

SUBSTANCE INDUCED PSYCHOSIS

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Definitions

Psychotic disorders – DSM V

Defined by abnormalities in one or more of the following **five** domains:

- **delusions**
- **hallucinations**
- **disorganized thought** (speech)
- grossly **disorganized** or **abnormal motor** behavior (including catatonia)
- **negative** symptoms.

also commonly cognitive deficits

Positive symptoms: hallucinations, delusions

Delusions: fixed false belief not bound by cultural or social norms

Hallucinations: "perception without an object"

Negative symptoms: lessening/absence of behaviour related to motivation and expression of emotion

- ("alogia – poverty of speech "avolition – lack of goal directed behaviour, "anhedonia" – reduced experience of pleasure)

Illusion: perceived object and mental image = false perception



Substance Induced Psychosis

DSM-V

Psychotic disorders may be induced by **substances**, **medications**, **toxins**, and other medical conditions.

In substance/medication-induced psychotic disorder, the psychotic symptoms are judged to be a **direct physiological consequence** of a **drug** of abuse, a **medication**, or **toxin** exposure and **cease** after **removal** of the agent.

Substance Induced Psychosis

A. Presence of one or both of the following symptoms:

- Delusions
- Hallucinations

B. There is evidence from the **history, physical examination**, or laboratory findings that either (1) or (2):

- The symptoms in Criterion A developed **during, or within a month of, substance intoxication or withdrawal**
- Medication used is etiologically related to the disturbance

C. The disturbance is **not more accounted for by a psychotic disorder that is not substance-induced**.

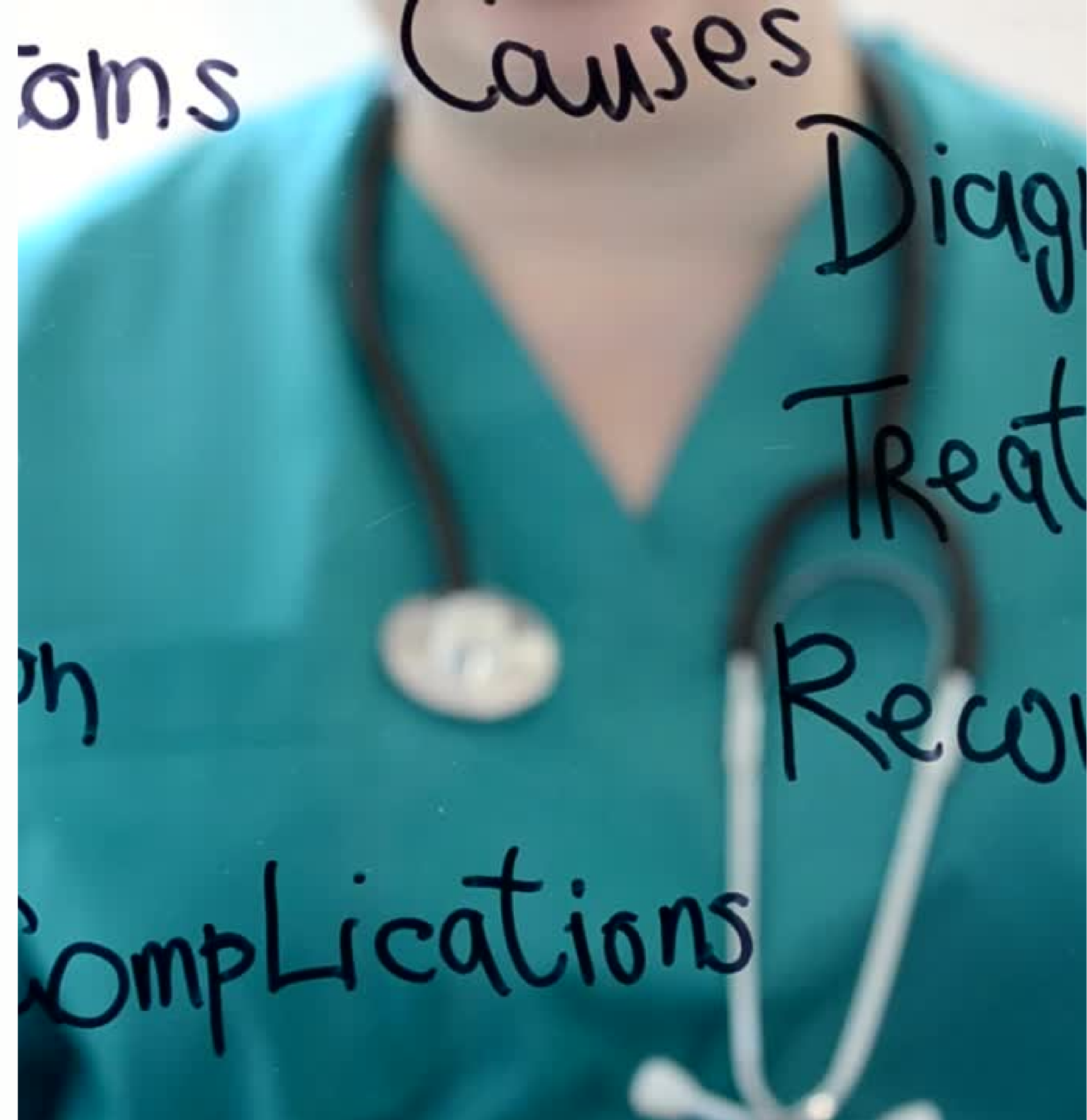
D. The disturbance does not occur exclusively during delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.



Diagnostic Dilemma!

- **Substance Induced Psychosis (SIP) or Primary Psychotic Disorder**
 - Temporal relationship between substance used and presence of psychotic symptoms
 - intoxication
 - withdrawal
 - Period of abstinence
 - Poly-substance use
 - Symptoms: Similarities vs Differences between Schizophrenia and Substance Induced Psychosis
 - pre-existing psychotic disorder
 - presence of confounding/similar risk factors



Just Illicit "Drugs"

A drug with psychotomimetic ("psychoto" – psychosis, "mimetic" – an imitation of) actions is one which induces temporary states of altered perception, often mimicking the symptoms of psychosis including delusions and/or hallucinations

- **Cannabinoids**
- **Synthetic Cannabinoids**
- **Methamphetamine**
- **Hallucinogens** (LSD/DMT)
- Enactogens (MDMA)
- Cocaine
- Phencyclidine (PCP) + Ketamine

Examples:

- antimalarial agents (i.e. mefloquine)
- antiretroviral agents (i.e. Interferon beta)
- antiepileptic agents (i.e. levetiracetam)
- Corticosteroids (i.e. Prednisolone)

Who is at Risk?

Liability to psychosis is highly heritable but monozygotic twin concordance < 50% –
Nature vs **NURTURE**

Risk factors:

- poly-substance use
- family hx of mental illness (i.e. psychotic disorder)
- Ultra High Risk of Psychosis
 - premorbid personality – (i.e. Schizotypal PD/ cluster B)
 - Higher risk of conversion to Psychosis
 - Young Age
 - duration and dose
 - self harm episodes after substance induced psychosis



How?

Complex and multifactorial, many neurotransmitter systems identified.

- Dopamine
- Serotonin
- Cannabinoid
- Glutamate and NMDA receptors
- Opioid receptors



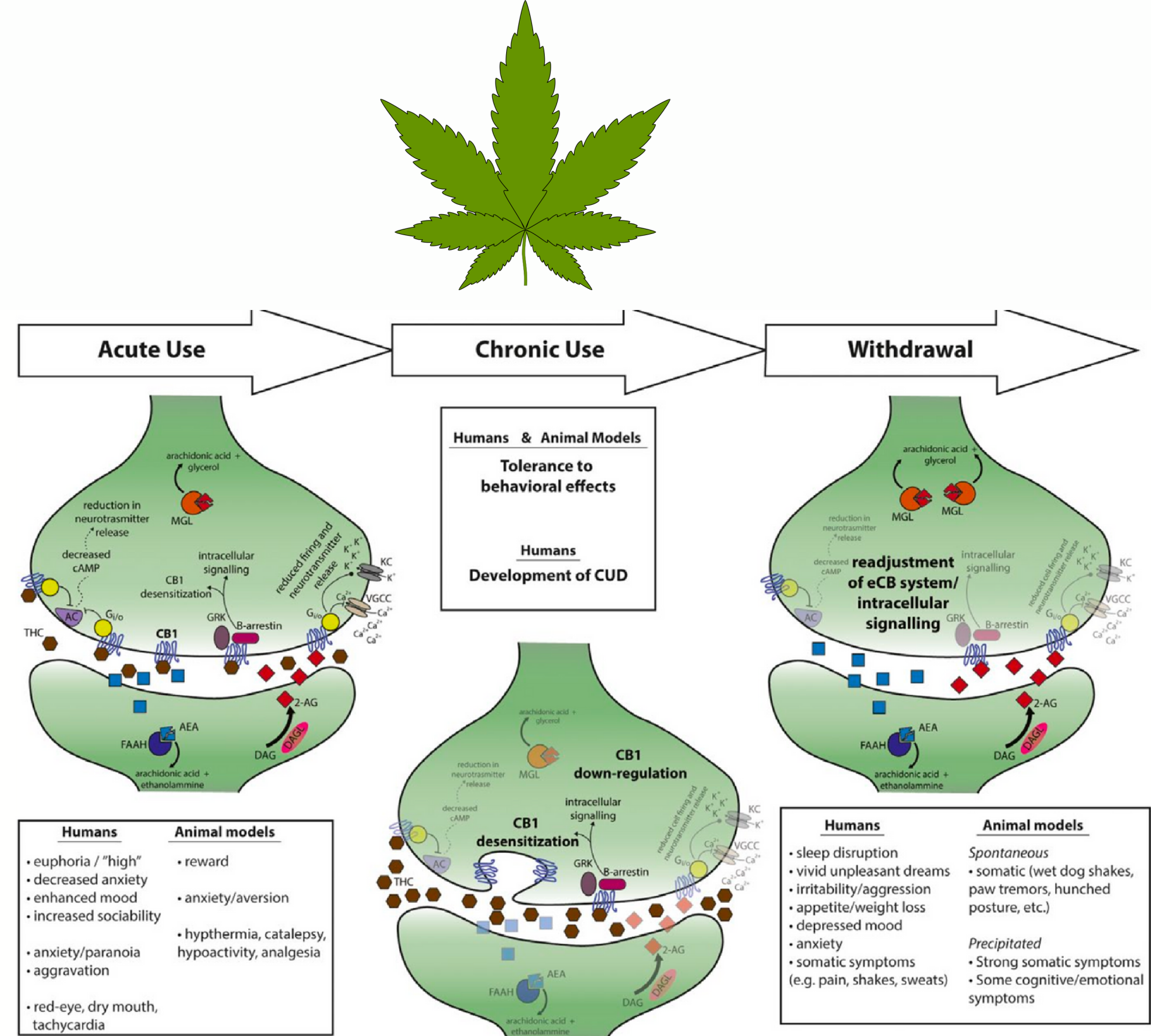
Cannabinoids

Epidemiology

- Cannabis – most widely used illicit used substance in the world
 - 15.3% of US population *
- Psychotic features: dependent on THC (delta9 – THC) content in cannabis

Pharmacology

- psychotropic ingredient: delta9- THC (delta-9-tetrahydrocannabinol)
 - partial agonist on CB1 (Cannabinoid Receptor 1) – widely expressed in CNS
 - multiple downstream signaling effects
- Cognitive deficits/psychotic/anxiogenic effects



Cannabinoids

Symptoms/Clinical characteristics

- psychoactive
 - psychotic: paranoia/hallucinations
 - negative sx
 - disinhibition
 - heightened senses (music/sounds/colours/tastes)

Cannabis has the **HIGHEST** conversion rate to Schizophrenia c.f other substance induced psychosis.

- higher risk with family hx of psychosis/UHR groups/ dose/duration
 - **< 15yo + continued use – HIGH** risk of transition to SCZ
 - neuroimaging studies – detrimental effects on brain resting connectivity, intelligence & cognitive function \



Starzer MSK, Nordentoft M, Hjorthøj C. Rates and predictors of conversion to schizophrenia or bipolar disorder following substance-induced psychosis. Am J Psychiatry. (2018) 175:343–50. doi:10.1176/appi.ajp.2017.17020223

Synthetic Cannabinoids (Spice/Kush)

Background

- since '60s – synthetic derivatives of cannabis produced
- composed of herbal mixtures sprayed with various SC
- not detected by Drug screens
- purchased from adult entertainment stores
- limited studies (mostly case reports)

Pharmacology

- mimics the action of delta-9-tetrahydrocannabinol
 - FULL agonist on CB1 (Cannabinoid Receptor 1) – widely expressed in CNS
 - HIGH affinity



Synthetic Cannabinoids (Spice/Kush)

Symptoms/Clinical characteristics

- Psychoactive
 - similar to Cannabis
- Physical
 - Nausea/vomiting
 - Acute kidney injury
 - Seizures

Higher risk for psychosis with pre-morbid psychiatric history (SCZ/BPAD)



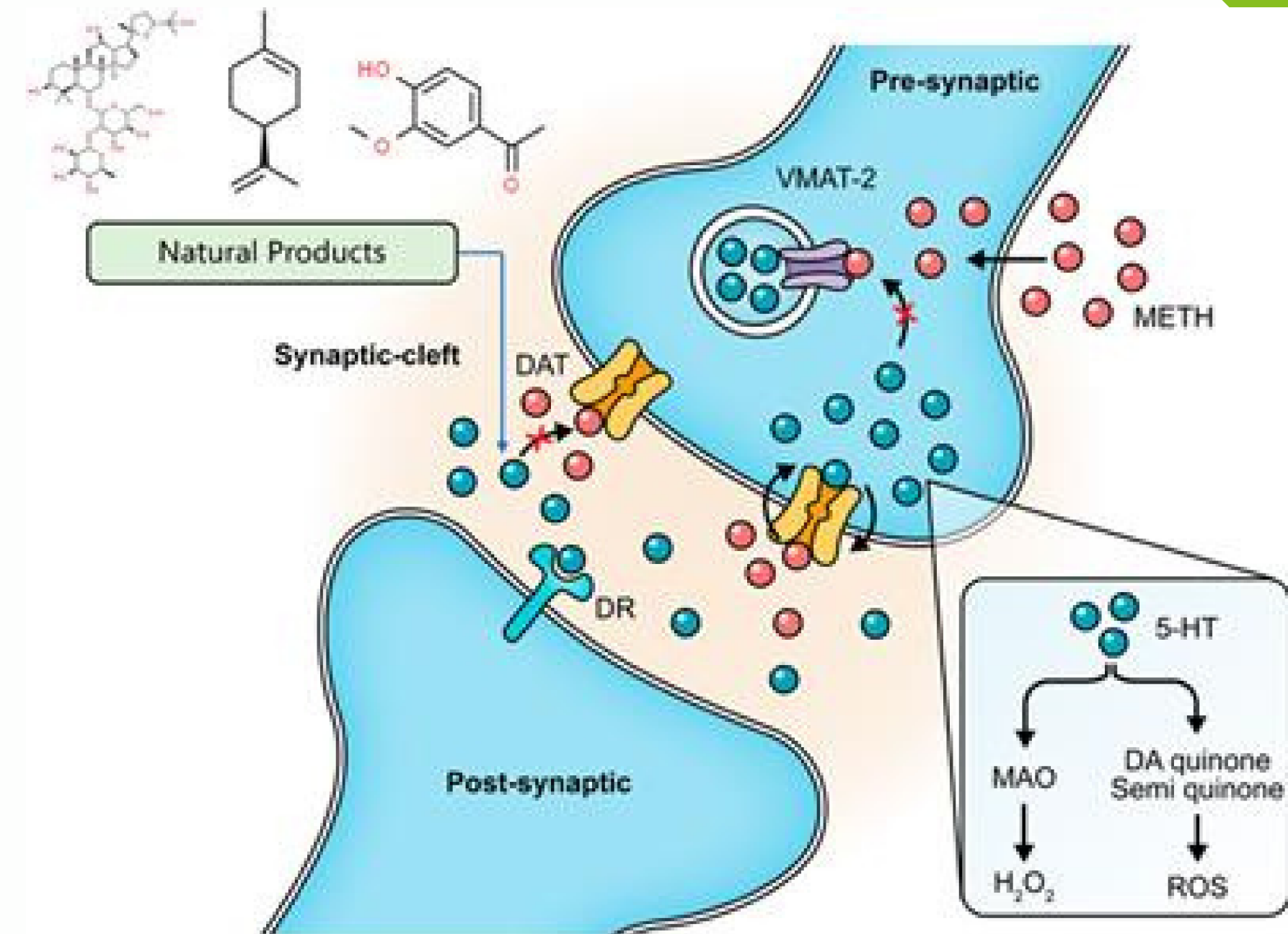
Methamphetamine (ICE)

Background

- (alpha- methylphenethylamine)
- 90's epidemic of methamphetamine use in SE asia - rapid rise of MIP -> Australia/NZ
- 2017 - 28.9 million users of amphetamine (0.6% global pop aged 15-64)*
- 37.1 % of methamphetamine users - psychosis (5 -fold increase c.f non users)
- DTNBI - genetic polymorphism for propensity to develop psychosis

Pharmacology

- Reverses both VMAT-2 and DAT - increases synaptic dopamine in Nigrostriatal pathway
- release of Dopamine in Mesolimbic/Mesocortical pathways in VTA -> excessive glutamate release - damage to NMDA receptors -> psychosis



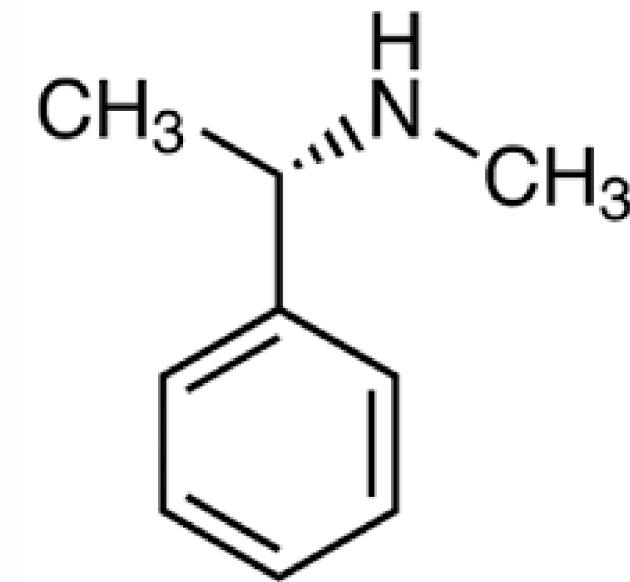
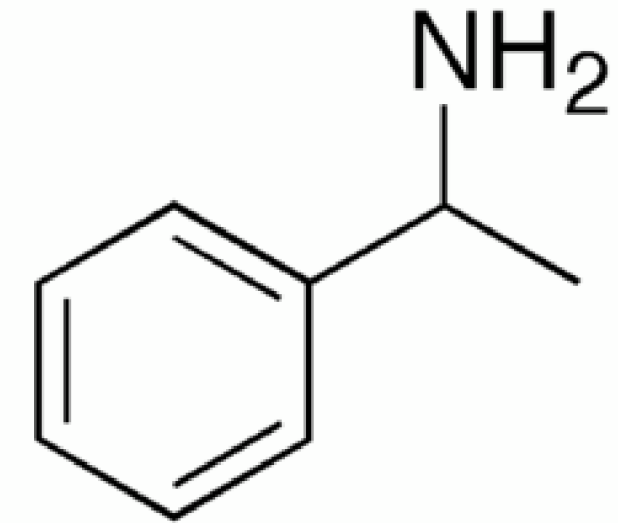
*UNODC. World Drug Report (2019).

Methamphetamine (ICE)

Symptoms/Clinical characteristics

- psychoactive
 - paranoia (persecution)
 - referential delusions
 - hallucinations
 - auditory , tactile, visual, gustatory, olfactory
 - disorganisation of thought
 - absence of negative symptoms
 - limited insight
 - "fear" "panic" "defensive violence"

Majority users experience a Brief Psychotic reaction when intoxicated that dissipate after withdrawal.
up to **25%** experience persistent psychosis



Hallucinogens

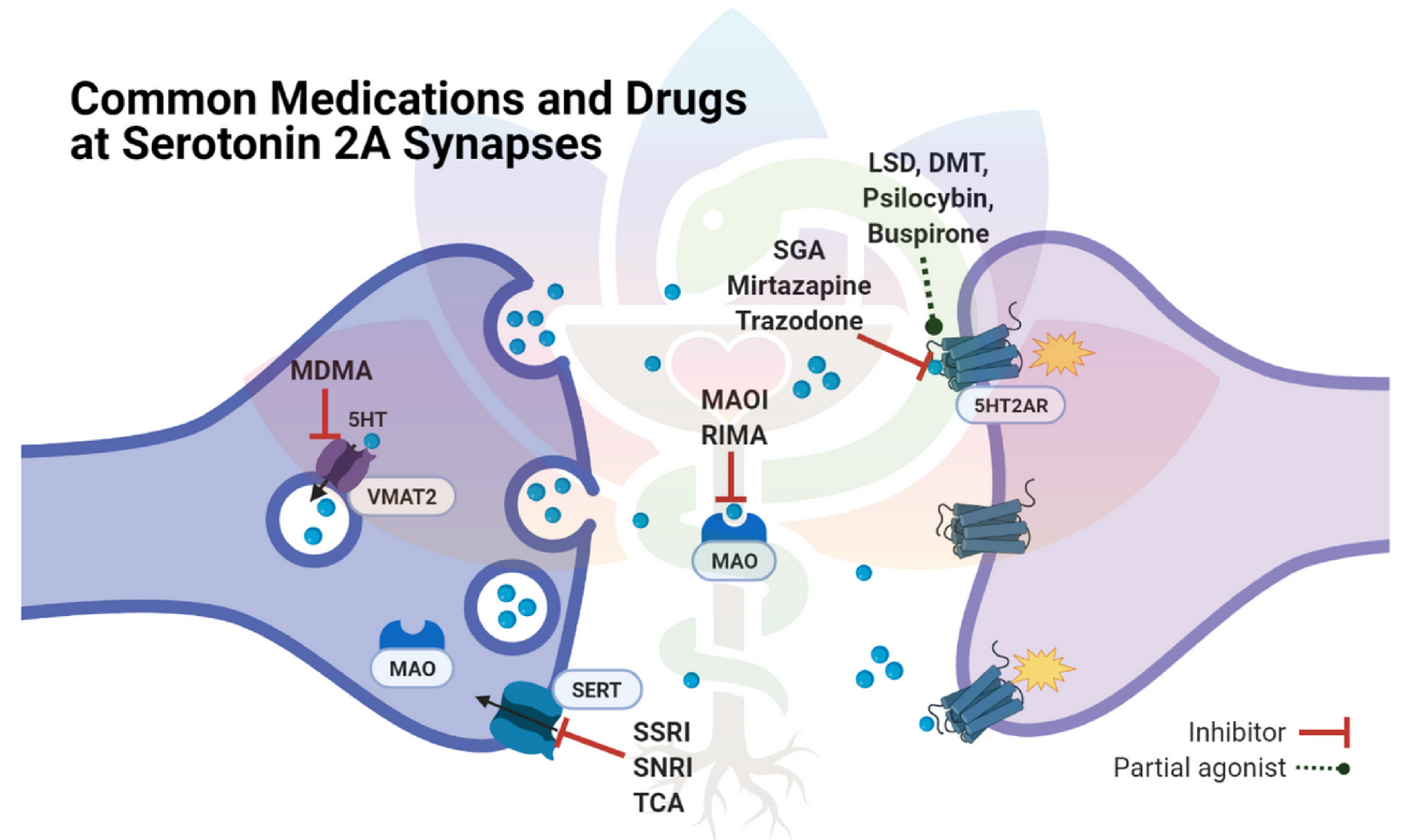
Background

- "psychedelic" – Hoffman
- 2 classes:
 - Tryptamines/phenylethylamines
 - tryptamines – DMT/Psilocybin/LSD
 - phenylethylamines – mescaline/synthetic hallucinogens
- limited epidemiological data on psychosis

Pharmacology

- agonist/partial agonist activity on 5-HT receptors
- 5-HT_{2A} agonist – main target modulating Dopamine in mPFC

Common Medications and Drugs at Serotonin 2A Synapses



Serotonin reuptake inhibitors (SSRI), serotonin norepinephrine reuptake inhibitors (SNRI), tricyclic antidepressants (TCA), second generation antipsychotic (SGA), monoamine oxidase inhibition (MAOI), reversible inhibitor of monoamine oxidase (MAOI), 3,4-methylenedioxymethamphetamine (MDMA), N,N-dimethyltryptamine (DMT), Lysergic acid diethylamide (LSD)

Hallucinogens

Clinical Characteristics:

- dependent on type, dose, mental state, environment
- visual perceptual changes – size, shape, colour, illusion of movement
- LSD – cognitive changes, positive mood state in a proportion of subjects

Limited evidence re: cases of prolonged psychosis w psychedelics

Retrospective cross-sectional study – no significant associations between lifetime use of psychedelics and increased rate of mental health outcomes



References

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Thank You