

Substance-related mental disorders

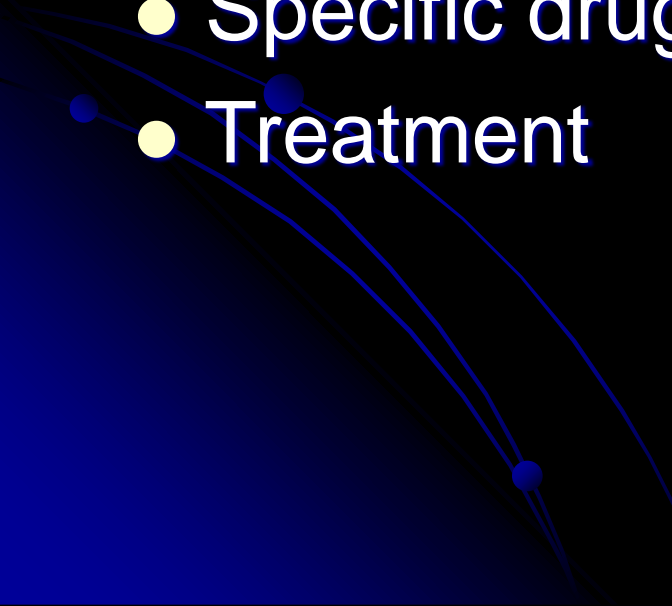
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Outline

- Basic definitions
 - Etiology: psychological theories, neurobiology
 - Specific drugs and related syndromes
 - Treatment
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Substances listed in the DSM IV.

- Alcohol
- Amphetamine or amphetamine-like
- Caffeine
- Cannabis
- Cocaine
- Hallucinogens
- Inhalants
- Nicotine
- Opioid
- Phencyclidine or phencyclidine-like
- Sedative, Hypnotic or Anxiolytic
- Anabolic steroid
- Other (e.g. MDMA, GHB/gamma-hydroxybutyrate, designer drugs: mephedrone, 3-4-methylene-dioxy-pyrovalerone)

DSM-IV-TR substance-related mental disorders

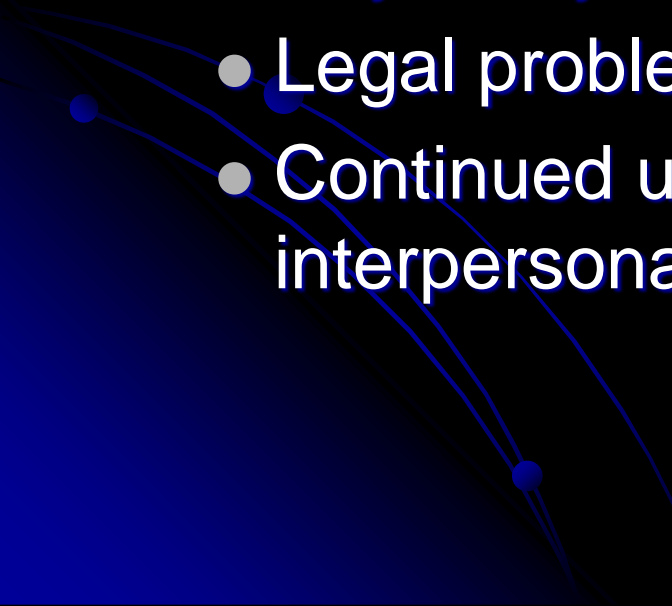
1. Substance use disorders (DSM-IV):

- Substance **abuse**
- Substance **dependence**

2. Substance -induced disorders:

- Substance **intoxication**
- Substance **withdrawal** with or without **delirium**
- Substance -induced amnestic disorder / dementia
- Substance -induced **psychotic disorder** (e.g. delusion of jealousy and hallucinations)
- Substance -induced mood, personality, anxiety, sexual, and sleep disorder

Basic definitions: substance abuse

- Maladaptive pattern of substance use:
 - Failure to fulfill role obligations at work, school or home
 - Physically hazardous situations
 - Legal problems
 - Continued use despite serious social and interpersonal problems
- 

Basic definitions: substance dependence

- (Heavy and prolonged substance use);
- Tolerance (need for increase amounts; diminished effect of the same amount)
- Withdrawal (certain symptoms when stop substance use, substance cures the syndrome)
- Persistent desire or unsuccessful efforts to cut down substance use
- Great amount of time is spent on activity related to the substance
- Social, work or recreational activities are given up
- Continued use despite of knowledge of serious social, psychological, and physical problems

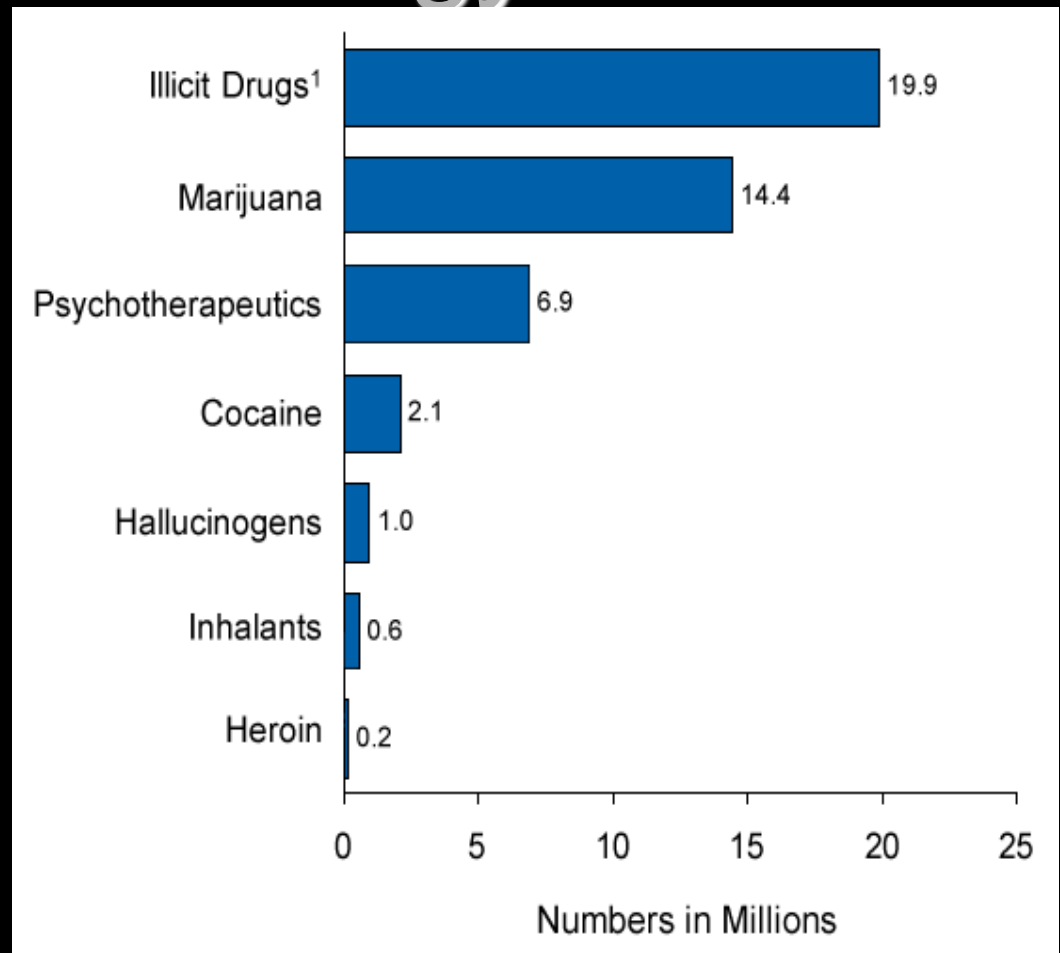
DSM-5: Substance use disorder

- Substance used in **larger** amounts or over a **longer** period of time than intended
- Persistent **desire** or unsuccessful attempts **to cut down** or control substance use
- Significant **time** spent obtaining, using, and recovering from the effects of substance
- **Craving** to use substance (new in DSM-5!)
- Recurrent substance use leading to **failure** to fulfil major role obligations at work, school, or home
- Recurrent use of substance, despite having persistent or recurring **social or interpersonal problems** caused or worsened by substance
- Recurrent substance use despite having persistent or recurring **physical or psychological problems** caused or worsened by substance
- **Giving up** or missing important social, occupational, or recreational **activities** due to substance use
- Recurrent substance use in hazardous situations
- **Tolerance**: markedly increased amounts of substance are needed to achieve intoxication or the desired effect, or continued use of the same amount of substance achieves a markedly diminished effect (somatic dependence)
- **Withdrawal**: there is the characteristic substance withdrawal syndrome, or substance is taken to relieve or avoid withdrawal symptoms (somatic dependence)
- **Mild – 2-3; Moderate – 4-5; Severe – 6 or more**

Epidemiology

- 40 % of USA population reports one or more illicit substances in their lifetime
- lower educational and lower income predicts dependence
- Race, ethnicity and urban environment does not predict dependence
- Rate of use among 12-13 yo. slightly declining
- Marijuana is most common illicit drug

/2000 NHSDA/



Past month illicit drug use among US citizens age > 12 yo. /Results from the 2007 National Survey on Drug Use and Health <http://www.oas.samhsa.gov/>

Etiology

Psychological explanations

- psychodynamic theories: masturbatory equivalent, manifestation of oral regression, inability to deal with reality
- behavioral theories: positive reinforcement, adverse effects, negative reinforcement, cues associated to the drug use

Genetics

Alcohol abuse has a genetic component, other drugs: less conclusive data.

Twin studies: higher concordance in stimulant dependence and in opioid dependence

Social and neurodevelopmental factors

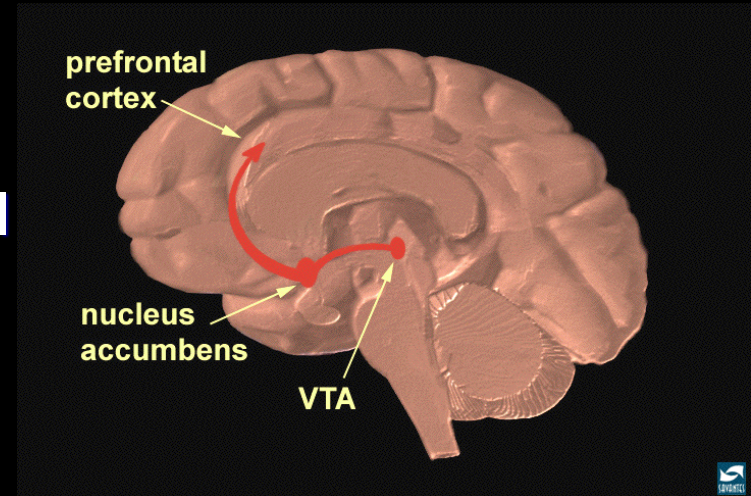
Childhood adverse events and stress might lead neurodevelopmental changes and vulnerability

Prevention!

Etiology

Neurobiology:

- Substances effect different neurotransmitter receptors:
 1. All substances activate the **brain dopaminergic reward system**: ventral tegmental area, n. accumbens (psychological dependence, craving and reinforcing effects)
 2. Particular receptors for some drugs: opioid receptors, anandamide receptors,
 3. Other targets: cocaine on dopamin transporter, hallucinogens on serotonerg neurons, phencyclidin on glutamaterg neurons, GHB on GABA-B receptors
- 2+3 might cause somatic dependence – tolerance and withdrawal symptoms



Case reports and questions



CASE 1: 16 year old girl arrives to the outpatient ward with her mother. In the last few months she has lost 20 kgs, she goes jogging every day, and has insomnia. Which diagnose would you think of?

- amphetamine abuse
- hyperthireosis
- anorexia nervosa
- alcohol dependency

CASE 2: A 18 year old boy is taken to hospital by his friends on a Sunday morning. Symptoms are sweating, tachycardia, pupilla dilatation, psychomotor agitation. Behaves angrily, hostile.

- alcohol withdrawal
- alcohol intoxication
- amphetamine withdrawal
- amphetamine intoxication

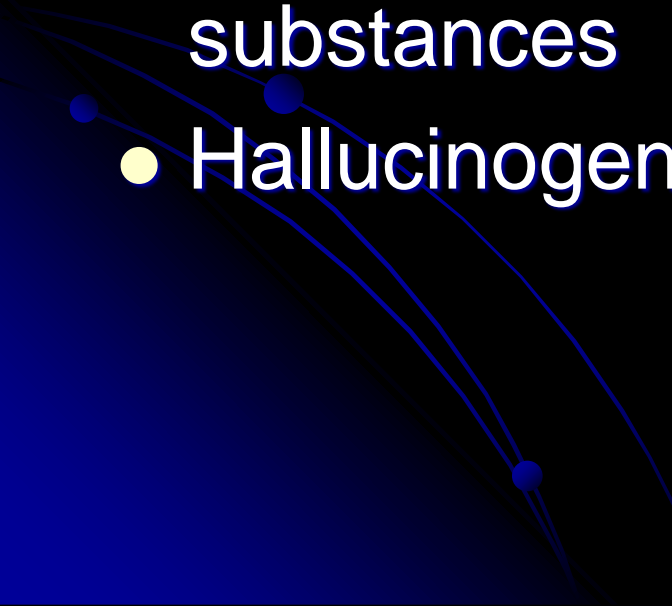
CASE 3: 23 year old boy complains he had transient hallucination in the last two weeks: while travelling on the metro, while having dinner at home, while having a bath. They lasted some minutes. He drinks alcohol on weekends, and used to use LSD and cannabis but he stopped both one month ago. What is the most probable reason of his symptoms?

- schizophrenia
- alcohol withdrawal
- cannabis withdrawal
- flashback

Question: Which of the followings can occur also as 'cannabis-induced' disorders?

- Major depression
- Anxiety
- Intoxication
- Psychotic disorder with hallucinations or delusions

„Classical” illicit drugs

- Cannabis
 - Opioids
 - Cocaine
 - Amfetamin and amfetamine-like substances
 - Hallucinogenic drugs
- 

Cannabis I.

History: Central Asia and China for 4000 years, today: most common illicit drug in the USA

Neuropharmacology: D9-tetrahydrocannabinol, cannabinoid receptors: basal ganglia, hippocampus (role in memory), cerebellum, cortex, limbic system

Affects GABA and dopaminerg neurons

Intoxication: „red eye”, tachycardia, dry mouth, increased appetite; depersonalization, derealization, less sensitivity to external stimuli

Cannabis-induced psychosis: paranoid ideation

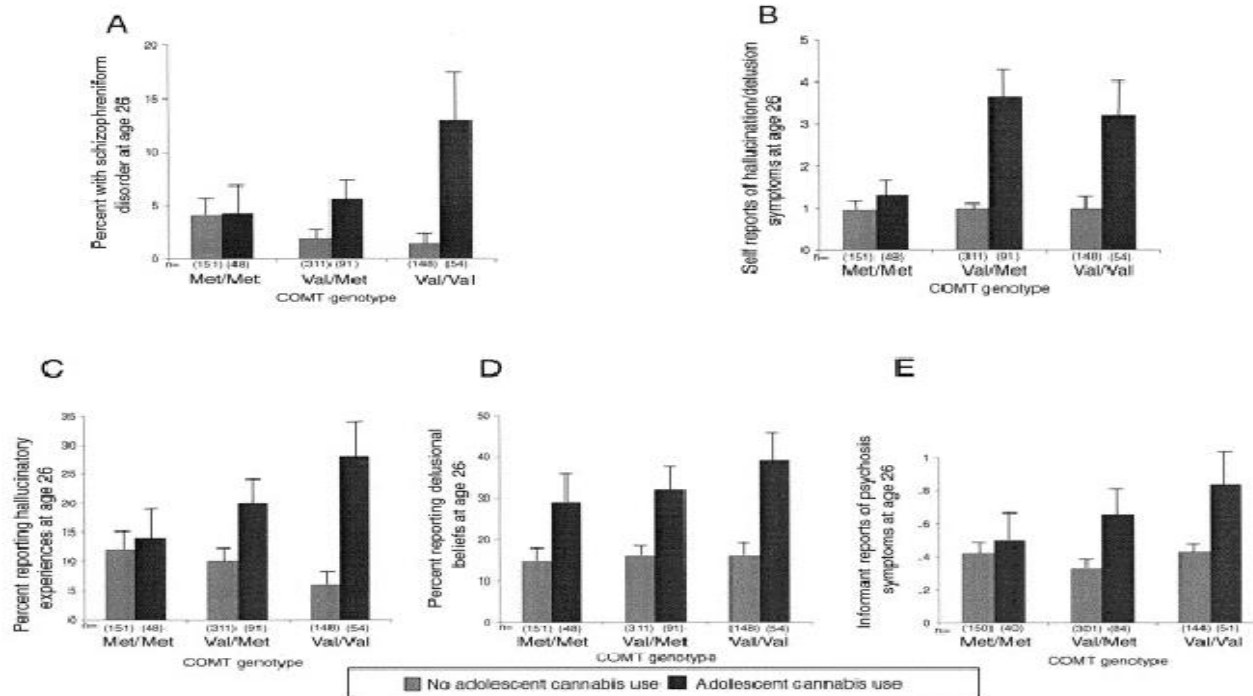
Other cannabis-induced disorders:

anxiety

persisting perceptual abnormalities („flashback”)

amotivational syndrome (apathy, anergy, lack of persistence in a task – controversial)

Cannabis II. – Long-term effects



Caspi et al, 2005

Gene-environment interaction: COMT (Catechol-O-Methyltransferase) gene Val/Val genotype AND cannabis use increases the risk of schizophreniform disorder

Opioids I.

History: opium used for approx 3500 years

1806: morphine synthesized

1832. Codein

Heroin introduced as a treatment for morphine addiction

Today: more than 20 chemically distinct opioid drugs in medical use;
dependence mostly associated with heroin (diacetylmorphine)

Neuropharmacology:

opioid receptors

μ- receptors: analgesia, respiratory depression, constipation,
dependence

K – receptors: analgesia, diuresis, sedation

δ – receptors: analgesia

Endogenous opiates: endorphines and encephalines, involved in
neural transmission and pain supression

Dopaminergic neurons in VTA: reward

Opioids II. – related syndromes

Intoxication: euphoria and rush (orgasm-like feeling) followed by sedation, psychomotor agitation or retardation, pupillary constriction, drowsiness or coma, blurred speech, impairment in attention or memory

Abuse

Dependence - somatic

Tolerance is very high, hundredfold increase of doses; does not develop uniformly to all actions of opioids

Withdrawal: dysphoria, nausea or vomiting, muscle pain, lacrimation, pupillary dilatation, diarrhoea, yawning, fever, insomnia, sweating, piloerection; intense craving for opioids

Neonatal withdrawal

Opioid-induced psychotic disorder

Mood disorder

Sleep-disorder

Sexual dysfunction

1976: several cases of irreversible Parkinson-syndrome due to opioid contaminated with MPTP (methyl-phenyl-tetrahydro-pyridin) – destroyed substantia nigra neurons

Cocaine I.

History: leaves chewed in South-America

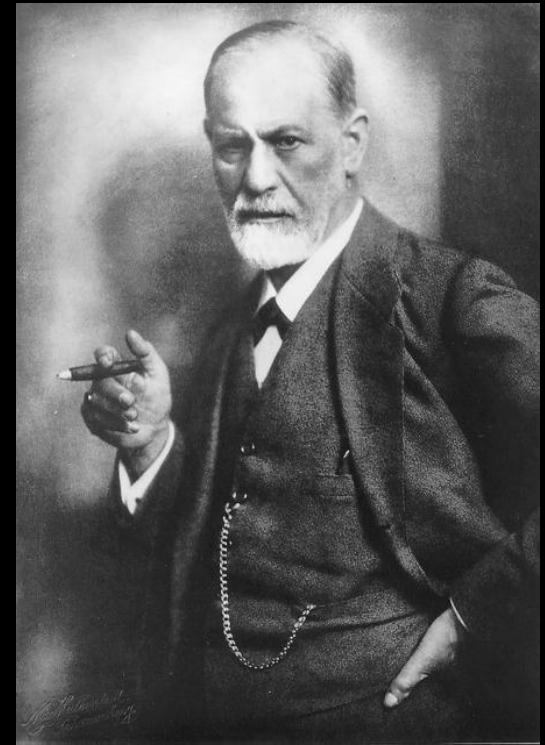
Local anaesthetic since 1880 (today in ear, nose, throat surger)

1880-1914 cure for many illnesses: cough, depression, heroin addiction

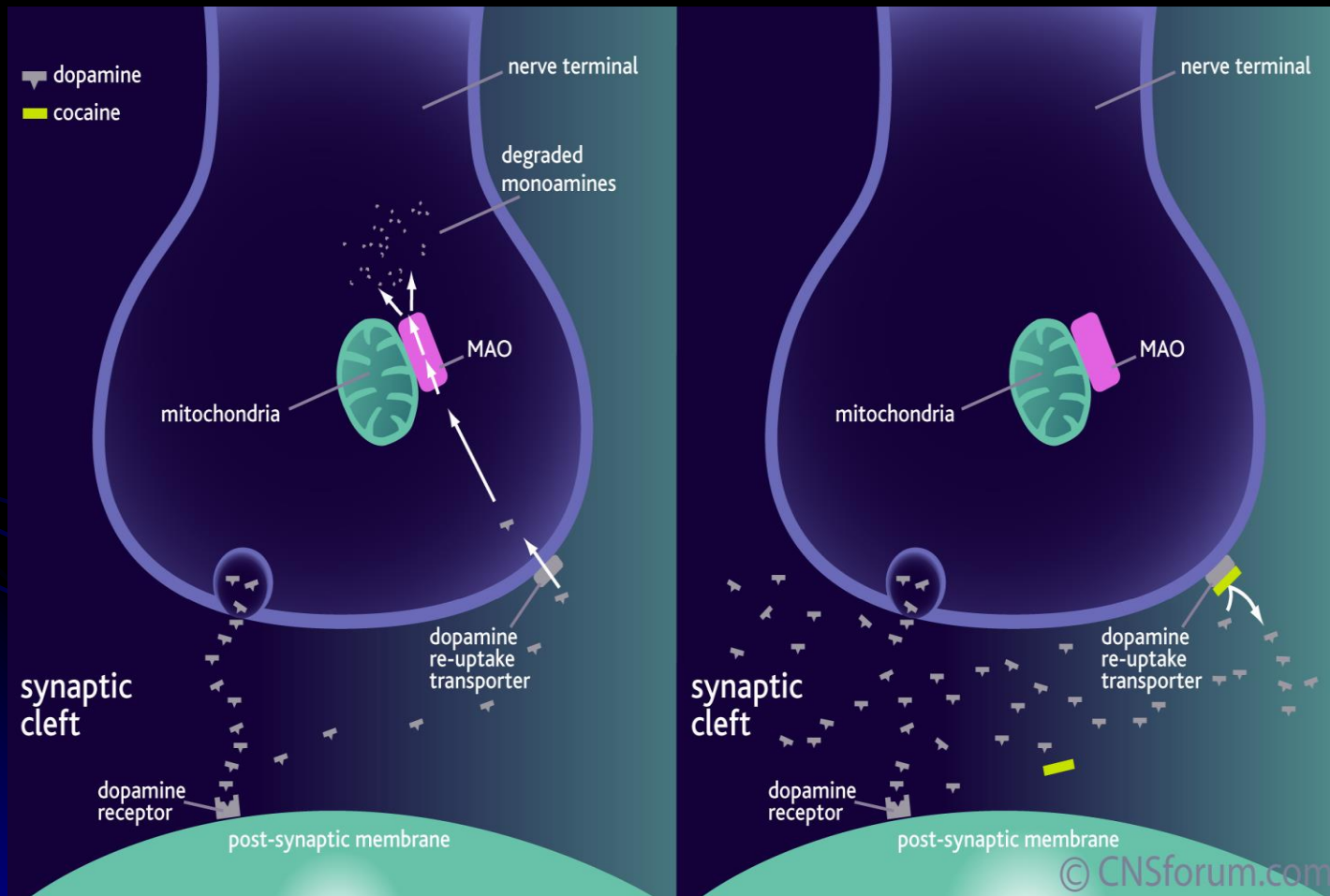
1914. Classified as a narcotic

Forms: powder inhaled, crack (free base of cocain) iv injected or smoked

Neuropharmacology: competitive bockade of dopamin reuptake by the dopamin transporter



Cocaine II.



Cocaine III. – Related symptoms

Dependence

Abuse

Intoxication: very similar to amfetamin intox

Withdrawal: fatigue, nightmares, insomnia or hypersomnia, increased appetite, psychomotor agitation, anhedonia

Cocain-induced psychotic disorder: paranoid delusions in 50 % of users; visual and acoustic hallucinations, „formication”

Other: mood disorder, anxiety, sleep disorder, sexual dysfunction

Amphetamine and amphetamine-like substances

History: 1932. nasal drop, antidepressant, 1970. regulations, today: illicit drug, approved in ADHD treatment (e.g. methylphenidate)

Neuropharmacology: dopamine release in VTA, cortex and n. accumbens

„Designer” amphetamines (MDMA = XTC): also serotonin release

Diagnosis of **intoxication**: tachycardia or arrhythmia, pupillary dilatation, elevated blood pressure, perspiration or chills, nausea or vomiting, psychomotor agitation, muscular weakness, confusion, seizures, coma + perceptual disturbances (especially with designer A-s)

Amphetamine-induced psychotic disorder:

- symptoms are similar to positive schizophrenia symptoms – schizophrenia animal models
- mostly visual hallucinations, hyperactivity, confusion and incoherence, ideas of reference, paranoid delusions

Treatment: short-term antipsychotic medication

Hallucinogenic drugs

History: natural substances used in ancient South-America (psilocybin, peyotl, ayahuasca); 1938: LSD synthesized and accidentally used by Albert Hoffmann. Model of psychotic syndromes.

(Designer amphetamines)

Neuropharmacology: serotonergic system

LSD: partial agonist at postsynaptic serotonin receptors

Related syndromes:

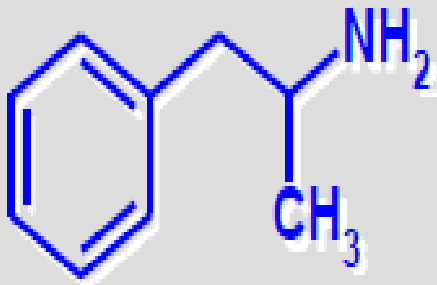
Intoxication: perceptual changes: depersonalization, derealisation, illusions, hallucinations, tachycardia, sweating, tremor, blurred vision, incoordination. Psychotic symptoms – „bad trip”. Death caused by hypertension or hypertermia can occur.

• **Psychotic disorder** – similar to schizophrenia positive symptoms

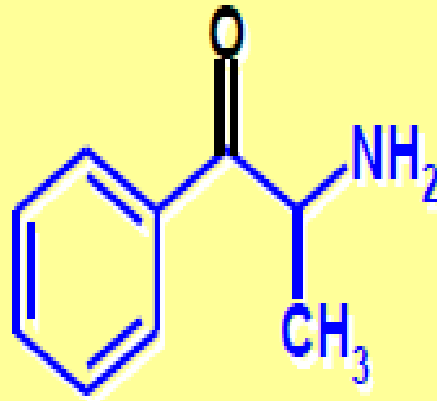
Hallucinogen-Induced Persisting Perception Disorder = Flashback:

spontaneous re-experiencing of perceptual symptoms which occurred at former hallucinogen use: hallucinations, false perception of movement, flashes or intensified colors, macropsia, micropsia

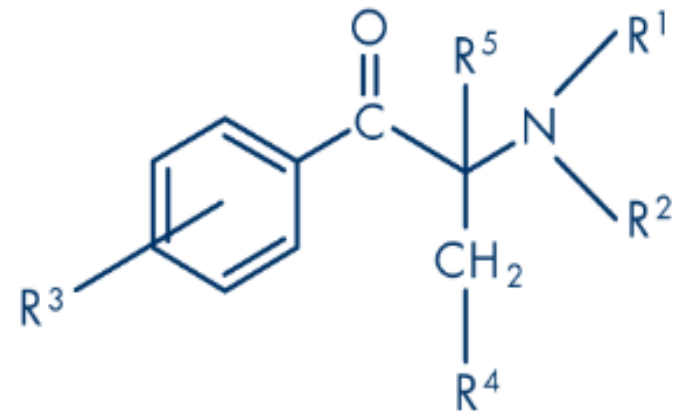
Designer drugs



Amphetamin



Cathinon

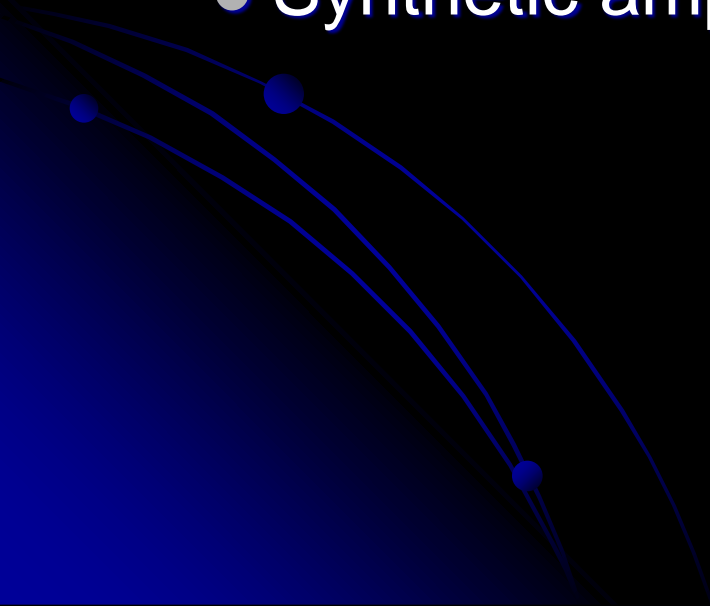


Designer drugs - definition

- Synthesized in chemical laboratories
- Powerful psychoactive drugs
- Mimic the effects of more commonly used illicit drugs
- Relatively cheap
- Not detected with standard urine drug screens
- Available at head shops and on the Internet – not always illegal
- **Worldwide trend of the rapidly increasing use of these substances**
- Effects, adverse-effects are unknown - **potential somatic or psychiatric risks**

Designer drugs - categories

- Synthetic cathinons (beta-keto-amphetamines)
- Synthetic cannabinoids
- Synthetic opioids
- Synthetic amphetamines



Designer drugs – designer amphetamines/cathinons

- Mephedrone, 3-4-methylene-dioxy-pyrovalerone, pentedrone, A-PVP, 4-MEC, 4-EMC...
- **Intoxiation:** Amphetamine-like and/or hallucinogen effects
- Severe psychological **dependence** – withdrawal symptoms and craving
- **Psychiatric consequences:** anxiety, agitation, delirium-like or hallucinatory states, psychotic episodes
- **Somatic consequences:** cardiac, neurological, GI problems, hepatotoxicity, hyperthermia, hyponatraemia, infections.....

Synthetic cannabinoids

- Cannabinoid receptor agonists
- Variable chemical structure, variable (and not well-known) pharmacodynamic and pharmacokinetic properties and adverse effects - psychosis?
- K2, Spice, Smoke, Herbal Mix...
 - JWH (John W. Huffman) group – JWH-018
 - CP (created by Pfizer) group – CP 55,940
 - HU (Hebrew University) group
 - AM (Alexandros Makriyannis) group

Therapy

Pharmacotherapy
Psychotherapy
Social interventions

Relapse rates in 6 months:

alcohol – 50 %

opioid – 40 %

cocaine – 45 %

nicotine – 70 %

/O'Brien, McLellan 1996/

Pharmacotherapy

- Substitution: methadon, LAAM (l-acetylmethadol), buprenorphin
(no iv use, no criminality, no fetal withdrawal, less severe neonatal withdrawal)
- Drugs used to reduce craving: naltrexone, nalmephe
- Treatment of comorbid depression, anxiety

Long-term management of substance dependence: psychosocial treatment and rehabilitation

- Psychoeducation and **motivational interviewing** according to individual needs and capacity to change (brief interventions)
- Focusing on and treatment of **co-morbid** mood and anxiety disorders (30-40%)
- **Family-level** interventions
- Rehabilitation centers and therapeutic communities
- Harm-reducing interventions – needle exchange
- **Counseling** and community-level intervention:
 - motivation to maintain abstinence and prevent relapse – showing the consequences
 - cope with everyday stress
 - stimulus control and craving
 - build-up alternative lifestyle

Self-help groups

Alcoholics Anonymous, Narcotics Anonymous

- Sober peer group, 12-step treatment from confrontation to spiritual awakening
- Role modeling of social functioning without drinking
- Peer help available 24 hours
- Strong group coherence („we-ness”)
- Religion and spirituality

potential problems: confrontation with the medical model, may be dogmatic, requires changes in view of life

Other organizations: LifeRing Secular Recovery, Rational Recovery, SMART Recovery

Thank you for your attention!

