

# Substance-related disorders

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# Substance Use

## Several aspects:

- Moral
- Legal
- Economical
- Medical
- Scientific

# Terminology

- Brain-altering substances
- Psychoactive substances
- Legal-illegal substances
- Substance  $\cong$  drug (manufactured chemical)
  
- Addiction
- Dependence: withdrawal + tolerance
  - Physical – behavioral
  - Psychological (= habituation)
- Abuse
- Misuse

# DSM-IV-TR Criteria for Substance Intoxication

A. The development of a reversible substance-specific syndrome due to recent ingestion of (or exposure to) a substance.

**Note:** Different substances may produce similar or identical syndromes.

B. Clinically significant maladaptive behavioral or psychological changes that are due to the effect of the substance on the central nervous system (e.g., belligerence, mood lability, cognitive impairment, impaired judgment, impaired social or occupational functioning) and develop during or shortly after use of the substance.

C. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

# DSM-IV-TR Diagnostic Criteria for Substance Dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by **three (or more)** of the following, occurring at any time in the same 12-month period:

- (1) **tolerance**, as defined by either of the following:
  - (a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect
  - (b) markedly diminished effect with continued use of the same amount of the substance
- (2) **withdrawal**, as manifested by either of the following:
  - (a) the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for Withdrawal from the specific substances)
  - (b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms

- (3) the substance is often taken in larger amounts or over a longer period than was intended
- (4) there is a persistent desire or unsuccessful efforts to cut down or control substance use
- (5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
- (6) important social, occupational, or recreational activities are given up or reduced because of substance use
- (7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

# DSM-IV-TR Criteria for Substance Abuse

- A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by **one (or more)** of the following, occurring within a 12-month period:
- (1) recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences, suspensions, or expulsions from school; neglect of children or household)
  - (2) recurrent substance use in situations in which it is physically hazardous (e.g., driving an automobile or operating a machine when impaired by substance use)

# DSM-IV-TR Criteria for Substance Abuse

- (3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
  - (4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)
- B. The symptoms have never met the criteria for Substance Dependence for this class of substance.



# DSM-IV-TR Criteria for Substance Withdrawal

- A. The development of a substance-specific syndrome due to the cessation of (or reduction in) substance use that has been heavy and prolonged.
- B. The substance-specific syndrome causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

# Etiology 1.

**Dependence:** *result from a person's taking a substance in an abusive pattern. Why that person?*

**Psychodynamic theory:**

- Substance abuse  $\cong$  masturbation,  $\cong$  oral regression,  $\cong$  defense against anxious impulses
- disturbed ego functions

**Psychosocial theories:**

- Societal factors
- Unstable childhood, family, subculture, etc.

# Etiology 2.

**Behavioral theory** (all substances, all dependencies)

*„Substance seeking behavior“*

Physical dependence is not determinative

Positive reinforcers:

Positive experience after first use  $\Rightarrow$  substance seeking

Adverse effects of an other substance

Discrimination between substances

## **Neurochemical factors**

Particular neurotransmitters (opiate, dopamine, GABA)

low endogenous agonist activities

High endogenous antagonist activity

Exogenous substance: long-term use modulates the receptor system

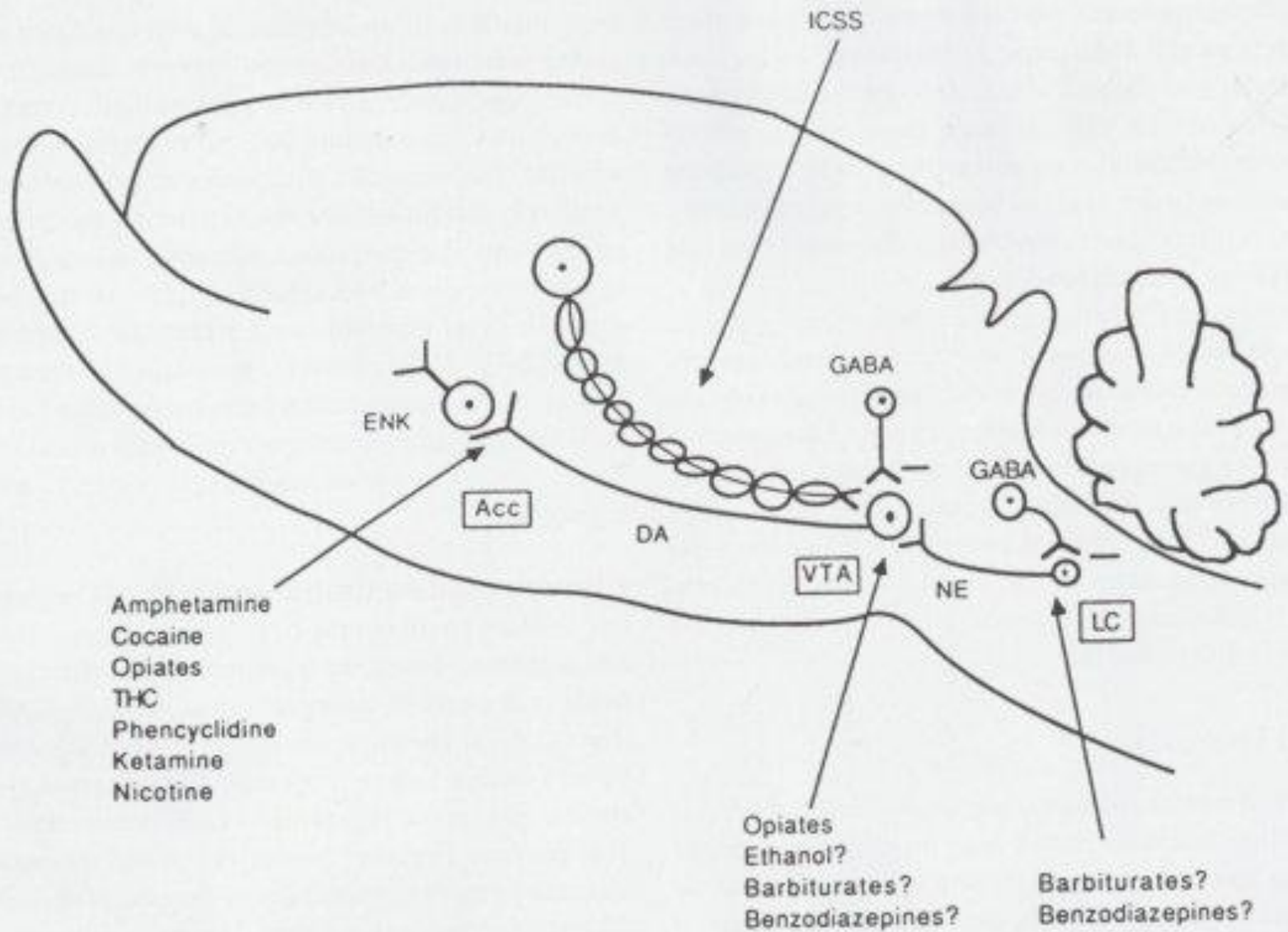
## **Brain reward circuitry:**

**VTA:** dopaminergic neurons  $\Rightarrow$  cortex, limbic regions, NA: Amphetamins, cocaine

**LC:** noradrenergic neurons: opiates

## **Genetic factors (twins, siblings, adoptees studies)**

Conclusive data about alcohol dependency



# Comorbidity

2 or more psychiatric disorder in a single patient

- Depression (life-time prevalence of major depressive disorder)
  - 33-50% of opioid dependents
  - 40% of alcohol dependents
- **Suicide**
  - 20 X more likely to commit suicide
- Antisocial Personality Disorder
  - Prevalence: 35-60% of patients with substance abuse or dependence

# Amphetamine (like) Related Disorders

- Amphetamine sulfate (1887)
- Treatment of nasal congestion, asthma, narcolepsy, postencephalotic parkinsonism, lethargy, depression, obesity, chronic fatigue etc.
- FDA: the only approved indications: Attention deficit/hyperactivity disorder and narcolepsy.
- Amphetamins: stimulants, psychostimulants, analeptics, sympatomimetics
  - Increase preformance: students, truck drivers, pilots, athletes, businesspeople
- Widely used illicit, addictive drugs

# Amphetamines

## „Classic” or legal preparations:

- mextroamphetamine (Dexedrine)
- methamphetamine (Desoxyn) „ice”
- dextroamphetamine-amphetamine salt (Adderall)
- methylphenidate (Ritalin)
- phenylpropranolamin
- ephedrine

Catecholamin (dopamine) release from presynaptic terminals  
(VTA ⇒ cortex, limbic areas = reward circuit pathway)

# Amphetamin-like substunces

(„designer” or substituted  
amphetamines)

- effects on the serotonergic
- and dopaminergic systems
- hallucinogen-like activites



- MDMA (3,4-methylenedioyamphetamine) Extasy, XTC, Adam
- MDEA (N-ethyl-3,4-methylenedioxyamphetamine) Eve
- MMDA (5-methoxy-3,4-methylenedioxyamphetamine)
- DOM (2,5-dimethoxy-4-methylamphetamine) STP



# DSM-IV-TR Diagnostic Criteria for Amphetamine Intoxication

- A. Recent use of amphetamine or a related substance (e.g., methylphenidate).
  
- B. Clinically significant maladaptive behavioral or psychological changes (e.g., euphoria or affective blunting; changes in sociability; hypervigilance; interpersonal sensitivity; anxiety, tension, or anger; stereotyped behaviors; impaired judgment; or impaired social or occupational functioning) that developed during, or shortly after, use of amphetamine or a related substance.

C. Two (or more) of the following, developing during, or shortly after, use of amphetamine or a related substance:

- (1) tachycardia or bradycardia
- (2) pupillary dilation
- (3) elevated or lowered blood pressure
- (4) perspiration or chills
- (5) nausea or vomiting
- (6) evidence of weight loss
- (7) psychomotor agitation or retardation
- (8) muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias
- (9) confusion, seizures, dyskinesias, dystonias, or coma

D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder. *Specify* if: With perceptual disturbances

# Amphetamine intoxication

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- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder. *Specify* if: With perceptual disturbances

# DSM-IV-TR Diagnostic Criteria for Amphetamine Withdrawal

- A. Cessation of (or reduction in) amphetamine (or a related substance) use that has been heavy and prolonged.
- B. Dysphoric mood and two (or more) of the following physiological changes, developing within a few hours to several days after Criterion A:
  - fatigue
  - vivid, unpleasant dreams
  - insomnia or hypersomnia
  - increased appetite
  - psychomotor retardation or agitation
- C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

# Amphetamine-induced Psychotic Disorder

≅ paranoid schizophrenia (positive symptoms)

- urine drug screen
- Resolution of the symptoms in a short time

# A-induced Mood disorder

- Intoxication – manic/mixed symptoms
- Withdrawal – depressive features

# Amphetamine Intoxication Delirium

- High doses
- Sleep deprivation
- Combination with other substances
- Preexisting brain damage

# Adverse Effects of Amphetamines

- Psychological:
  - Dysphoria
  - Restlessness
  - Irritability, hostility
  - Confusion
  - Insomnia
  - Anxiety disorders
- Physical:
  - AMI
  - Stroke
  - Hypertension
  - Ischaemic colitis
  - Tetany
  - Coma
  - Seizures
  - Iv. use: HIV, HCV, HBV and other infections

# Khat

- *Catha edulis* (East Africa)
- Cathinone (norpseudoephedrine)

Absorbed buccally (chewing)

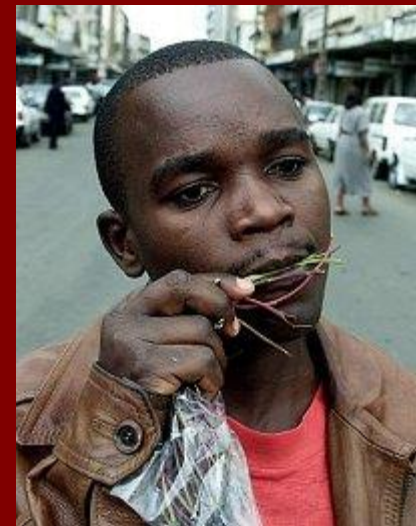
Rapid metabolism

Amphetamin-like effects

elevates mood

decreases hunger

alleviates fatigue



# Caffeine-related disorders

- Most widely consumed psychoactive substance
- Well integrated into the daily cultural practices
  - USA: 200 mg/day
  - A cup of coffee: 100-150mg, a cup of tea: 50mg
- Cocoa, chocolate, soft drinks, medications
- Comorbidity: large amounts of daily caffeine consumption
  - abuse of sedative, hypnotic drugs
- **Methylxanthine:**
  - Acts as an antagonist on the adenosine receptors  $\Rightarrow$  blocks the inhibitory G protein  $\Rightarrow$  blocks the inhibition of cAMP.
  - Activation of dopaminergic and noradrenergic neurons
  - Mild euphoria – anxiety, dysphoria
  - Tolerance
  - Effects on CBF: global cerebral vasoconstriction



# DSM-IV-TR Diagnostic Criteria for Caffeine Intoxication

Recent consumption of caffeine, usually in excess of 250 mg (e.g., more than 2-3 cups of brewed coffee).

B. Five (or more) of the following signs, developing during, or shortly after, caffeine use:

- restlessness
- nervousness
- excitement
- insomnia
- flushed face
- diuresis
- gastrointestinal disturbance
- muscle twitching
- rambling flow of thought and speech
- tachycardia or cardiac arrhythmia
- periods of inexhaustibility
- psychomotor agitation



C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

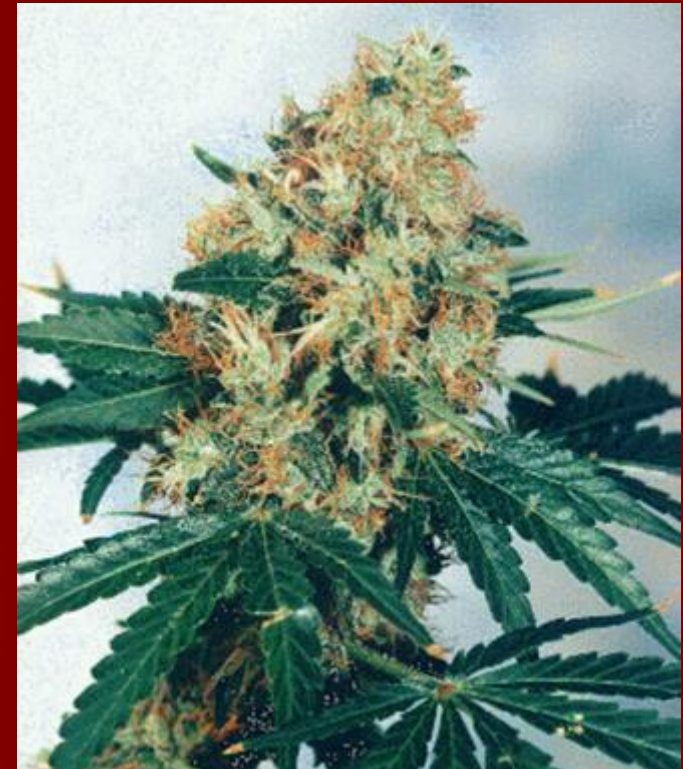
D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder

# DSM-IV-TR Research Criteria for Caffeine Withdrawal

- A. Prolonged daily use of caffeine.
- B. Abrupt cessation of caffeine use, or reduction in the amount of caffeine used, closely followed by headache and one (or more) of the following symptoms:
  - marked fatigue or drowsiness
  - marked anxiety or depression
  - nausea or vomiting
- C. The symptoms in criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to the direct physiological effects of a general medical condition (e.g., migraine, viral illness) and are not better accounted for by another mental disorder.

# Cannabis related disorders

- Cannabis sativa (Central Asia, China)
- Cannabis: the world's most commonly used illicit drug
- Cannabinoids:  $\Delta 9$ -THC
  - Flowering top of the plant or dried resinous exudate from the leaves (*hashish*)
- The plant is cut, dried, chopped and rolled into cigarettes (*joint*)
- $\Delta 9$ -THC  $\Rightarrow$  11-hydroxy- $\Delta 9$ -THC (active)
- Cannabinoid receptor – G-protein linked: basal ganglia, hippocampus, cerebellum
- Animal studies: effects on monoamines, GABA neurons
- „Hemp insanity”
- Medical use of marijuana ???
  - Nausea after chemotherapy
  - Chronic pain
  - AIDS
  - Glaucoma
  - SM



**Cannabis**

**Marihuana**

**Haschisch**







# DSM-IV-TR Cannabis-Related Disorders

## **Cannabis dependence**

- **Cannabis abuse**
- **Cannabis-induced disorders**
- **Cannabis intoxication** Specify if:
  - With perceptual disturbances
- **Cannabis intoxication delirium**
- **Cannabis-induced psychotic disorder, with delusions**  
Specify if:
  - With onset during intoxication
- **Cannabis-induced psychotic disorder, with hallucinations**, Specify if:
  - With onset during intoxication
- **Cannabis-induced anxiety disorder** Specify if:
  - With onset during intoxication

# DSM-IV-TR Diagnostic Criteria for Cannabis Intoxication

- A. Recent use of cannabis.
- B. Clinically significant maladaptive behavioral or psychological changes (e.g., impaired motor coordination, euphoria, anxiety, sensation of slowed time, impaired judgment, social withdrawal) that developed during, or shortly after, cannabis use.
- C. Two (or more) of the following signs, developing within 2 hours of cannabis use:
  - conjunctival injection
  - increased appetite
  - dry mouth
  - Tachycardia
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.
  - *Specify* if: **With perceptual disturbances**

- **Cannabis intoxication delirium** (high doses)
  - level of consciousness
  - Cognition
  - Perception
  - Attention
  - Motor coordination
- **Cannabis-induced Anxiety Disorder**
  - Inexperienced users
  - Dose dependent
  - Short-lived anxiety states (panic)
- **Cannabis-induced Psychotic Disorder**
  - Long-term use
  - Paranoid ideations
  - „bad trip” experience
  - Vulnerability



# Cocaine-related Disorders

- „*Erythroxylon coca*” shrub,
- indigenous in South-America
- Stimulant: leaves are chewed by local inhabitants
- 1860: the alkaloid was isolated
- Narcotic drug: vasoconstrictive, analgesic affects
- 1880: it was used as a local anesthetic: eye, nose, throat surgery
- S. Freud
- Commonly used drug in the US
  - 10% of population tried cocaine
  - Highest among 18-35 years (cc.1,2%)
  - Crack (freebase of cocaine) very potent
- Methods of use: snorting, smoking, subcutaneous, iv
- Dangerous drug (iv, smoking). cardiac and cerebrovascular diseases

# Cocain-related Disorders II.

- **Comorbidity:**
  - Mood disorders
  - Alcohol-related disorders
  - Anxiety disorders
  - Personality disorders
  - Attention-deficit/hyperactivity disorder
- **Etiology:**
  - Genetic factors
  - Sociocultural factors (availability)
  - Learning and conditioning
    - yields a rush, euphoria, wellbeing
    - Reinforce the drug-seeking behavior
    - Enhances sexual performances ?



# Additional Psychiatric Diagnoses among Cocaine Users Seeking Treatment

Psychiatric Diagnosis	Current Disorder	Lifetime Disorder
• Major depression	4.7	30.5
• Cyclothymia/hyperthymia	19.9	19.9
• Mania	0.0	3.7
• Hypomania	2.0	7.4
• Panic disorder	0.3	1.7
• Generalized anxiety disorder	3.7	7.0
• Phobia	11.7	13.4
• Schizophrenia	0.0	0.3
• Schizoaffective disorder	0.3	1.0
• Alcoholism	28.9	61.7
• Antisocial personality disorder—RDC	7.7	7.7
• Antisocial personality disorder—DSM-III	32.9	32.9
• Attention-deficit disorder		34.9



# Cocain-related Disorders III.

- Neuropharmacology:
  - Competitive blockade of dopamine reuptake
  - Increases the concentration of the dopamine in the synaptic cleft
  - Increased activation of D1 and D2 receptors
  - Blocks the reuptake of norepinephrine and serotonin
  - Decrease the CBF
  - Behavioral effects are felt immediately, but it last a brief time (30-60 minutes)
  - Repeated doses for maintain intoxication
  - Powerful addictive qualities
    - Psychological dependence after a single use
    - Crack: 1-2 experience can cause craving (violence)

# DSM-IV-TR Diagnostic Criteria for Cocaine Intoxication

- A. Recent use of cocaine.
- B. Clinically significant maladaptive behavioral or psychological changes (e.g., euphoria or affective blunting; changes in sociability; hypervigilance; interpersonal sensitivity; anxiety, tension, or anger; stereotyped behaviors; impaired judgment; or impaired social or occupational functioning) that developed during, or shortly after, use of cocaine.
- C. Two (or more) of the following, developing during, or shortly after cocaine use:
  - (1) tachycardia or bradycardia
  - (2) pupillary dilation
  - (3) elevated or lowered blood pressure
  - (4) perspiration or chills
  - (5) nausea or vomiting
  - (6) evidence of weight loss
  - (7) psychomotor agitation or retardation
  - (8) muscular weakness, respiratory depression, chest pain, or cardiac arrhythmias
  - (9) confusion, seizures, dyskinesias, dystonias, or coma
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

# DSM-IV-TR Diagnostic Criteria for Cocaine Withdrawal

- A. Cessation of (or reduction in) cocaine use that has been heavy and prolonged.
- B. Dysphoric mood and two (or more) of the following physiological changes, developing within a few hours to several days after Criterion A:
  - (1) fatigue
  - (2) vivid, unpleasant dreams
  - (3) insomnia or hypersomnia
  - (4) increased appetite
  - (5) psychomotor retardation or agitation
- C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

- **Cocaine intoxication delirium**
  - High doses
  - Mixed with other psychoactive substances
  - Preexisting brain disorder
- **Cocaine-induced Psychotic Disorder**
  - Hallucinations and delusions are common
  - Depends on dose, duration of use, method of use, the user's sensitivity, sex
  - Paranoid delusions, auditory hallucinations
  - „sensation of bugs” (crawling beneath the skin)
  - Inappropriate behavior (violent, homicidal actions)
- **Cocaine-induced Mood Disorder, Anxiety Disorder, Sexual disorder (delay orgasm, aphrodisiac) Sleep disorder**



# Adverse effects of cocaine

- Nasal congestion
- Inflammations, infections
- Bleeding
- Ulceration of nasal mucosa
- Lung damage (smoking)
- Embolism
- Acute dystonia, tics
- Migraine-like headache
- Cerebrovascular effects: nonhemorrhagic infarctions (vasoconstriction)
- Seizures
- Cardiac effects: AMI, arrhythmias, cardiomyopathies
- Death: seizures, respiratory depression, stroke, AMI

# Hallucinogen-related Disorders

- Psychedelics, psychotomimetics
  - Many natural and some synthetic substances
  - Hallucinations
  - loss of contact with reality
  - Expanded, heightened consciousness
  - No medical use
  - High abuse potential
  - Long-term use is not common
  - No physical addiction – psychological dependence
  - Ingested by inhalation, smoking, iv.
- Epidemiology:
  - Most common among 15-35 years of age
  - 10 % of persons had used at least once (US)
  - Cultural and other factors

# Hallucinogens

- LSD (lysergic acid diethylamide)
  - A. Hoffman (1938)
  - fungus in rye yields lysergic acid
- Mescaline (Peyote cactus, *L. williamsii*)
- Psilocybine (mushroom)
- Nutmeg, mace
- MDA (methylene-dioxyamphetamine)
- MDMA (methylene-dioxymethamphetamine)

## Neuropharmacology:

- Serotonergic system
  - LSD: partial agonist on postsynaptic 5-HT receptors
- Rapid tolerance (but reverses quickly)
- No withdrawal symptoms, psychological dependence

„**Bad trip**“: adverse effect, panic-like symptoms or psychotic symptoms (Hallucinogen-induced Psychotic Disorder)

# DSM-IV-TR Diagnostic Criteria for Hallucinogen Intoxication

- A. Recent use of a hallucinogen.
- B. Clinically significant maladaptive behavioral or psychological changes that developed during, or shortly after, hallucinogen use.
- C. Perceptual changes occurring in a state of full wakefulness and alertness (e.g., subjective intensification of perceptions, depersonalization, derealization, illusions, hallucinations, synesthesias) that developed during, or shortly after, hallucinogen use.
- D. Two (or more) of the following signs, developing during, or shortly after, hallucinogen use:
  - (1) pupillary dilation
  - (2) tachycardia
  - (3) sweating
  - (4) palpitations
  - (5) blurring of vision
  - (6) tremors
  - (7) incoordination
- E. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

# DSM-IV-TR Hallucinogen-Related Disorders

## *Hallucinogen use disorders*

**Hallucinogen dependence**

**Hallucinogen abuse**

## *Hallucinogen-induced disorders*

**Hallucinogen intoxication**

**Hallucinogen persisting perception disorder (flashbacks)**

**Hallucinogen intoxication delirium**

**Hallucinogen-induced psychotic disorder, with delusions**

*Specify if: With onset during intoxication*

**Hallucinogen-induced psychotic disorder, with hallucinations**

*Specify if: With onset during intoxication*

**Hallucinogen-induced mood disorder**

*Specify if: With onset during intoxication*

**Hallucinogen-induced anxiety disorder**

*Specify if: With onset during intoxication*

**Hallucinogen-related disorder not otherwise specified**

# DSM-IV-TR Diagnostic Criteria for Hallucinogen Persisting Perception Disorder (Flashbacks)

- A. The reexperiencing, following cessation of use of a hallucinogen, of one or more of the perceptual symptoms that were experienced while intoxicated with the hallucinogen (e.g., geometric hallucinations, false perceptions of movement in the peripheral visual fields, flashes of color, intensified colors, trails of images of moving objects, positive afterimages, halos around objects, macropsia, and micropsia).
- B. The symptoms in Criterion A cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The symptoms are not due to a general medical condition (e.g., anatomical lesions and infections of the brain, visual epilepsies) and are not better accounted for by another mental disorder (e.g., delirium, dementia, schizophrenia) or hypnopompic hallucinations.

# Inhalant-related Disorders

- Solvents, Glues, Adhesives, Aerosol propellants, Paint thinners, Fuels, Lighter fluid

CNS depressants

Tolerance can develop – withdrawal is mild

Alcohol-like effects: enhancing

GABA system, membrane fluidation

Easily available, legal,  
inexpesive ⇒ poor and  
young persons

80% users are male

Antisocial personality disorder



# DSM-IV-TR Inhalant-Related Disorders

## ***Inhalant use disorders***

**Inhalant dependence**

**Inhalant abuse**

## ***Inhalant-induced disorders***

**Inhalant intoxication**

**Inhalant intoxication delirium**

**Inhalant-induced persisting dementia**

**Inhalant-induced psychotic disorder, with delusions**

*Specify if: With onset during intoxication*

**Inhalant-induced psychotic disorder, with hallucinations**

*Specify if: With onset during intoxication*

**Inhalant-induced mood disorder**

*Specify if: With onset during intoxication*

**Inhalant-induced anxiety disorder**

*Specify if: With onset during intoxication*

**Inhalant-related disorder not otherwise specified**



# DSM-IV-TR Diagnostic Criteria for Inhalant Intoxication

- A. Recent intentional use or short-term, high-dose exposure to volatile inhalants (excluding anesthetic gases and short-acting vasodilators).
- B. Clinically significant maladaptive behavioral or psychological changes (e.g., belligerence, assaultiveness, apathy, impaired judgment, impaired social or occupational functioning) that developed during, or shortly after, use of or exposure to volatile inhalants.
- C. Two (or more) of the following signs
  - (1) dizziness
  - (2) nystagmus
  - (3) incoordination
  - (4) slurred speech
  - (5) unsteady gait
  - (6) lethargy
  - (7) depressed reflexes
  - (8) psychomotor retardation
  - (9) tremor
  - (10) generalized muscle weakness
  - (11) blurred vision or diplopia
  - (12) stupor or coma (13) euphoria

# Nicotine-related disorders

- 1 billion smokers worldwide
- 60% of direct health care costs
- Kills more than 3 million people per year
- Psychiatric patients
  - Bipolar 70%
  - Schizophrenia 90%
  - Substance use disorders 70%
  - Patients with depressive or anxiety disorders are less successful to quit smoking
- Nicotine:
  - Agonist at the nicotinic subtype of ACh receptors
  - Activating the dopamine reward system
  - Stimulatory effects

# DSM-IV-TR Diagnostic Criteria for Nicotine Withdrawal

- A. Daily use of nicotine for at least several weeks.
- B. Abrupt cessation of nicotine use, or reduction in the amount of nicotine used, followed within 24 hours by four (or more) of the following signs:
  - (1) dysphoric or depressed mood
  - (2) insomnia
  - (3) irritability, frustration, or anger
  - (4) anxiety
  - (5) difficulty concentrating
  - (6) restlessness
  - (7) decreased heart rate
  - (8) increased appetite or weight gain
- C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.



# Opioid-related disorders

- Used for at least 3500 years
- Crued opium or alcoholic solutions
- Morphine (1806), Codeine (1832)
- Medical use
- Heroin (diacetylmorphine)
  - Introduced as a treatment for morphine addiction
  - More potent
  - Crosses faster the blood-brain barrier
  - More addictive
  - Lifetime users. 2 million (US)
  - Current users 6-800.000



# Opioids

## Proprietary Name

## Trade Name

Morphine

Heroin (diacetylmorphine)

Hydromorphone (dihydromorphinone)

Oxymorphone (dihydrohydroxymorphinone)

Levorphanol

Methadone

Meperidine (pethidine)

Fentanyl

Codeine

Hydrocodone (dihydrocodeinone)

Drocode (dihydrocodeine)

Oxycodone (dihydrohydroxycodeinone)

Propoxyphene

Buprenorphine

Pentazocine

Nalbuphine

Butorphanol

Dilaudid

Numorphan

Levo-Dromoran

Dolophine

Demerol, Pethadol

Sublimaze

Hycodan, others

Synalgos-DC, Compal

Roxicodone, OxyContin, Percodan, Percocet

Darvon, others

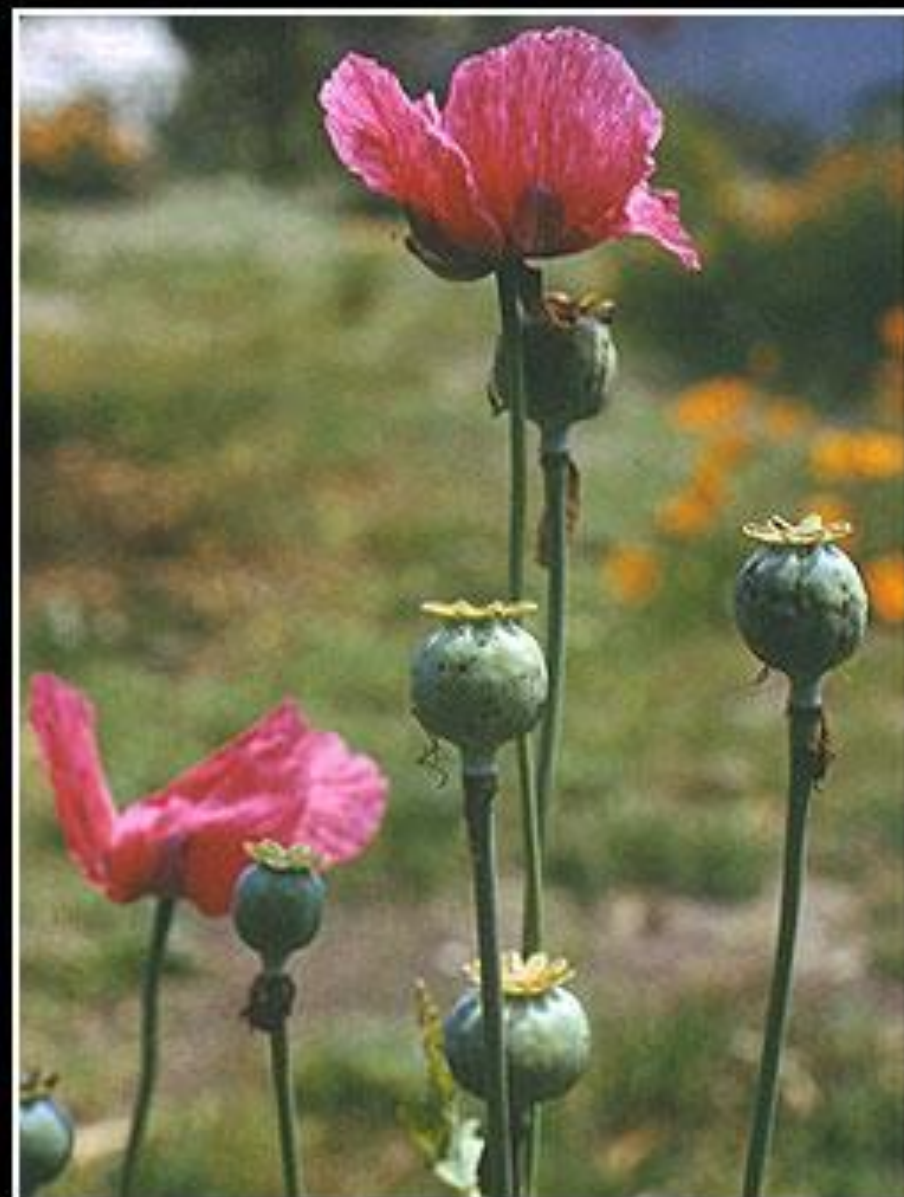
Buprenex

Talwin

Nubain

Stadol





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# Opioid-related Disorders

- Neuropharmacology
  - Opioid receptors:
    - $\mu$  receptors: analgesia, respiratory depression, constipation, dependence
    - $\kappa$  receptors: analgesia, diuresis, sedation
    - $\delta$  receptors: analgesia
  - Endogenous opioids:
    - Endorphines
    - Enkephalines
    - Neural transmission
    - Pain suppression
    - VTA: activating dopaminergic neurons
  - Tolerance:
    - 60 mg morphine can be fatal for a naive person
    - 200-300mg morphine is needed for a cancer patient





# DSM-IV-TR Opioid-Related Disorders

## Opioid use disorders

Opioid dependence and Opioid abuse

## Opioid-induced disorders

Opioid intoxication

*Specify if:* With perceptual disturbances

## Opioid withdrawal

## Opioid intoxication delirium

## Opioid-induced psychotic disorder, with delusions

*Specify if:* With onset during intoxication

## Opioid-induced psychotic disorder, with hallucinations

*Specify if:* With onset during intoxication

## Opioid-induced mood disorder

*Specify if:* With onset during intoxication

## Opioid-induced sexual dysfunction

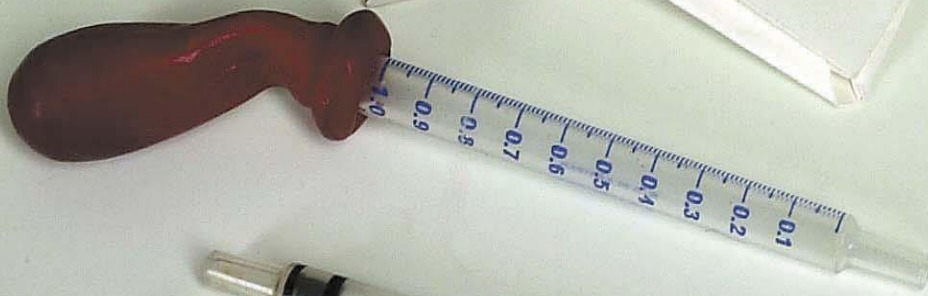
*Specify if:* With onset during intoxication

## Opioid-induced sleep disorder

*Specify if:* With onset during intoxication With onset during withdrawal

# DSM-IV-TR Diagnostic Criteria for Opioid Intoxication

- A. Recent use of an opioid.
- B. Clinically significant maladaptive behavioral or psychological changes (e.g., initial euphoria followed by apathy, dysphoria, psychomotor agitation or retardation, impaired judgment, or impaired social or occupational functioning) that developed during, or shortly after, opioid use.
- C. Pupillary constriction (or pupillary dilation due to anoxia from severe overdose) and one (or more) of the following signs, developing during, or shortly after, opioid use:
  - (1) drowsiness or coma
  - (2) slurred speech
  - (3) impairment in attention or memory
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder. *Specify* if: **With perceptual disturbances**



# DSM-IV-TR Diagnostic Criteria for Opioid Withdrawal

- A. Either of the following:
  - (1) cessation of (or reduction in) opioid use that has been heavy and prolonged (several weeks or longer)
  - (2) administration of an opioid antagonist after a period of opioid use
- B. Three (or more) of the following, developing within minutes to several days after Criterion A:
  - (1) dysphoric mood
  - (2) nausea or vomiting
  - (3) muscle aches
  - (4) lacrimation or rhinorrhea
  - (5) pupillary dilation, piloerection, or sweating
  - (6) diarrhea
  - (7) yawning
  - (8) fever
  - (9) insomnia
- C. The symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.



# Phencyclidine-Related disorders

- PCP, „angel dust”,
- anaesthetic (human and veterinary)
- Ketamine
- Similar effects like hallucinogens
- More dangerous: behavioral, psychological, neurological toxicity
- Inexpensive, easy to synthesize
- Tolerance
- Physical dependence are rare
- Model of schizophrenia
  - Antagonist of NMDA subtype of glutamate receptors
  - Activates the dopaminergic neurons of the VTA

# DSM-IV-TR Phencyclidine-Related Disorders

## **Phencyclidine use disorders**

**Phencyclidine dependence and abuse**

## **Phencyclidine-induced disorders**

### **Phencyclidine intoxication**

*Specify if: With perceptual disturbances*

### **Phencyclidine intoxication delirium**

### **Phencyclidine-induced psychotic disorder, with delusions**

*Specify if: With onset during intoxication*

### **Phencyclidine-induced psychotic disorder, with hallucination**

*Specify if: With onset during intoxication*

### **Phencyclidine-induced mood disorder**

*Specify if: With onset during intoxication*

### **Phencyclidine-induced anxiety disorder**

*Specify if: With onset during intoxication*

### **Phencyclidine-related disorder not otherwise specified**

# DSM-IV-TR Diagnostic Criteria for Phencyclidine Intoxication

- A. Recent use of phencyclidine (or a related substance).
- B. Clinically significant maladaptive behavioral changes (e.g., belligerence, assaultiveness, impulsiveness, unpredictability, psychomotor agitation, impaired judgment, or impaired social or occupational functioning) that developed during, or shortly after, phencyclidine use.
- C. Within an hour (less when smoked, "snorted," or used intravenously), two (or more) of the following signs:
  - (1) vertical or horizontal nystagmus
  - (2) hypertension or tachycardia
  - (3) numbness or diminished responsiveness to pain
  - (4) ataxia
  - (5) dysarthria
  - (6) muscle rigidity
  - (7) seizures or coma
  - (8) hyperacusis

*Specify if:* **With perceptual disturbances**



# Sedative, Hypnotic and Anxiolytic Related Disorders

- Benzodiazepines
- Barbiturates
- Barbituratelike substances
  
- Antiepileptics
- Muscle relaxants
- Anesthetics, adjuvants
- Drugs of this class have a cross-tolerance with alcohol
- Physical and psychological dependency
- Withdrawal syndrome

# DSM-IV-TR Diagnostic Criteria for Sedative, Hypnotic, or Anxiolytic Intoxication

- A. Recent use of a sedative, hypnotic, or anxiolytic.
- B. Clinically significant maladaptive behavioral or psychological changes (e.g., inappropriate sexual or aggressive behavior, mood lability, impaired judgment, impaired social or occupational functioning) that developed during, or shortly after, sedative, hypnotic, or anxiolytic use.
- C. One (or more) of the following signs, developing during, or shortly after, sedative, hypnotic, or anxiolytic use:
  - (1) slurred speech
  - (2) incoordination
  - (3) unsteady gait
  - (4) nystagmus
  - (5) impairment in attention or memory
  - (6) stupor or coma
- D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

# DSM-IV-TR Diagnostic Criteria for Sedative, Hypnotic, or Anxiolytic Withdrawal

- A. Cessation of (or reduction in) sedative, hypnotic, or anxiolytic use that has been heavy and prolonged.
- B. Two (or more) of the following, developing within several hours to a few days after criterion A:
  - (1) autonomic hyperactivity (e.g., sweating or pulse rate greater than 100)
  - (2) increased hand tremor
  - (3) insomnia
  - (4) nausea or vomiting
  - (5) transient visual, tactile, or auditory hallucinations or illusions
  - (6) psychomotor agitation
  - (7) anxiety
  - (8) grand mal seizures