Substance-related mental disorders

Erika Szily Semmelweis University 11. 14. 2016.

Outline

- Basic definitions
- Etiology: psychological theories, neurobiology
- Specific drugs and related syndromes
 Treatment

Substances listed in the DSM IV.

- Alcohol
- Amphetamine or amphetamine-like
- Caffeine
- Cannabis
- Cocaine
- Hallucinogens
- Inhalants
- Nicotine
- Opioid
- Phencyclidine or phencyclidine-ike
- Sedative, Hypnotic or Anxiolitic
- 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

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





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
- behaviorial 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 lost 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-tetrahidrocannabinol, 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 presistence in a task – controversial)

Cannabis II. – Long-term effects



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

Opioids I.

History: opium used for approx 3500 years 1806: morphine synthetized 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 feling) 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-tetrahidro-piridin) – 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 delusons in 50 % of users; visual and acustic hallucinatins, "formication" Other: mood disorder, anxiety, sleep disorder, sexual dysfunction

Amphetamine and amphetaminelike substances

History: 1932. nasal drop, antidepressant, 1970. regulations, today: illicit drug, approved in ADHD treatment (e.g. methylphenydate)
Neuropharmacology: dopamin release in VTA, cortex and n. accumbens
"Designer" amphetamines (MDMA = XTC): also serotonin release

Diagnosis of intoxication: tachycardia or arrythmia, 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 symptomes – 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 (psylocibin, peyotl, ayahuasca); 1938: LSD synthetized 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 symptomes – "bad trip". Death caused by hypertension or hypertermia can occur.

Psychotic disorder – similar to schizophrenia positive symptoms

Hallucinogen-Induced Persisting Perception Disorder = Flashback: spontaneus re-experiencing of perceptual symptoms which occured at former halluconigen use: hallucinations, false perception of movement, flashes or intensified colors, macropsia, micropsia

Designer drugs



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 - cathegories

Synthetic cathinons (beta-keto-amphetamines)

Synthetic cannabinoids

Synthetic opioidsSynthetic 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, deliriumlike or hallucinatory states, psychotic episodes
- Somatic consequences: cardial, neurological, GI problems, hepatotoxicity, hyperthermia, hyponatraemia, infections....

Synthetic cannabinoids

- Cannabinoid receptor agonists
- Variable chemical stucture, variable (and not well-known) pharmakodinamic and –khinetic 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 Psychoterapy Social interventions

Relapse rates in 6 months:

alcohol – 50 % opioid – 40 % cocaine – 45 % nicotine – 70 %

/O'Brien, McLellan 1996/

Pharmacotherapy

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

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

- Confrontation with reality and motivating 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!