependent! Act 3

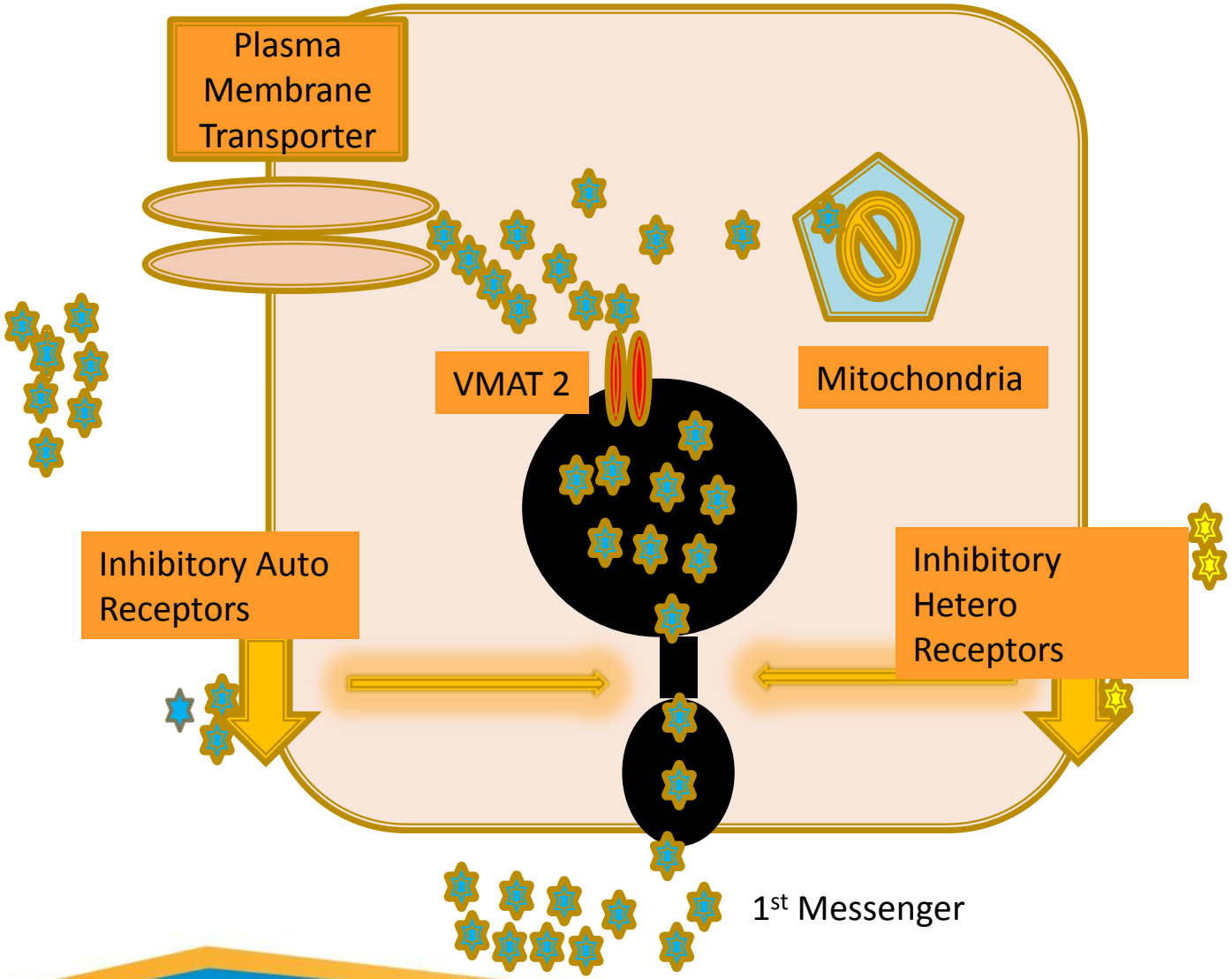
Up regulation of NMDA receptors

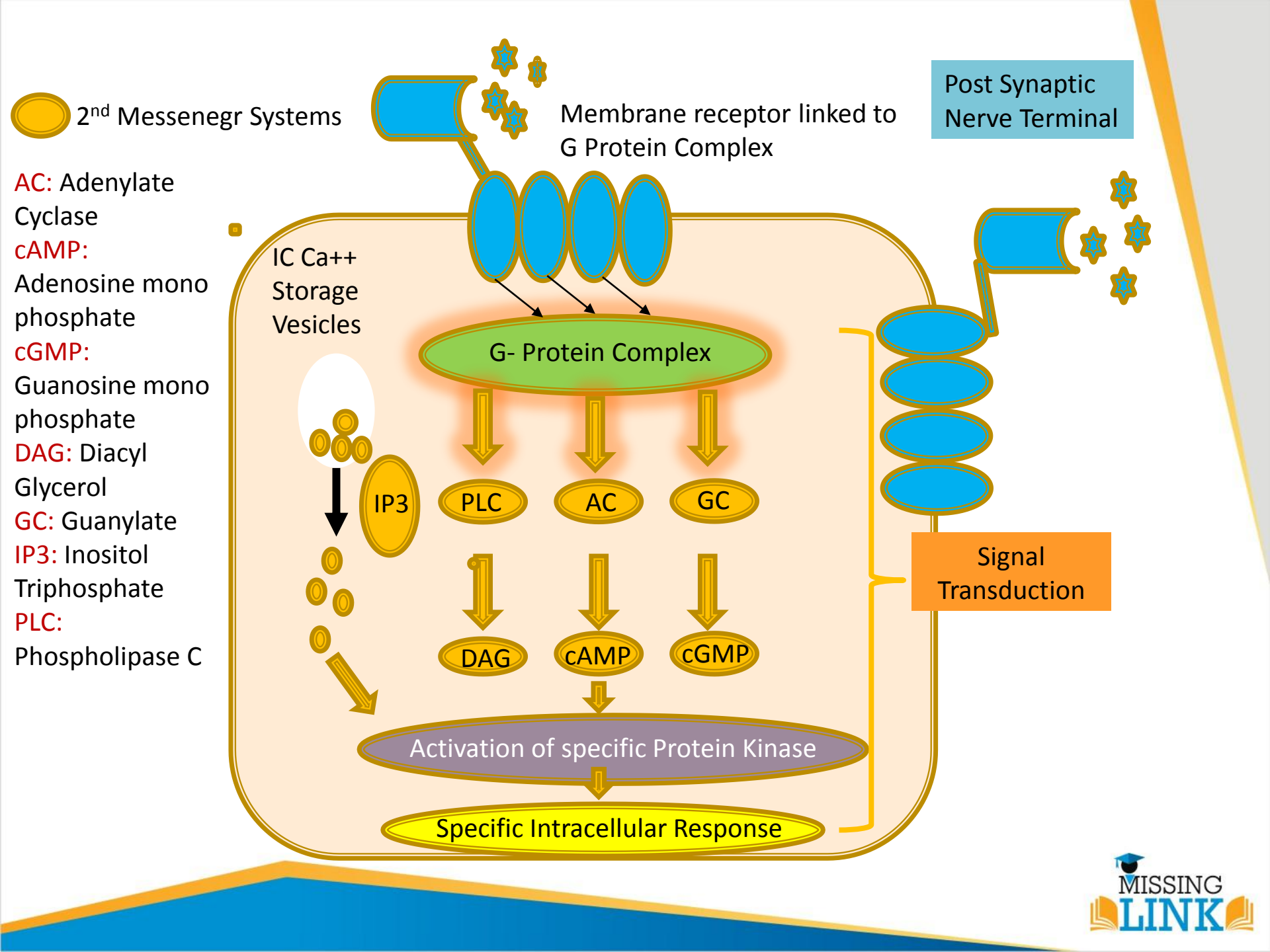


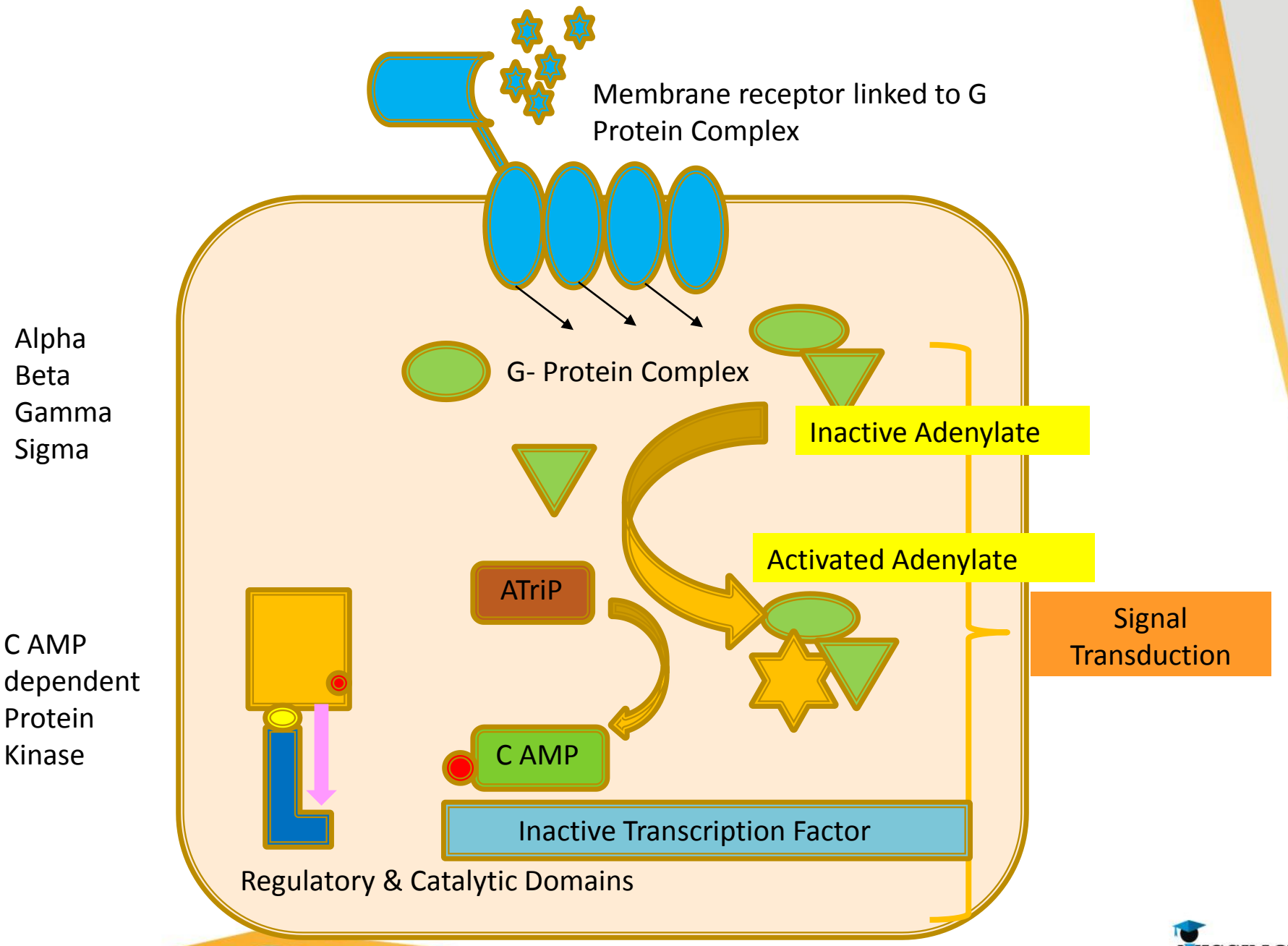
Pre Synaptic Neuronal Terminal

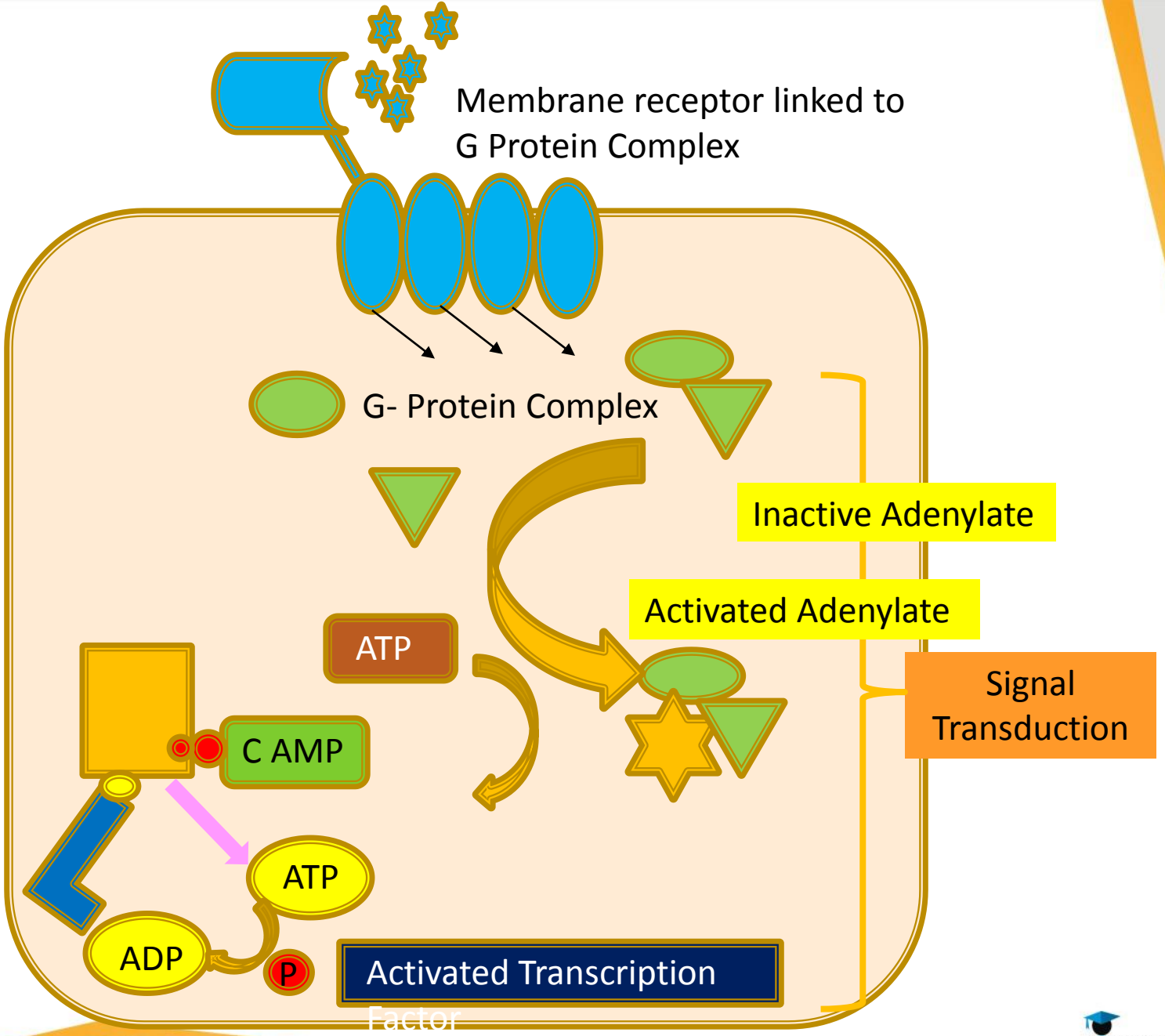


Pre Synaptic Neuronal Terminal




2nd Messenegr Systems
AC: Adenylate Cyclase
cAMP: Adenosine mono phosphate
cGMP: Guanosine mono phosphate
DAG: Diacyl Glycerol
GC: Guanylate
IP3: Inositol Triphosphate
PLC: Phospholipase C
Membrane receptor linked to G Protein Complex
Post Synaptic Nerve Terminal
IC Ca++ Storage Vesicles
G- Protein Complex
IP3
PLC
AC
GC
DAG
cAMP
cGMP
Signal Transduction
Activation of specific Protein Kinase
Specific Intracellular Response


Membrane receptor linked to G Protein Complex
Alpha
Beta
Gamma
Sigma
G- Protein Complex
Inactive Adenylate
Activated Adenylate
ATriP
Signal Transduction
C AMP dependent Protein Kinase
C AMP
Inactive Transcription Factor
Regulatory & Catalytic Domains


Membrane receptor linked to
G Protein Complex
Alpha
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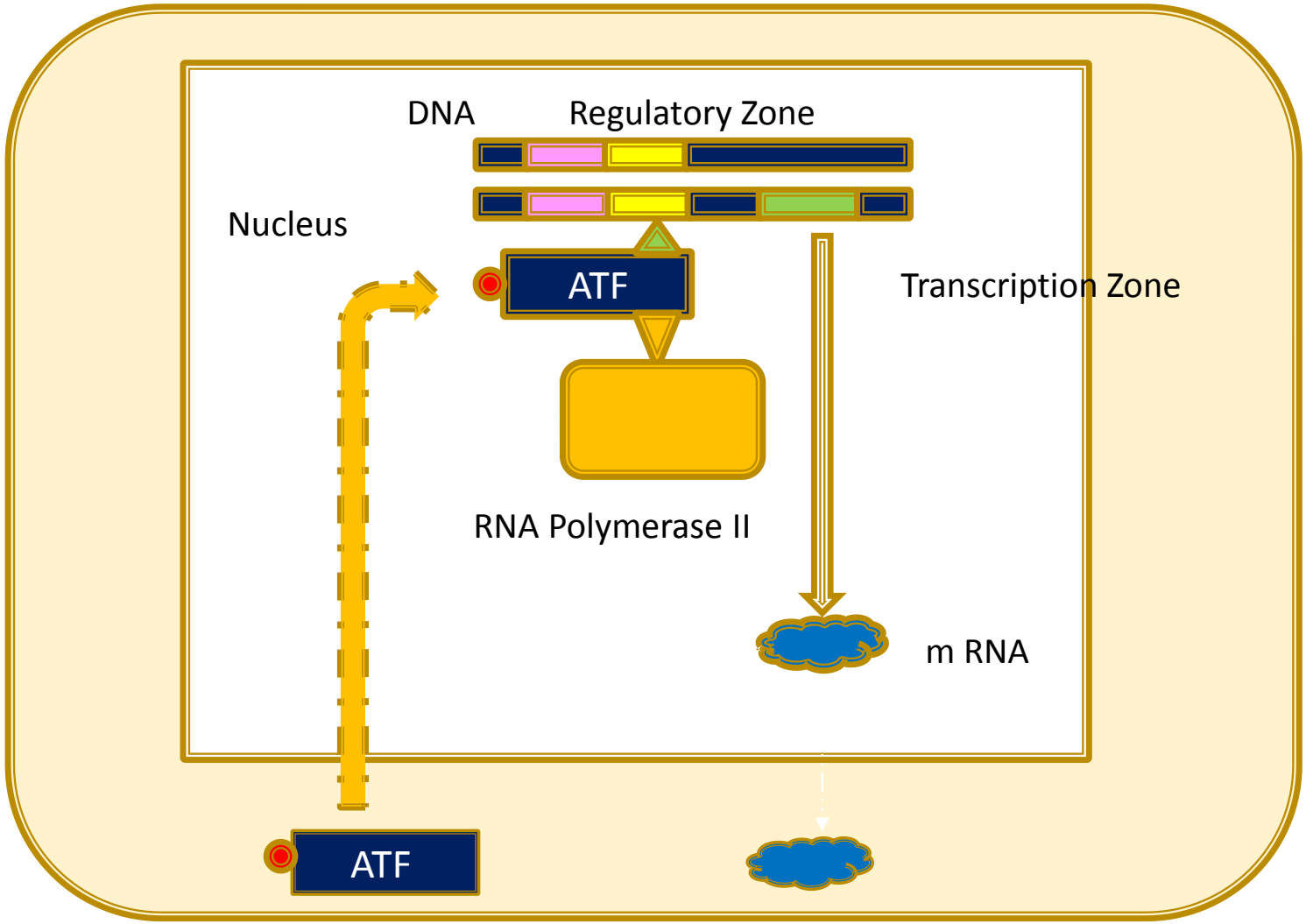
G- Protein Complex
Inactive Adenylate
Activated Adenylate
ATP
Signal
Transduction
C AMP
dependent
Protein
Kinase
C AMP
ATP
ADP
P
Activated Transcription
Factor

Post Synaptic Neuron Nucleus

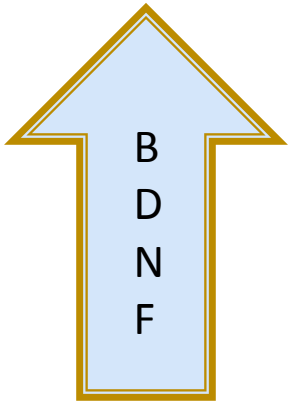


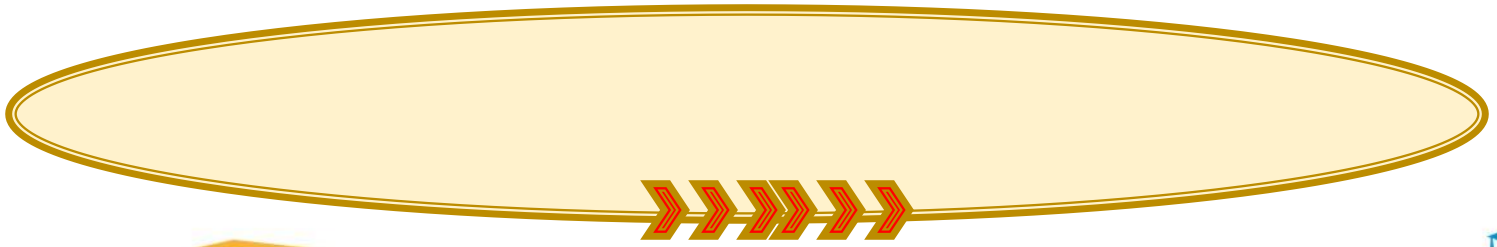
Activation of G-Protein Complex

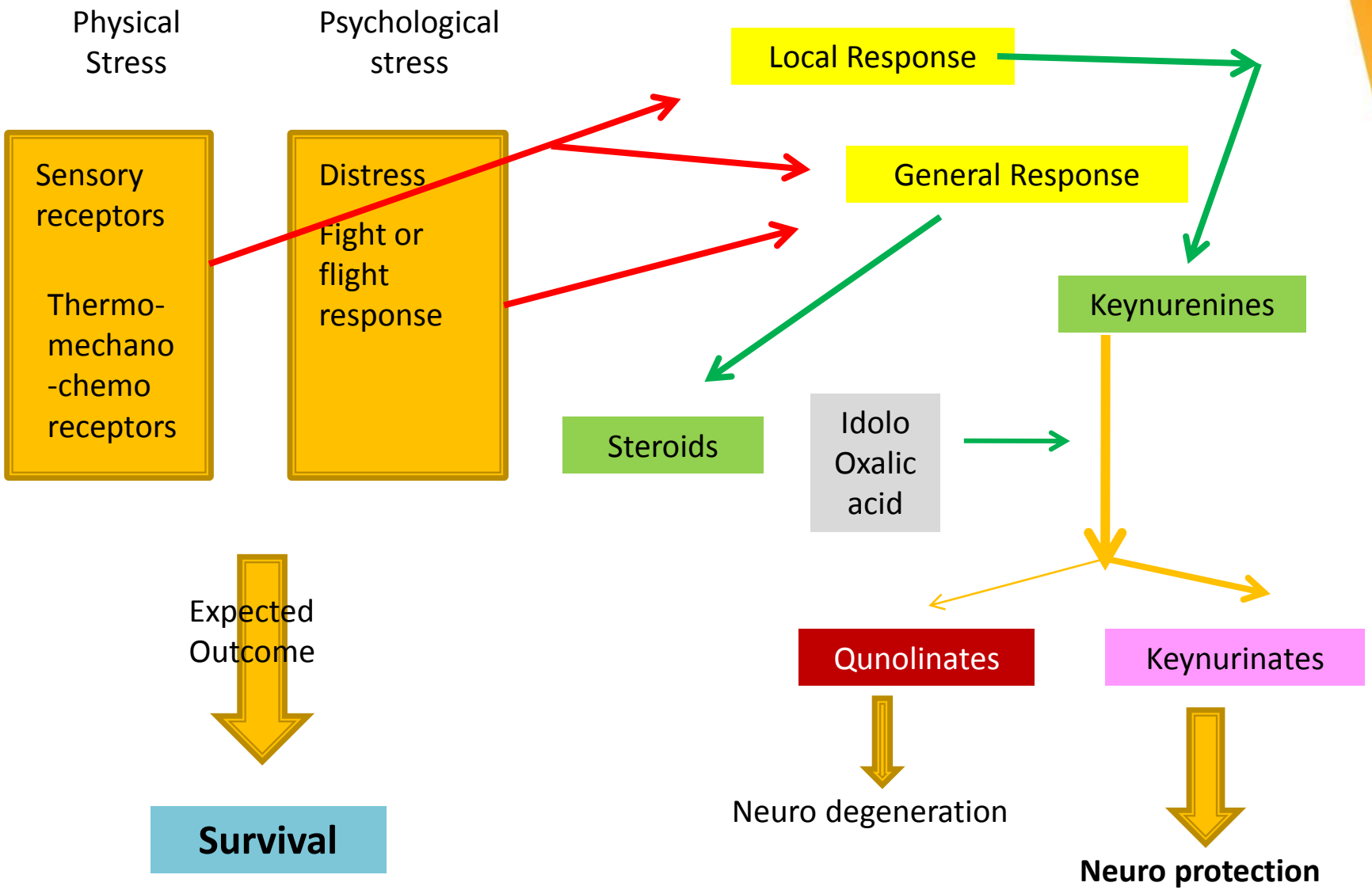
- Disintegration of alpha, beta, gamma and ‘S’ units of G- protein.
- De-phosphorylation of Adenosine tri phosphate to C-AMP that activates Protein Kinase.
- C-AMP dependent PK when attached with C-AMP, dephosphorylates ATP to ADP, resultant free P, phosphorylates the Trasncription Factor that can alter cell differentiation, cell metabolism, cell membrane properties, gene responses.
- Activated Transcription factor enters the nucleus, attaches with the regulatory element of the DNA, leading to exposure of the transcribed region, and formation of specific mRNA in the nucleus. Protein synthesis.
- Change of gene expression.

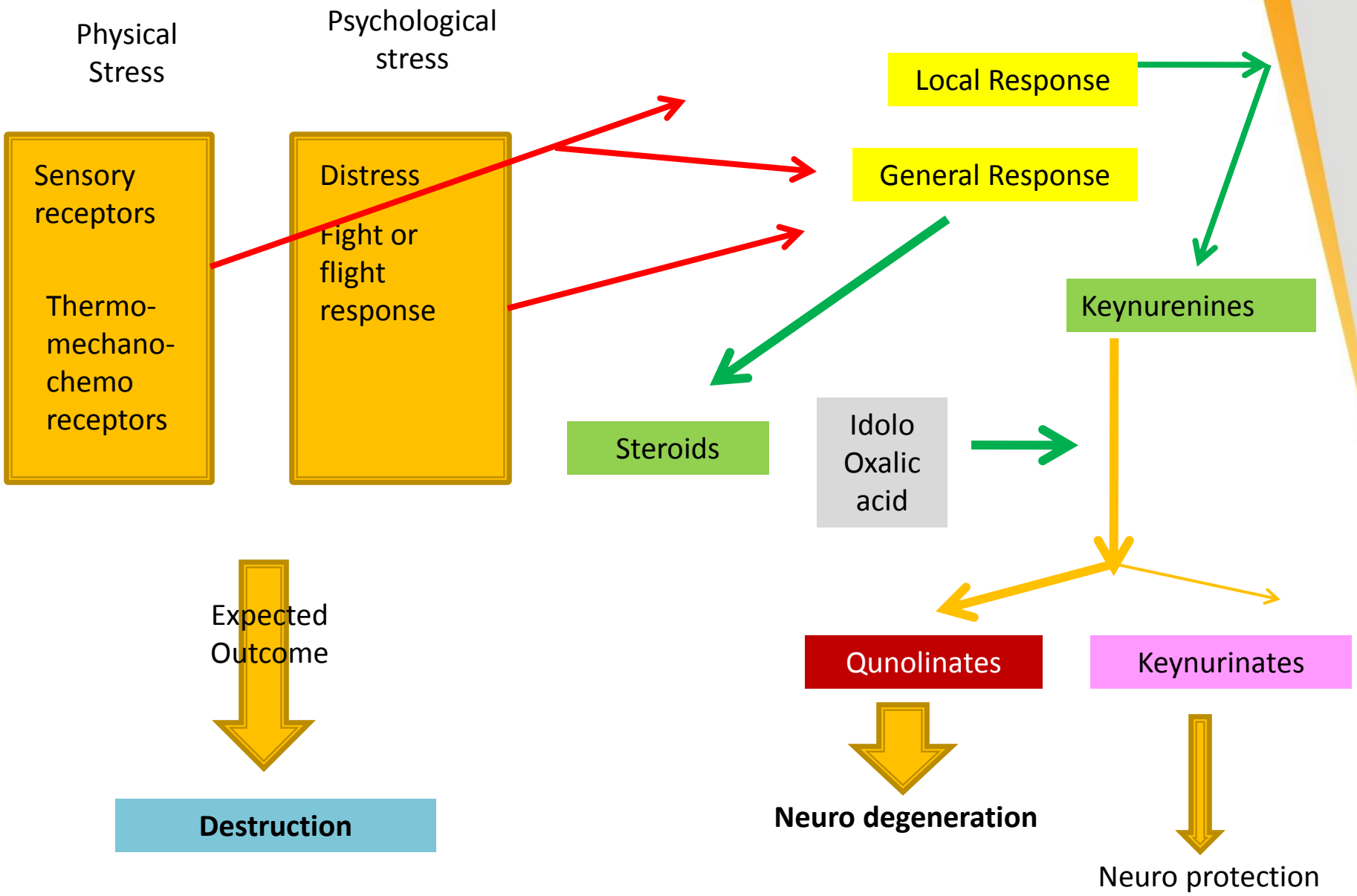
Normal Signal Transduction

Mesolimbic Paths
Meso Cortical Paths
Temptation-Reward circuits
Basal Ganglia
Prefrontal Cortex
Hypothalamo-Pituitary Axis






Physical Stress
Psychological stress
Local Response
Sensory receptors
Thermo-mechano-chemo receptors
Distress
Fight or flight response
General Response
Keynurenines
Steroids
Idolo Oxalic acid
Expected Outcome
Survival
Qunolinates
Keynurinates
Neuro degeneration
Neuro protection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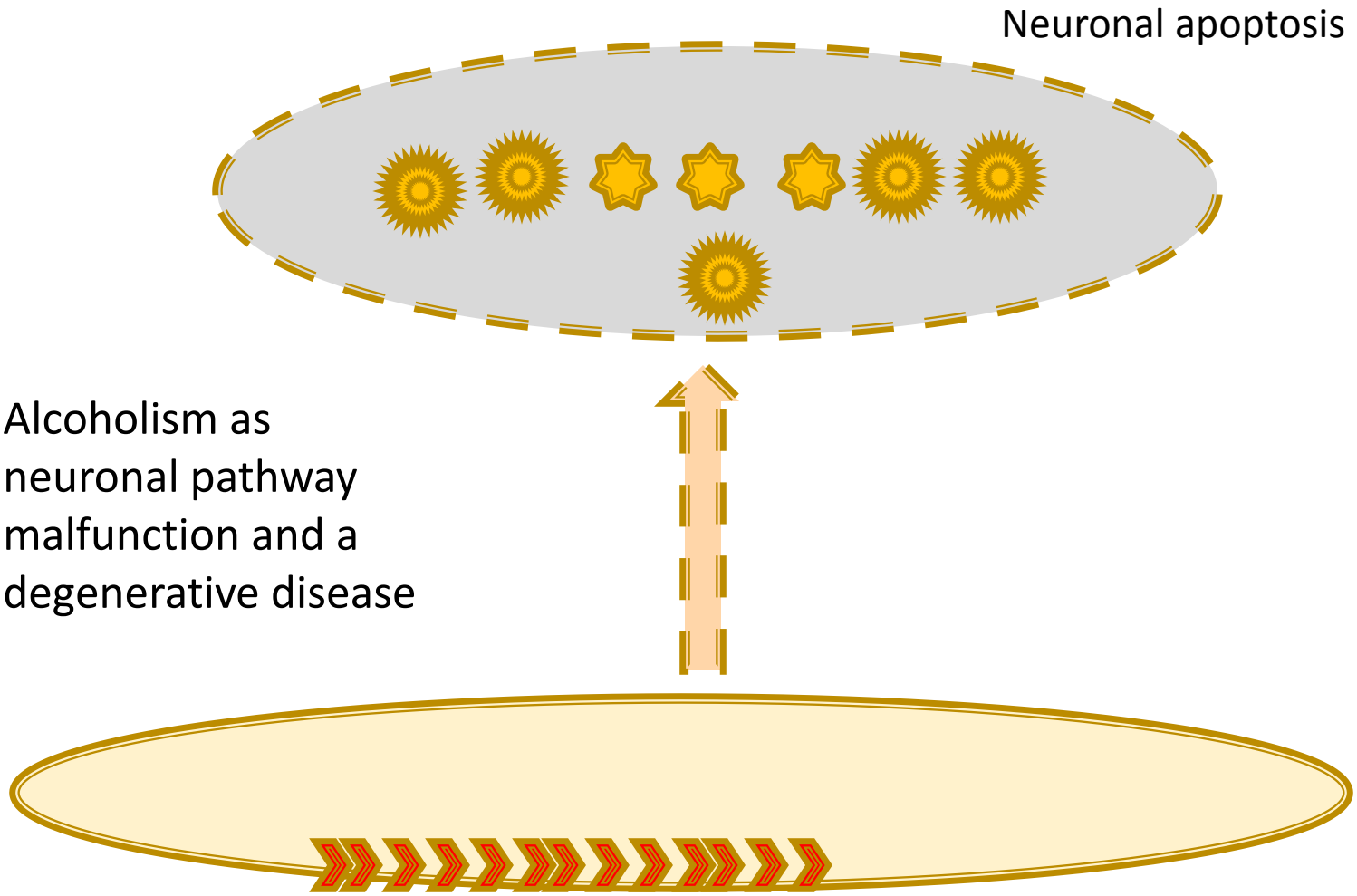
Local Response
General Response
Keynurenines
Steroids
Idolo Oxalic acid
Expected Outcome
Destruction
Qunolinates
Keynurinates
Neuro degeneration
Neuro protection

Alcohol interfering with Stress Response

- Corticotrophin Releasing Factor: CRF: High CRF in amygdala during withdrawals; CRF antagonists block anxiety during withdrawals. (High CRF→High Angst→ high drinking.
- Neuropeptide Y (NPY): High NPY→low alcohol self administration; low NPY→ high anxiety→ increased alcohol consumption

Flawed Signal transduction



Genetics of Alcohol Dependence

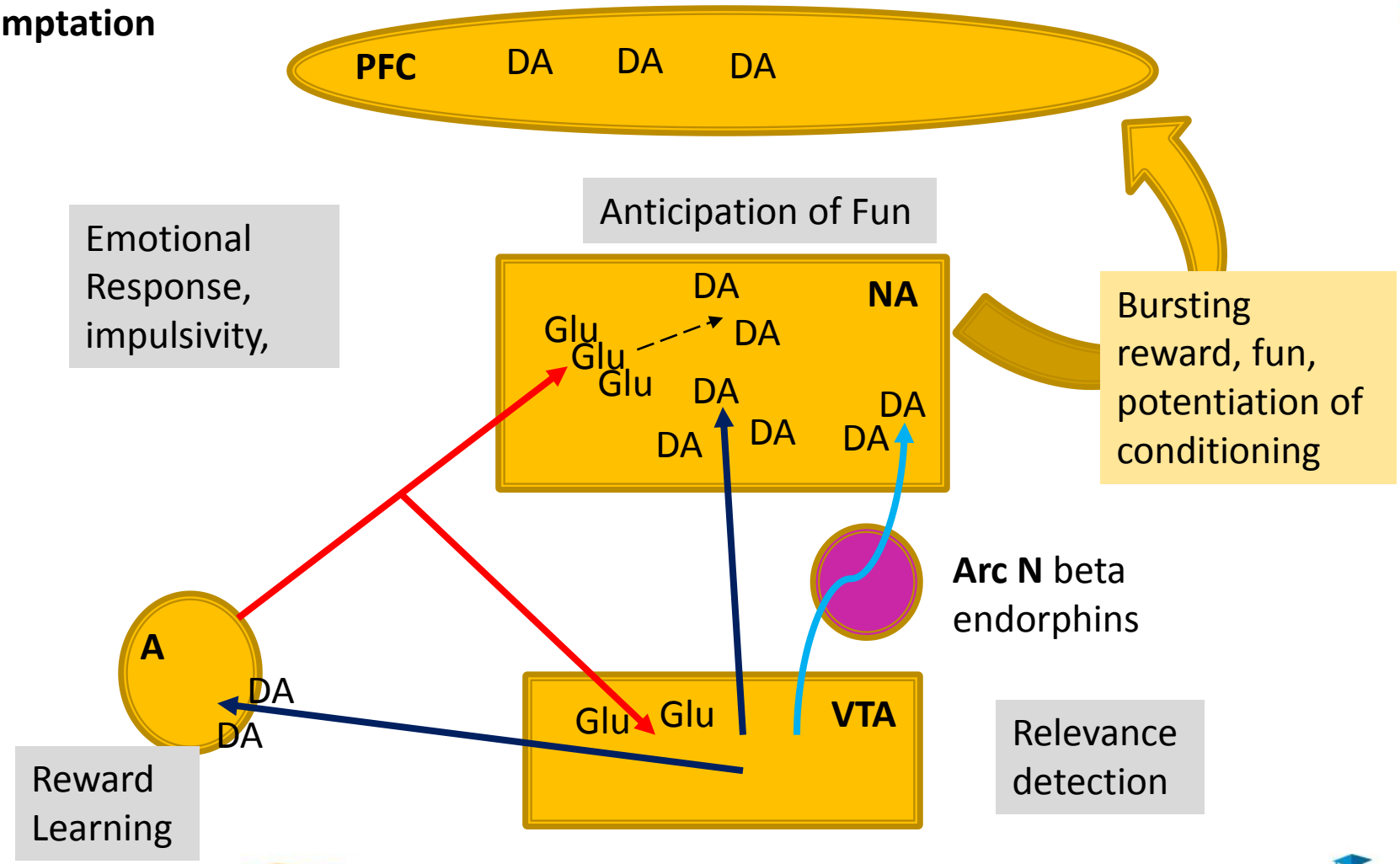
- Heritability rate of 50%-65%
- Social attitudes interplay of 40-50%
- Specific Polymorphisms associated: GABRG3; NPY geneLeu7Pro; 5HT-transporter; A118G PM (G-variant) of OPRM1 gene; D4 rec variable number tandem repeats (DRD4 VNTR) PM
- HLA- 28 A offers some protection from ALD

Reflections in Families

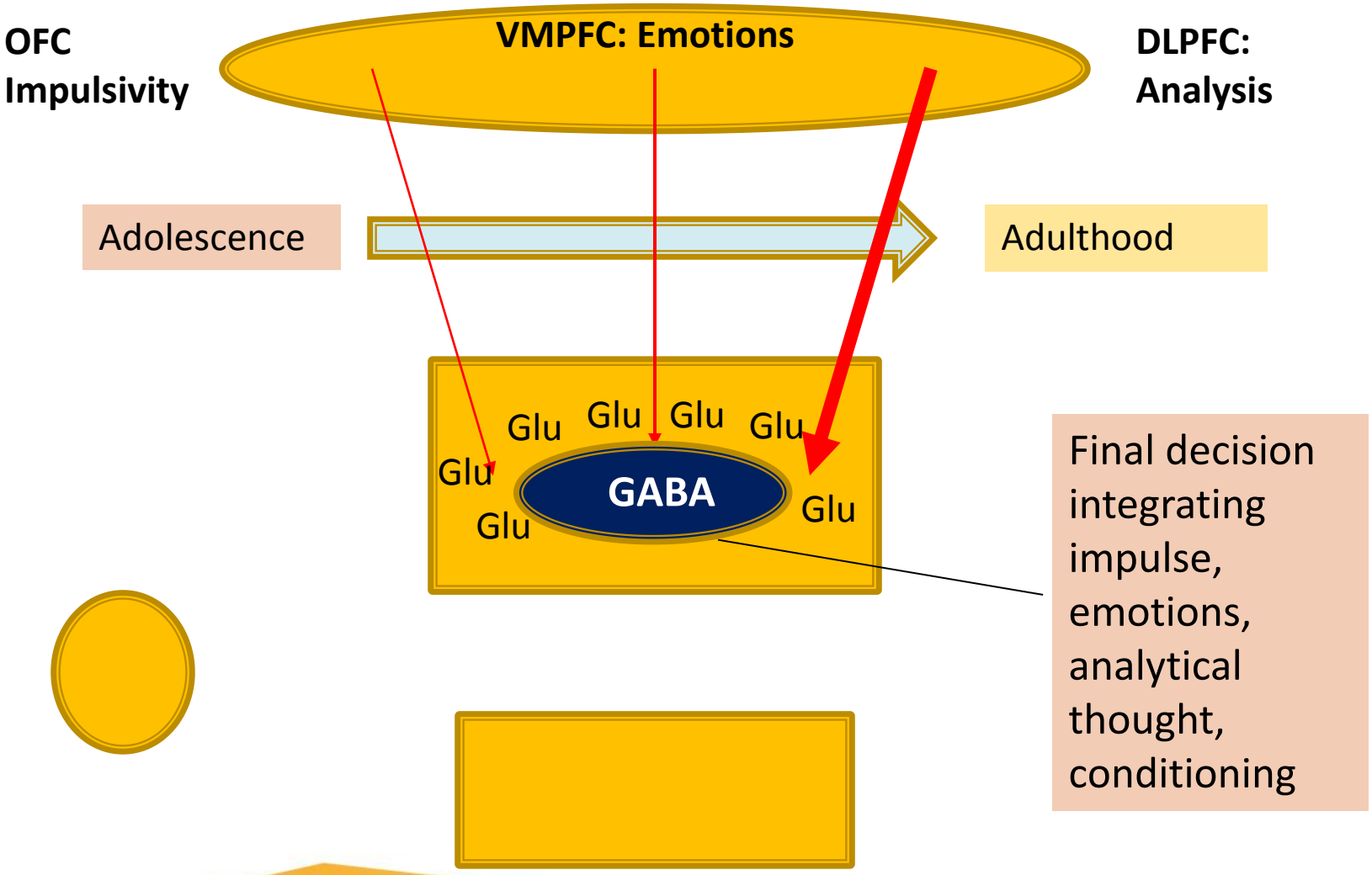
- Relatives of alcoholics have 3-5 times increased risk
- Biological parents vs Adoptive parents
- Identical twins adopted into alcoholic families do not show increased risk. Vice versa true.
- Alcoholism, Bipolar Disorder, Suicide run in families.

Temptation, Reward & Motivation

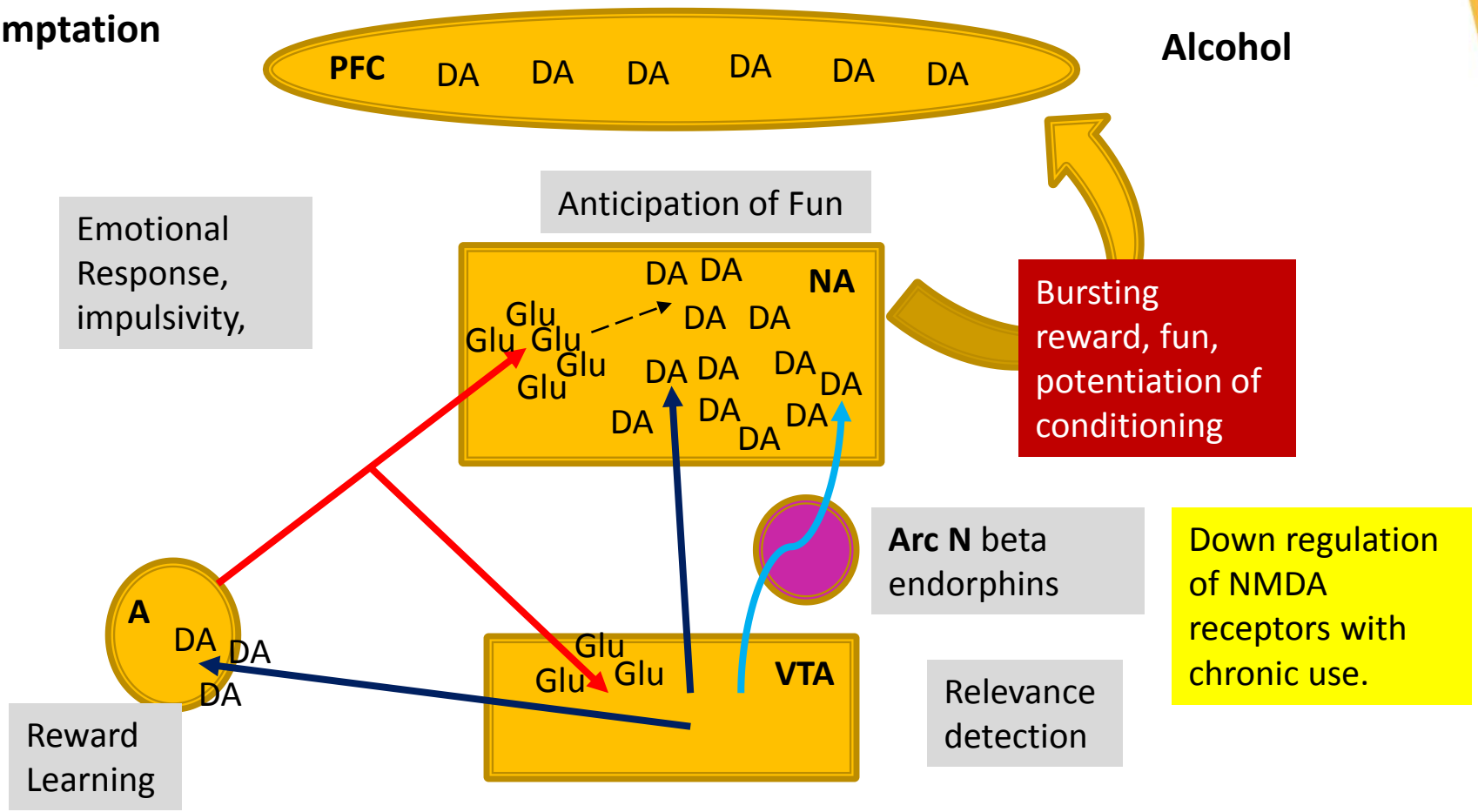
Temptation



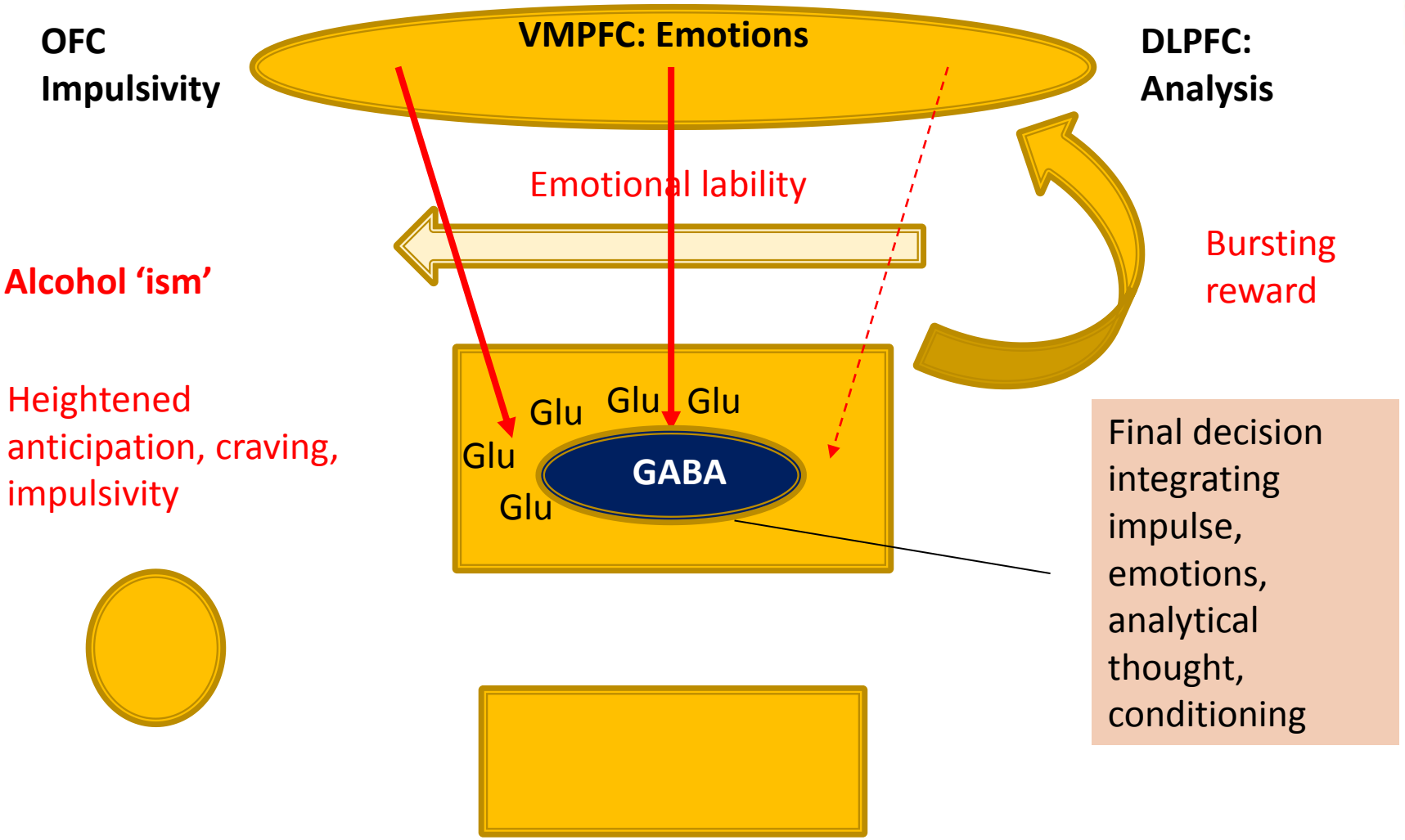
Mechanisms of Dependence 3



Mechanisms of Dependence 2



Mechanisms of Dependence 4



Types of Alcoholics: Moss et al.

- **Young Antisocial Type** 21%: Avg age 26, 50% of them would have ASPD, age of onset 15, pattern by 18, co-consumption of tobacco, pot.
- **Functional 19%:** middle aged, working. Stable relationships, financially better, educated.
- **Intermediate familial type** 18%: 50% have family history, first drink at 17, disease by 30.
- **Chronic severe type** 9%: Men, social deterioration more, illicit drug use more.
- **Young adult**: 32%: Disease at 20, More of binge drinking.

Biomarkers in Alcohol Use and Abuse: State Markers

Marker	Sensitivity	Specificity	Use	Availability
GGT	61	Data not available	Chr Alc Abuse	Y Y
ALT	Method dep	DNAvailable	Chr Alc Abuse	Y Y
AST	56	DNAvailable	Chr Alc Abuse	Y Y
Carb Deficient transferrin	26-83	92	Heavy Alc Use	Y Y
N-acetyl-beta hexosaminidase	94	91	Heavy Alc Use	N N
Whole Bld associated acetaldehyde	100	95	Recent alcohol	Y N

State Markers contd

Marker	Sensitivity	Specificity	Use	Availability	
MCV	47	Data not available	Heavy Alc Use	Y	Y
Apolipoprotein J	DNAvail	DNAvail	Heavy Alc Use	N	N
5-Hydroxytryptophol	DNAvail	DNAvail	Recent alc Use	N	
Salsolinol	DNAvail	DNAvail	Chr Alc Use	N	
Fatty Acid Ethyl Esters	100	90	Recent heavy use	N	
Ethyl glucuronides	DNAvail	Method dependent	Recent alc use	N	

Trait Markers

- Proteomics: Study of proteins that are matched to certain genes. Fragment of **Fibrinogen alpha E chain and apoprotein A-II** levels low in alcoholics; increase one week after sobriety.
- Carried from generation to generation; associated with the disease, not associated with the state of disease.

Trait Markers

- Adenylate Cyclase Activity: Less in platelets of sober alcoholics; increases when in relapse.
- GABA: Lower levels in alcoholics than controls
- Dopamine: Withdrawals increased DA levels; extended remission DA gradually decrease. Not dependable
- Beta endorphins: Alc have lower levels than controls, children have lower number of receptors.
- Serotonin: Lower Serotonin in alc; Alc in remission higher SERT activity in platelets; children too have higher SERT activity.

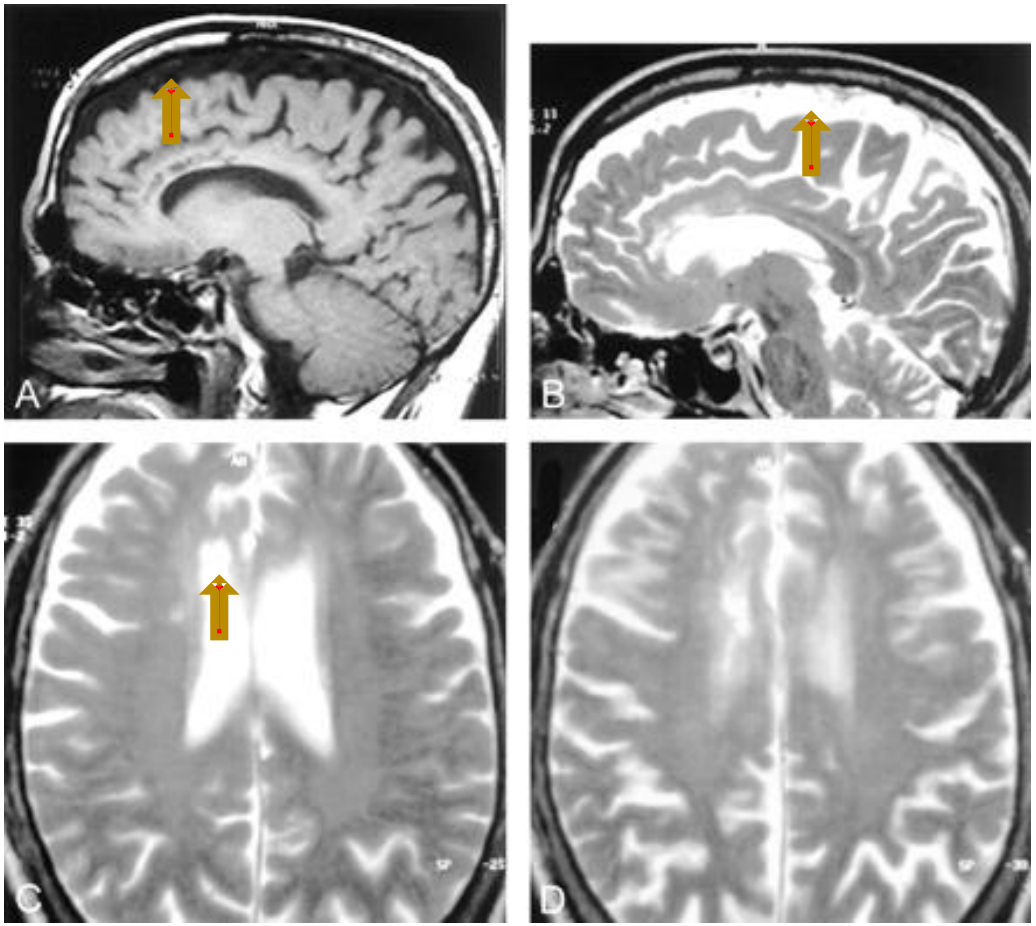
Organic Conditions with Alcoholism

- Head injuries: SDHs, Concussions, Lacerative injuries, Contre le Coup injuries etc
- CVAs: IC haemorrhages.
- Optic nerve atrophy, central pontine myelinosis
- Dementia: Nutritional/ vascular/ mixed; generalized atrophy.
- Wernicke's Encephalitis: A, O, N, C, B1, Contrast enhancement in Mammillary bodies, periaqueduatal regions and walls of 3^{rd} ventricle;
- Korsakoff's Psychosis: PolyNeuthy, Confabuln, hallucinations

Marchiafava Bignami Disease

- Marchiafava-Bignami Disease: **Acute**: C, Disor, NeuCog, Seiz; **Sub acute**:Dem, Dysarthria, Hypertonia; **Chronic**: Chronic dementia; MB disease is a primary degeneration of the **corpus callosum** (body, genu & the splenium involved sparing the subcortical U fibres) associated with chronic alcohol consumption but is occasionally seen in nonalcoholic patients. Mainly due to a deficiency in the vitamin B complex.

Marchiafava-Bignami Disease



A: T1 weighted : decreased intensity in genu and anterior aspect of Corpus Callosum

B: T2 weighted: Hyperintense lesions in the ant portions of CC

C: Periventricular hyperintense lesions around the frontal horns

D: Periventricular hyperintensities.

Whom to treat?

- Egodystonic vs egosyntonic alcoholism
- Self harm vs harm to the society
- Self request vs family request
- Solitary alcoholism vs dual disorder
- Alcoholism vs its complications
- Individual (mind and body) vs family

How to treat?

- What is treatment?
- Sobriety and recovery
- Bio-psycho-social model of disease and treatment.
- Assessment of recovery.
- Importance of social and work laws for treatment of alcohol.

Steps in treatment

- Motivational stage based intervention.
- Early engagement in therapy.
- Induce motivation promotion
- Role of controlled drinking
- Detoxification
- Pharmacological intervention
- **Supportive and restructuring psychotherapy.**

Pre-detoxification intervention

- Pre-contemplation and contemplation stage of motivation
- Rapport building
- Engagement therapy
- Group or individual intervention.
- Role of Alcoholics Anonymous
- Medical support for biological damage

Dos

- Learn all you can about alcoholism.
- Talk to the care givers.
- Speak up and offer your support.
- Express love, concern and support.
- Don’t expect a person to stop without help.
- Support recovery as an ongoing process.
- For an unwilling patient, be patient. Record destructive behaviour.
- Know more about Al Anon groups.

Don’ts

- Don’t preach.
- Don’t be a martyr: Emotional appeals increase guilt and add to compulsive drinking.
- Don’t cover up.
- Don’t take responsibility or help them out of their ill deeds.
- Don’t argue when using
- Don’t feel guilty.
- Don’t join them.

Detoxification

- Residential, community based or hospital based.
- Chlordizepoxide 15mg= oxazepam 15mg= 5mg diazepam.
- Role of anticonvulsants (carbamazepine)
- Role of FGAs.
- Thiamine and vitamin B complex, C.

Chlordiazepoxide replacement therapy

- About 4 hrs after last drink; breathalyzers showing dropping levels.
- 3 hourly Clinical Alcohol Withdrawal Rating Scale
- Loading dose 5mgs to 50 mgms
- Baseline day dose: two hourly prn basis based on CAWRS. Max. 250mgms.
- 20% daily reduction

Special cases

- Liver damage: Oxazepam, lorazepam
- DT: NBM, TPR, BP 2 hourly, M/C urine, IVF, Inj. Thiamine, nutritional support, IV diazepam upto 100mgms in an ICU set up, Vit C IV, Carbamazepines, Acamprosate, electrolyte and sugar correction.
- Wernicke's encephalopathy: High dose injection thiamine (600 mg/day for 2 days) therapy.
- Hallucinosis: High dose BZ, rare cases FGAs.

Goals of treatment

- Engagement, Focusing, Evoking, Planning
- Empathize, Articulate discrepancy, avoid argument, role with resistance, support self sufficiency.
- Groups: engage, create member perspective and group perspective, build momentum, action.
- Education, reality/ insight orientation
- Family education (Al Anon)
- Introduction to Alcoholics Anonymous
- Continuation of nutritional support.

Extending Sobriety

- Supportive psychotherapy
- Restructuring psychotherapy
- Reconstructive psychotherapy
- Pharmacotherapy
- Group therapy
- Rehabilitation

Supportive psychotherapy

- Individual counseling: health, wealth, family, legal, work related, any other.
- Family counseling: EE, positive support & “enabling(Criticism, hostility, Over Involvement, intrusive attitude) belief systems, unresolved IP issues, Maladjusted behaviours, Substance Use; co-dependence(Preoccupation with Patient’s drinking, set of controlling behaviours, used to reciprocating benefits)”, disease education.
- Introduction to support groups.
- Counseling on short term and long term goals.
- AA and Al Anon call.

Restructuring Psychotherapy

- Personality assessment and alcohol as a coping mechanism.
- Cognitive distortion charting, analysis and basic counseling on help seeking behaviours.
- Family counseling: Enabling and help seeking behaviours, positive and negative support, Al Anon.
- Assessment for dual disorders.

Reconstructive Psychotherapy

- Established dual disorder diagnosis
- Early age alcoholism
- Gross personality change
- Absence of social/ vocational skills.
- Multi specialty help and educational support
- Long term rehabilitation effort.

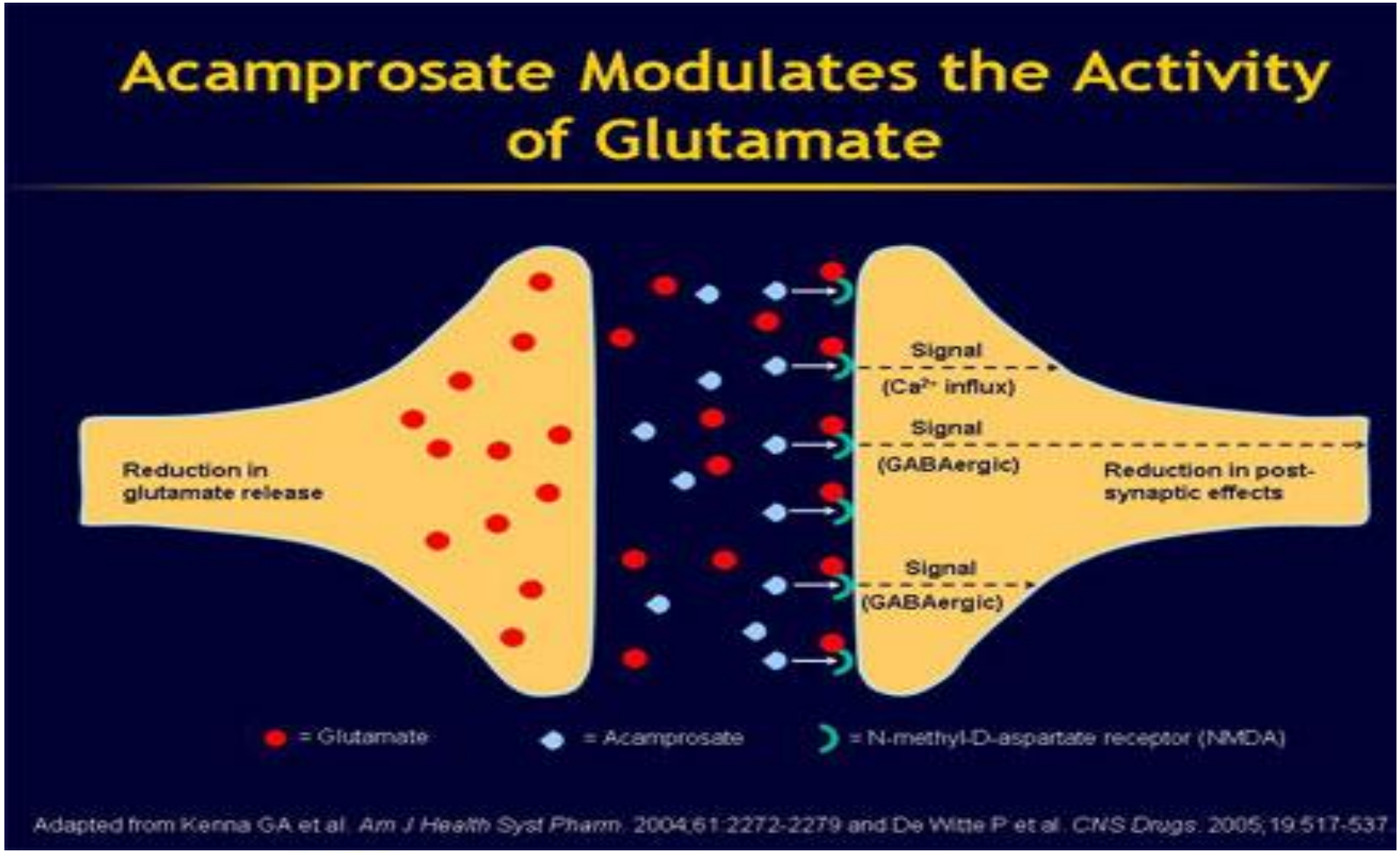
Pharmacotherapy

- Acamprosate,
- Baclofen,
- Naltrexon.
- SSRIs, Topiramate, APDs
- Disulfiram

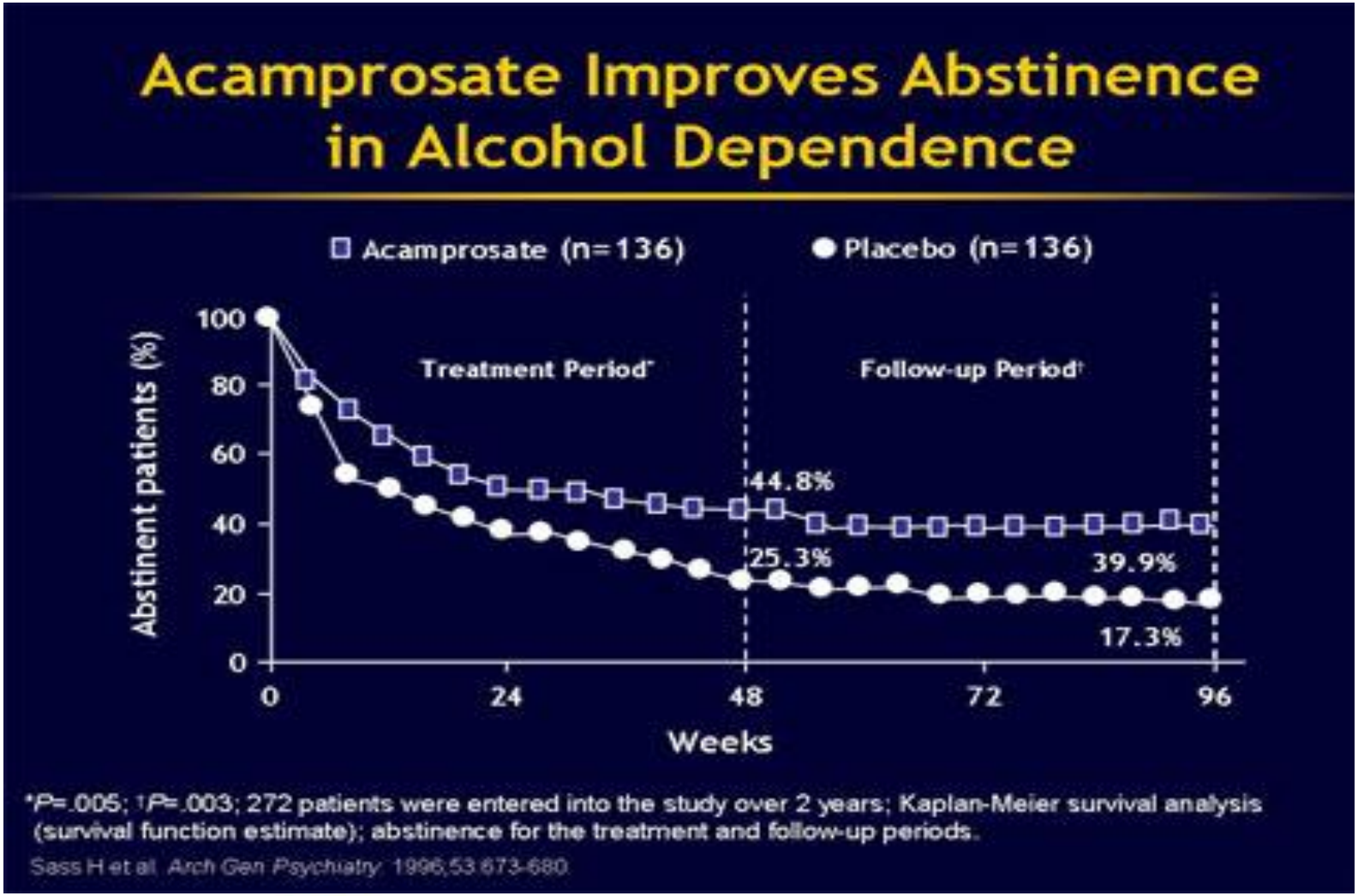
Acamprosate

- Glutamate and GABA-A receptor action
- Blocks the reverse reward circuit by stepping up the switch tolerance.
- Permits controlled drinking (?)
- Helps withdrawals as well as controlling drinking.
- Wt < 60kgms 1000- 1200 mgms; >60kgms 1500-1800 kgms.
- Check renal clearance.
- USFDA pending. EUFDA approved.

Inhn of GLU; Modulator of GABA; Blocks Ca++ channels



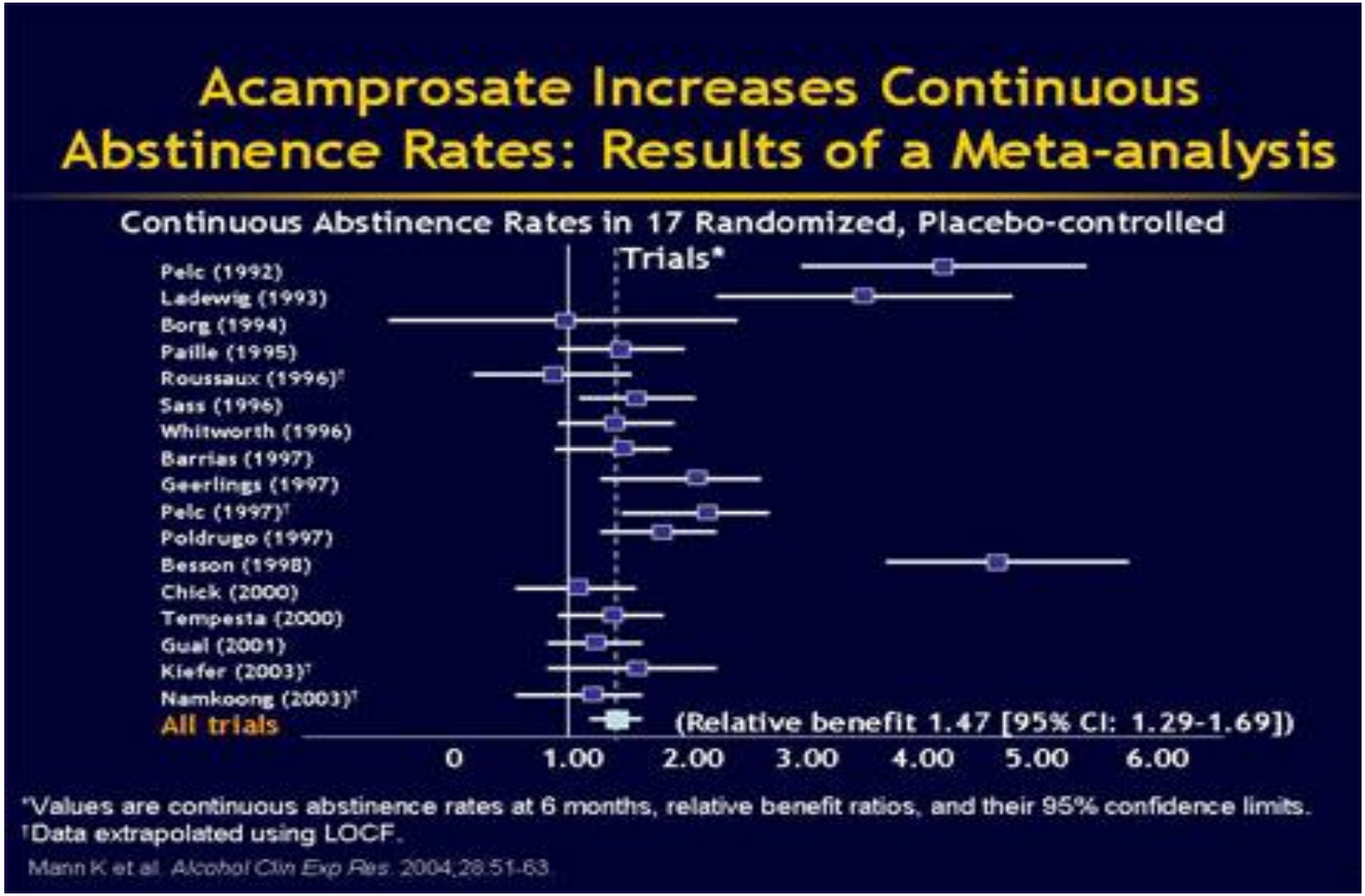
Acamprosate Effect Size:



Maisel et al 2012, MA of 64 RCTs

- Acamprosate and Naltrexon effect studied.
- Prior detoxification or alcohol free period preferred for both.
- Longer the alcohol free period larger the effect size.
- Acamprosate slightly more efficacious in promoting abstinence and Naltrexon slightly more efficacious in reducing heavy drinking and craving.

2004 Meta-analysis



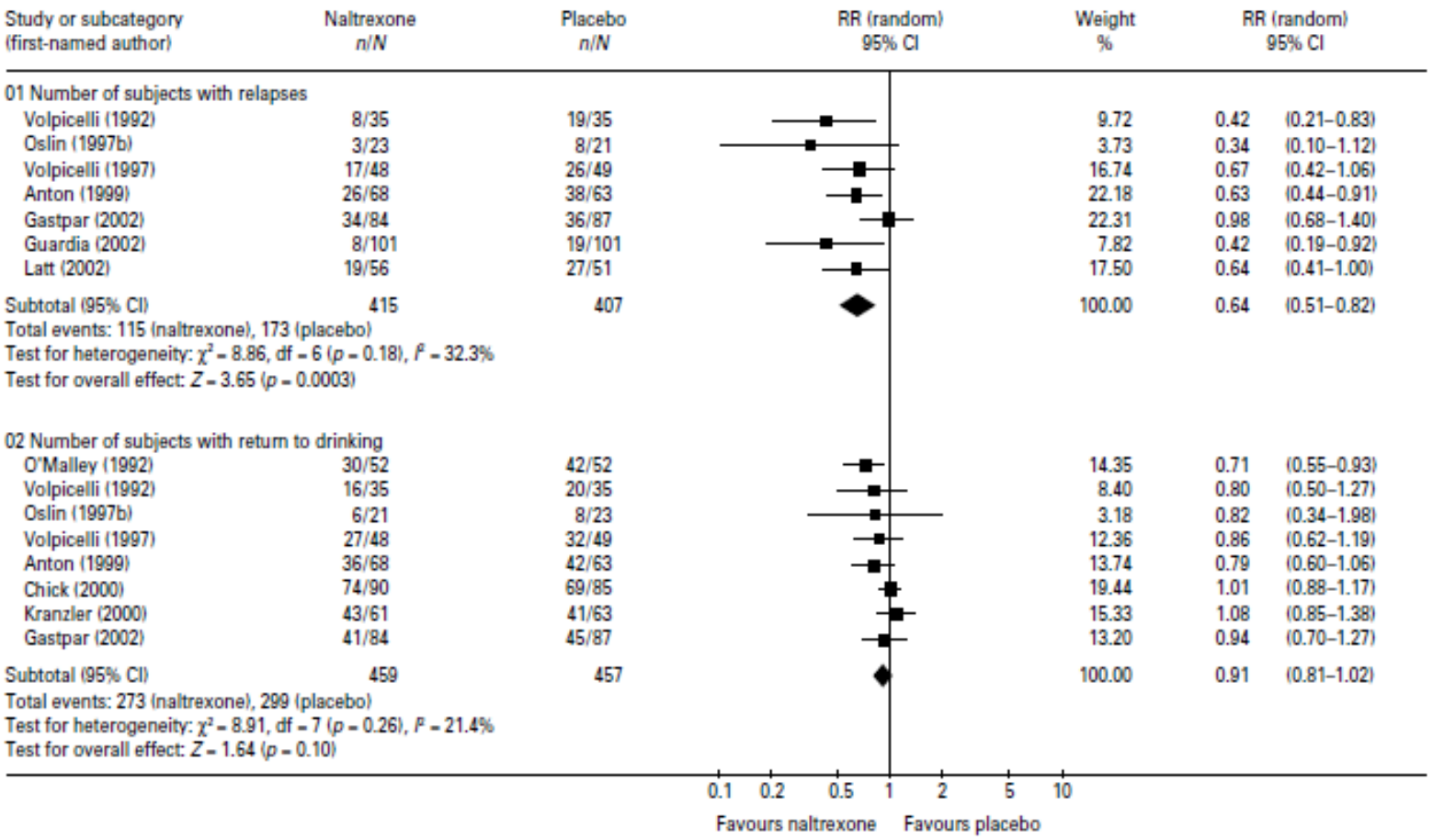
Baclofen

- New generation anti craving drug.
- AC action 60-150mgms/day.
- Controlled drinking, helps stopping drinking.
- Dopaminergic systems in VT nuclei and mesolimbic paths.
- Check hepatic damage.
- In research; pending USFDA, EUFDA approvals.

Naltrexon

- Only USFDA approved anti craving substance.
- 50-150 mgms orally/ day.
- Blocks the dopaminergic reward circuit at the mu receptors and amide receptors.
- Combination with acamprosate works better.

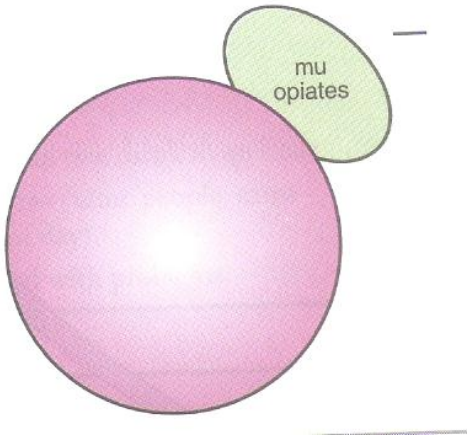
2005 28 RCT Meta-analysis of Naltrexon effect: Srisurapanont

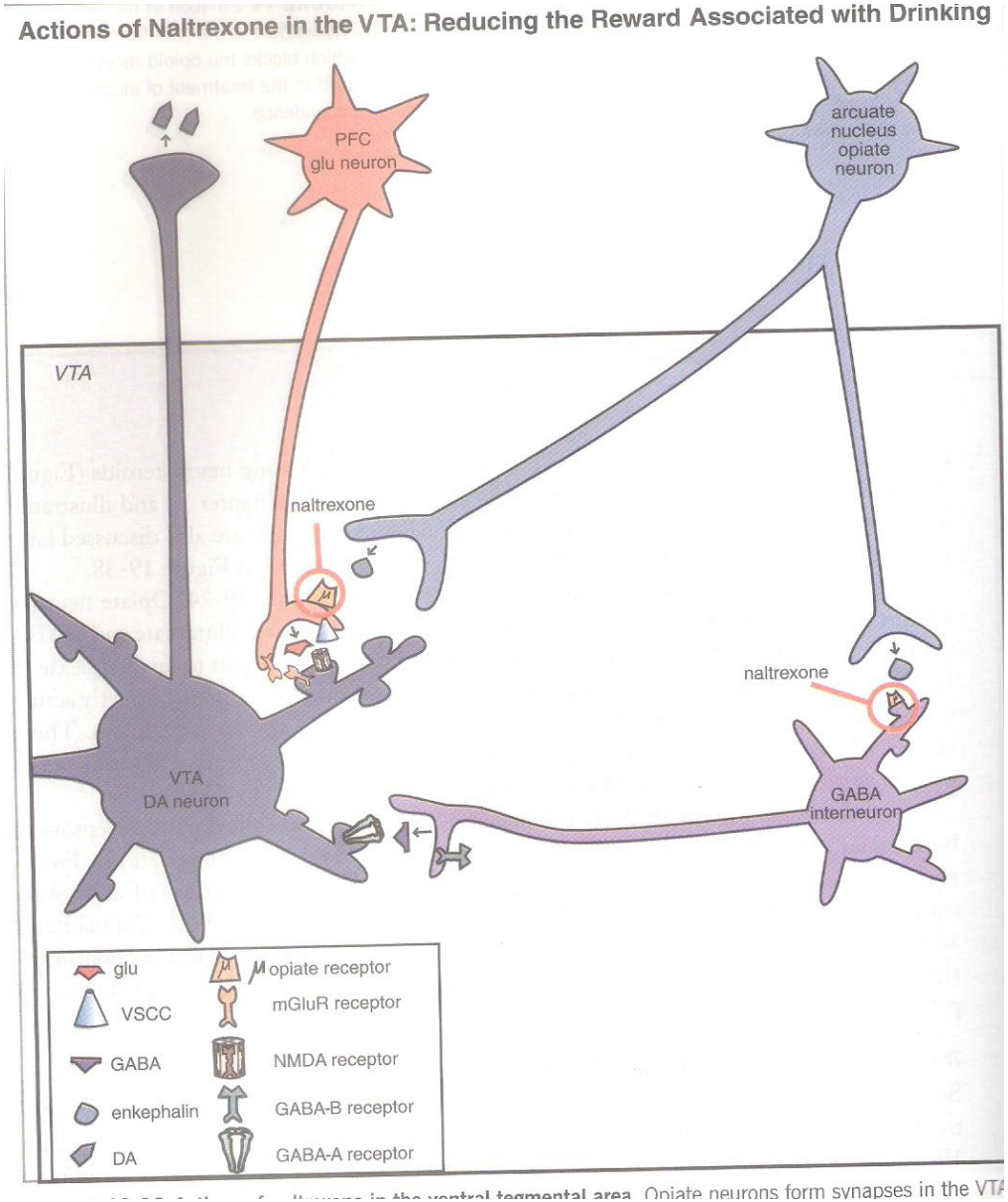


Naltrexon: Review

- Short term treatment with N decreases the risk of alcohol relapse by 36% (NNT =7)
- After 12 weeks, benefits in only time to first drink and craving but not in time to relapse.
- NNH of 8 (nausea); 12 (dizziness); 17 (fatigue)
- N can not lower the risk of discontinuation of treatment in alcoholics (36% in first 12 weeks)
- Intensive CBT does not show any benefit over community based in first 12 weeks. After 12 weeks it increases the time to first drink and decreasing the craving.

Naltrexone





Opiate neurons form synapses in the VTA

Disulfiram

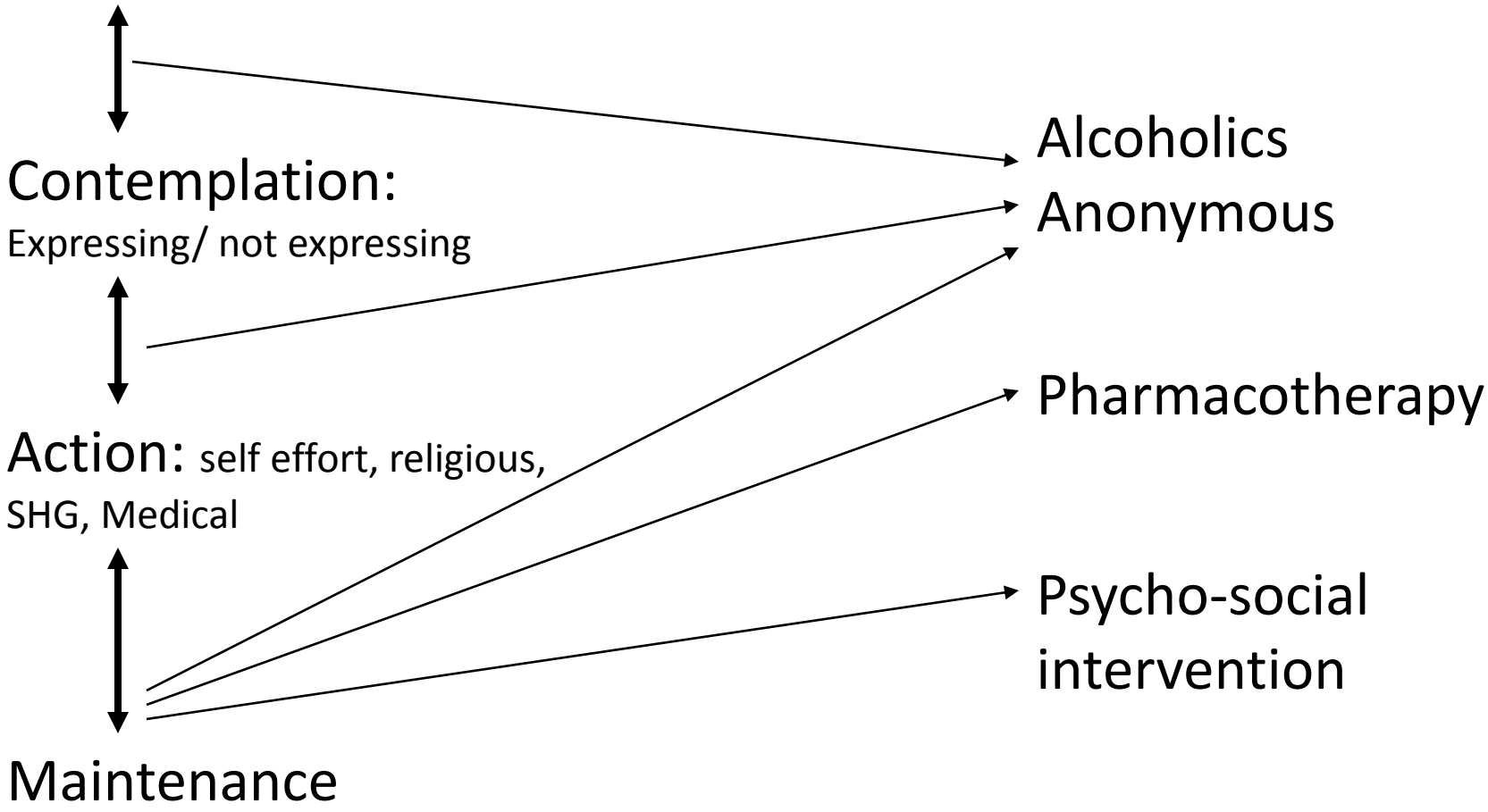
- Deterrent mechanism of action.
- Start after minimum 24 hours of last drink
- Importance of consent.
- Patient education
- Test dose of 125mgms followed by 125 mgms after 8 hours; 250-500mgms a day for 6-8 months
- Monitor blood glucose, LFTs, RFTs.

Problems with pharmacotherapy

- Cost
- Low rate of benefits (6 month RR of 12%-33%)
- S/E of medication.
- How long do we continue? And what after that?
- Is there an alternative for motivation?

Problems with motivation in Chemical Dependency

- Pre-contemplation (reluctant, rebellious, resigned, rationalizing)



Alcoholics Anonymous

- Fellowship of alcoholics for the suffering alcoholics.
- Meetings are platform for sharing their experiences and their hope so that…
- No charges but self supporting; singleness of purpose; no opinion on any other matter; apolitical; non profit organization.
- Organized services all over the world.

AA in India

- More than 50 years; more than 1050 groups; more than 30,000 sober members.
- GSO with board of trustees, class A trustees, delegates, inter-groups, state committees, district committees;
- 12 step program and structured service
- World approved literature in regional languages.

Why AA?

- Cost, reach, tested community intervention
- Approved literature.
- Multipoint intervention.
- Al Anon, Al-a-teen support
- Highest rates of long term sobrieties.
- High satisfaction amongst relatives of alcoholics.

How should we work with AA?

- AA is a “community resource”.
- AA helps people who have desire to give up their drinks.
- In AA, principles are above personalities.
- AA has no opinion (and knowledge) of medicine and psychiatry.
- But AA member knows what we can not (and should not) do!

What to expect from AA?

- Every patient will not get alright.
- Every patient will not understand.
- Expect more if “you” know more!
- Appreciation and criticism comes from members, not the philosophy!
- GSB will give you the right perspective.

AA not an option!

- Not ready for AA but going down!
- Ready but unable to sober up!
- Medically sick
- Suicidal
- Violent
- Dangerous

Rehabilitation Centres

- Half way home license from Directorate of Mental Health
- Availability of Mental Health Professionals
- Training of Peer Counselors
- Structured Process
- Structured Program
- Individual Work
- Family Work

Models

- Punitive model
- Correctional model
- Spiritual Correctional model
- Behavioural Deconditioning model
- 12 step model
- Medical model
- Eclectic model

The Process at HWHs

- Life has become unmanageable
- Can not differentiate b/w self & disease thoughts
- High impulsivity and low analytical thought
- The family disease that is set in

The Program

- Improve analytical thought
- Change choice of behaviour
- Live a life without alcohol
- 12 steps to recovery