Antidepressants
Affective disorders - mental illnesses characterized by pathological changes in mood (not thought – compare with schizophrenia)

1. **Unipolar disorders**
   - *Depression* – pathologically depressed mood (lifetime prevalence up to 17%)
   - *Mania* – excessive elation and accelerated psychomotoric activity (rare)

2. **Bipolar disorder** (manic-depressive illness) – „cycling mood“
   - = severe highs (mania, event. hypomania) and lows (major depressive episodes)
   - prevalence 1-5%, life-time illness, stronger genetic background
Depression

- Depression afflicts approximately 5% - 10% of the population, 1-2% with bipolar disorder.

- Suicide from depression is 25-30% of depressed population.

- Depression 2-3 X higher in women.

- 70% of patients have response to drugs.
Clinical symptoms of depression

- Loss of pleasure (anhedonia)
- Loss of energy
- Social withdrawal
- Psychomotor retardation or agitation
- Insomnia
- Loss of appetite
- Decreased hygiene
- Crying spells
- Difficulty concentrating
- Sad thoughts/thoughts of suicide
- Hopelessness
- Helplessness
- Guilt/shame
Biological Theories

Genetic Theory
Disordered genes predispose people to depression or bipolar disorder

Neurotransmitter theories
Dysregulation of neurotransmitters and their receptors

Neurophysiological abnormalities
Altered brain-wave activities affect mood

Neuroendocrine abnormalities
Chronic hyperactivity in the hypothalamic-pituitary-adrenal axis and slow return to baseline after stressor affect the functioning of neurotransmitters.
first great theory - role of monoamine neurotransmitters (NE, 5-HT)

deficiency of neurotransmitters – depression

simplistic theory
SEROTONIN - A key player

- Serotonin has widespread distribution and density of innervation in CNS (mood, memory, pleasure, aggression, hypothalamic control)

- Alterations of serotonin in depressed drug-free patients: The reduction point of view
  - decreased 5-HT levels in CSF
  - increased amounts of 5-HT2 receptors in brain
  - reduced levels of plasma tryptophan
Cont.

- Blunted neuroendocrine responses to the serotonin releasing drug fenfluramine
- Efficacy of SSRI’s in treating depression
- Loss of SSRI efficacy with tryptophan depletion
- Increased presynaptic $\alpha_2$ noradrenergic receptor sensitivity = greater reduction in 5-HT release
problem - timing of antidepressant effect on neurotransmitters is far from the timing of the antidepressant effect on mood
Onset of action of antidepressants. Synaptic effects and side effects of antidepressants begin before therapeutic effects are observed.
newer theories - role of neurotransmitter receptors

disturbancies in signal transduction
The purpose of antidepressants is the increase the neurotransmitters in the synapse
MAO inhibitors (IMAO)

- first antidepressive agents used clinically
- "classical" (e.g. tranylcypromine) ⇒ irreversible, nonselective inhibition of MAO-A and MAO-B
- for antidepressive effects - inhibition of MAO-A
- 2-3 weeks for antidepressive action
- use of "classical" MAOI is now limited - side effects, interactions (food, drugs)

- tyramine (cheese, red wine, beer) is normally inactivated by MAO-B in the gut

- tyramine causes release of stored atecholamines
  - tachycardia, hypertension,
  - headache, cardiac arrhythmias

- patients must avoid tyramine-containing foods
## MAOI Dietary Restrictions

<table>
<thead>
<tr>
<th>Food</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Tyramine Content—Not Permitted</strong></td>
<td></td>
</tr>
<tr>
<td>Aged, matured cheeses (unpasteurized)</td>
<td>Cheddar, bleu, Swiss</td>
</tr>
<tr>
<td>Smoked or pickled meats, fish or poultry</td>
<td>Herring, sausage, corned beef, salami, pepperoni</td>
</tr>
<tr>
<td>Aged/fermented meats, fish, or poultry</td>
<td>Chicken or beef-liver pate, game</td>
</tr>
<tr>
<td>Yeast extracts</td>
<td>Brewer's yeast</td>
</tr>
<tr>
<td>Red wines</td>
<td>Chianti, burgundy, sherry, vermouth</td>
</tr>
<tr>
<td>Italian broad beans</td>
<td>Fava beans</td>
</tr>
<tr>
<td><strong>Moderate Tyramine Content—Limited Amounts Allowed</strong></td>
<td></td>
</tr>
<tr>
<td>Meat extracts</td>
<td>Bouillon, consomme</td>
</tr>
<tr>
<td>Pasteurized light and pale beers</td>
<td></td>
</tr>
<tr>
<td>Ripe avocado</td>
<td></td>
</tr>
<tr>
<td><strong>Low Tyramine Content—Permissible</strong></td>
<td></td>
</tr>
<tr>
<td>Distilled spirits (in moderation)</td>
<td>Vodka, gin, rye, scotch</td>
</tr>
<tr>
<td>American and mozzarella cheeses</td>
<td>Cottage cheese, cream cheese</td>
</tr>
<tr>
<td>Chocolate and caffeine beverages</td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td>Figs, raisins, grapes, pineapple, oranges</td>
</tr>
<tr>
<td>Soy sauce</td>
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<tr>
<td>Yogurt, sour cream</td>
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</tbody>
</table>
**RIMA** (Reversible Inhibitors of MAO-A)

**Moclobemide**
- reversible inhibition of MAO-A
- inhibition of deamination of 5-HT, NE, D

**PK**
- good absorption in GIT
- 50% bound to plasma albumine
- 95% excreted in urine as an inactive metabolites

**Side effects**
- insomnia, nausea, headache, dizziness, desorientation, nervousness
- effect on CVS in combination with tyramine - less important
Tricyclic antidepressants (TCA)

- Many years ⇒ drug of choice
- Inhibition of re-uptake ⇒ increase of NE, 5-HT
- Also blockade of M, H₁, α₁ receptors
- 2-3 weeks for antidepressive action
- M-receptors ⇒ dry mouth, urine retention, constipation, blurred vision
- M⁺α₁-receptors - tachycardia, hypertension, postural hypotension,
- H₁-receptors ⇒ sedative effects, body weight gain
MECHANISM OF ACTION

Pharmacological properties:

Therapeutic effect
- Block presynaptic NE reuptake transporter
- Block presynaptic 5-HT reuptake transporter

Side effects
TCAs block other receptors:
- Muscarinic
- α1
- Histamine 1
Imipramine

- antidepressive effect after one week therapy
- for long term effect - 3 or more weeks of application

PK
- good absorption from GIT
- 90% bound to albumine
- main metabolite $\Rightarrow$ desipramine $\Rightarrow$ biologically active
- excreted by urine as a glucuronide

Side effects
- dry mouth, urine retention, constipation, blurred vision
- tachycardia, hypertension, postural hypotension,
- insomnia, anorexia, hallucination
TCA TOXICITIES

- lowers threshold for convulsions
- cardiac arrhythmias
- cardiac conduction defects
Selective Serotonin Reuptake Inhibitors (SSRI)

- most common prescribed antidepressants today
- inhibition of 5-HT re-uptake
- increase of 5-HT $\Rightarrow$ effect on postsynaptic 5-HT and 5-HT$_{1A}$ presynaptic receptors
- stimulation of 5-HT$_{1A}$ receptors $\Rightarrow$ „down-regulation“ $\Rightarrow$ lower effect on 5-HT release from presynaptic neurons
- inhibition of NE reuptake $\downarrow$
- blockade of $\alpha_1$, H$_1$ alebo M- receptors $\downarrow$ $\Rightarrow$ cardotoxic, hypotensive, sedative effects
MECHANISM OF ACTION

[Image: Diagram of neurotransmitter release with SSRI indicated.]
SIDE effects of SSRI’s

- nausea, GI disturbances
- headache
- nervousness
- insomnia
- some sedation
- anorgasmia/impotence
- possible fatal interaction with MAOI’s
Serotonin syndrome

- A potentially fatal interaction when SSRI’s and MAOI’s are combined

- Symptoms:
  - autonomic instability (labile HR/BP)
  - hyperthermia
  - rigidity and myoclonus
  - confusion, delirium
  - seizures
  - coma
**Fluoxetine**

- in depression of different etiology

**PK**

- food prolongs time of absorption
- 95% to plasma albumine
- metabolised in the liver → major metabolite (norfluoxetine) → similar effect as a fluoxetine

**Side effects**

- lower incidence and intensity
- GIT - nausea, anorexia,
- CNS - insomnia, tremor, headache, vertigo
- CVS - orthostatic hypotension
SSRI – cont.

Citalopram

- high selective for 5-HT
- no affinity to M, H₁ a α₁ receptors
- depression, panic fear, bulimia, anorexia nervosa

PK

- bioavailability - 80%,
- bound to albumine - 80%
- metabolised in the liver, no of metabolits has effect as a parent drug
- excreted via kidney

Side effects

- nausea, insomnia, in man - sexual disturbancies
Fluvoxamine

- bioavailability cca 53%
- other as a citalopram
Newer antidepressants
Norepinephrine Reuptake Inhibitors (NRI)

**Reboxetine**
- introduced in 1997
- inhibition of NE re-uptake
- minimal effect on 5-HT a D
- depression, narcolepsy, panic fear
- 98% bound to $\alpha_1$ acid glycoproteine

**Side effects**
- well tolerated
- obstipation, dry mouth, urine retention, insomnia, tachycardia
Bupropion

- weak inhibitor of D and NE re-uptake
- major metabolite - strong NE re-uptake inhibitor
- suitable for patients with intolerability or low response to SSRI
- suitable to suppress withdrawal symptoms in nicotine-dependent people
- contraindicated in epileptic patients - proconvulsive effect
Serotonin and Norepinephrine Reuptake Inhibitors (SNRI)

- action similar to TCA - NE and 5-HT re-uptake inhibition
- no effects on M, H₁ and α₁-adrenergic receptors

**Venlafaxine**

- low doses ⇒ 5-HT, moderate doses ⇒ NA, high doses ⇒ D
- metabolised in the liver - O-desmethylvenlafaxine - active metabolit

Side effects

- nausea, constipation, somnolece, nervousness, headache
- serotonine syndrome
blockade of presynaptic $\alpha_2$-receptors

$\alpha_2$-adrenergic autoreceptors $\Rightarrow$ regulation of NE release

$\alpha_2$-adrenergic heteroreceptors (on serotoninergic neurons) $\Rightarrow$ regulation of 5-HT release

blockade of $\alpha_2$-receptors $\Rightarrow$ ↑ release of NE a 5-HT
**NaSSA – cont.**

**Mirtazapine**
- high affinity to $\alpha_2$-receptors
- antagonist of $5-HT_2$, a $5-HT_3$ and $H_1$-receptors

**Side effects**
- somnolence, dry mouth, increase of apetite, body weight gain, constipation, serotonine syndrome

**Mianserine**
- selective antagonist of presynaptic $\alpha_2$-adrenergic receptors
- partial effect on $\alpha_1$, $5-HT_2$, $5-HT_3$ and $H_1$-receptors
- main metabolites $\Rightarrow$ biological activity

**Side effects**
- hypersensitivity, nausea, tremor
Mania
Symptoms of mania

- increased energy (buying, phoning, sex)
- pressured speech, talkativeness
- decreased sleep
- drunkenness
- combative, dangerous behavior
- racing thoughts
- impulsive actions and decisions
- elevated mood
- euphoria
- grandiosity
- irritability/hostility (easily angered)
Anti-manic therapy

*Lithium*

- used more than 50 years
- mechanism of action?

- Possible mechanism is the reduction of neuronal PI second messenger resulting in reduced response of neurons to ACh and NE
Clinical pharmacology

- primary therapy for mania
- a narrow therapeutic window
- absolutely necessary to monitor serum level (trough level approx. 5 days after initial dose)
- solely eliminated by kidney, therefore assess patient’s kidney function
Lithium – cont.

Side effects

- intensity depends on plasma concentration
- first days of therapy ⇒ tremor of hands, urination, nausea, thirst
- first signs of intoxication ⇒ vomiting, diarrhea, muscle weakness, loss of coordination
- higher doses ⇒ tinnitus, blurred vision, polyuria
- plasmatic concentration over 3,0 mmol.l⁻¹
Lithium – cont.

- **CNS**: tremor, convulsions, epileptiformic seizures, urine and feces incontinence, tinitus, halucination
- **CVS**: dysrhytmias, hypotension, periferal circulatory colaps, bradycardia
- **GIT**: anorexia, nausea, vomiting, diarrhea, gastritis, abdominal pain,
- **Urogenital tract**: glycosuria, albuminuria, polyuria
- **Skin**: acne, psoriasis, pruritus, skin ulcus, angioedema, alopecia
- **Other**: blurred vision, dry mouth, loss of body weight, leucocytosis, headache, fever
Warnings

- renal or cardiovascular diseases, dehydratation, hyponatremia increase risk of toxicity
- water 2-3 l/day is recomended
- suspect teratogen
Other medications

- Anticonvulsants: carbamazepine and valproic acid for rapid cyclers
- Olanzapine approved for treatment of mania
- St. John’s Wort: questionable efficacy, but high potential for drug-drug interactions
Anxiolytics
(antianxiety drugs)
What is anxiety?

Physical and emotional distress which interfere with normal life.
Common emotional symptoms of anxiety

- irrational and excessive fear and worry
- irritability
- restlessness
- trouble concentrating
- feeling tense
Common physical symptoms of anxiety

- sweating
- tachycardia
- stomach upset
- shortness of breath
- frequent urination or diarrhea
- sleep disturbances (insomnia)
- fatigue
Benzodiazepines (BDZ)

5-HT drugs
Mechanism of action

- BDZ receptor linked to GABA-A receptor complex (bound to Cl\(^{-}\) channels)
  - GABA: an inhibitory neurotransmitter
  - BDZ enhance GABA effect
- open Cl\(^{-}\) channels in response to GABA activation ⇒ hyperpolarization, decreased neuronal firing
- Effects: antianxiety, sedative, hypnotic, anticonvulsant, muscle-relaxant
BDZ receptors

GABA<sub>A</sub> Receptor Complex

- Barbiturates
- GABA
- Steroids
- BZ
- ETOH
- OUTSIDE
- INSIDE
- P
- CL<sup>-</sup>

BZ = BENZODIAZEPINES
ETOH = ETHANOL (ALCOHOL)
BZD: Pharmacokinetics

- **fast cross BBB**: rapid onset of action
- **biotransformation and half-life:**
  - **hepatic oxidation**: long-$t_{1/2}$, active metabolites
  - **glucuronidation**: short-$t_{1/2}$, no active metab.
BZD: Adverse Effects

- sedation, CNS depression
  - worse if combined with EtOH

- behavioral disinhibition
  - irritability, excitement, aggression (<1%),

- psychomotor & cognitive impairment
  - coordination, attention (driving)
  - ataxia, confusion
BZD: Adverse Effects

- Overdose: Rare fatalities if BZD alone
- Severe CNS and Respiratory Depression if combined with:
  - alcohol
  - barbiturates
  - narcotics
  - TCA

flumazenil
BZD: Withdrawal

- worse if stop abruptly
- symptoms
  - diaphoresis, ↑pulse, ↑BP
  - tremor, lethargy, dizziness, headaches
  - restlessness, insomnia, irritability, anxiety
  - depersonalization, perceptual disturbances
- also: depression, tinnitus, delirium, panic, hallucinations, abnormal muscular activity.
5-HT$_{1A}$ agonists
Buspirone

- has strong anxiolytic properties
- almost no sedative effect, drowsiness or hypnosis
- minimal amnesia and dementia
- does not potentiate other sedatives
- no abuse potential
- it is a weak 5-HT agonist
- has both antianxiety and antidepressant effects
- metabolized very quickly, grapefruit juice increases effect
- slow onset of action
Uses of buspirone

- as anxiolytic in mild anxiety & generalized anxiety disorders.
- not effective in severe anxiety/panic disorder.
Beta Blockers

- propranolol – atenolol
- act by blocking peripheral sympathetic system.
- reduce somatic symptoms of anxiety.
- decrease BP & slow HR.
- used in social phobia.
- are less effective for other forms of anxiety
Doxepin- imipramine

- act by reducing uptake of 5HT & NA.
- used for anxiety especially associated with depression.
- effective for panic attacks.
- delayed onset of action (weeks).
- dry mouth, postural hypotension, sexual dysfunction, weight gain.
## Conclusion of anxiolytics

<table>
<thead>
<tr>
<th>Classes of anxiolytics</th>
<th>USES</th>
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<tr>
<td>Benzodiazepines</td>
<td>Generalized anxiety disorders, OCD, phobia, panic attack</td>
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<tr>
<td>SSRIs (Fluoxetine)</td>
<td>Generalized anxiety disorders, OCD, phobia, panic attack</td>
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<td>Tricyclic antidepressants (doxepin, imipramine)</td>
<td>anxiety with depression. panic attacks</td>
</tr>
<tr>
<td>5HT1A agonists (Buspirone)</td>
<td>Mild anxiety. Not effective in panic attack</td>
</tr>
<tr>
<td>Beta blockers (propranolol, atenolol)</td>
<td>Phobia (social Phobia)</td>
</tr>
<tr>
<td>MAO inhibitors phenelzine</td>
<td>Panic attack, phobia</td>
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</tbody>
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## Conclusion of anxiolytics

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<th>Classes of anxiolytics</th>
<th>Adverse effects</th>
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<tr>
<td>Benzodiazepines</td>
<td>Ataxia, confusion, dependence, tolerance, withdrawal symptoms,</td>
</tr>
<tr>
<td>SSRIs <em>(Fluoxetine)</em></td>
<td>weight gain, sexual dysfunction</td>
</tr>
<tr>
<td></td>
<td>Dry mouth</td>
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<tr>
<td>Tricyclic antidepressants  <em>(doxepin, imipramine)</em></td>
<td>weight gain, sexual dysfunction, atropine like actions</td>
</tr>
<tr>
<td>5HT1A agonists  <em>(Buspirone)</em></td>
<td>Minimal adverse effects</td>
</tr>
<tr>
<td>Beta blockers  <em>(propranolol, atenolol)</em></td>
<td>Hypotension</td>
</tr>
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</table>
PSYCHOSTIMULANTS
Effects

- Behavioral manifestations of CNS stimulation
- Mild elevation in alertness, decrease in drowsiness and lessening of fatigue (analeptic effect)
- Increased nervousness and anxiety - convulsions.
Methylxantines

- **Caffeine:**
  - Coffee (100-150 mg/cup)
  - Tea (30-40 mg/cup)
  - Cocoa (15-18 mg/cup)

- **Theophylline:** Tea and cocoa

- **Theobromine:** Cocoa
Mechanisms of action

- Increase cyclic nucleotide concentration – PDE inhibition
- Blocks adenosine receptors
Caffeine

- commonly found in coffee, tea, soft drinks, chocolate and a wide variety of over-the-counter medications
- it is legal to buy and easily accessible
- caffeine is a physically addictive drug
Pharmacological activity/adverse effects

- **Low Doses:** 50-250mg/caffeine (oral doses) - increase mental alertness, decrease drowsiness, lessen fatigue
- **Larger Doses:** 250-600mg/caffeine - irritability, restlessness, tremor, insomnia, headache, palpitations
- **Large Doses:** > 1000 mg - excitement, delirium, and clonic seizures
- **CVS:** Increase rate and force of the heart by directly stimulating myocardium (low doses)
- Tachycardia and arrhythmias at higher doses.
- Peripheral vasodilation - decrease blood pressure (acute administration)
- Hypotension and cardiac arrest (rapid i.v. theophylline)
Smooth Muscles: relaxes vascular smooth muscle (theophylline > caffeine)

Kidney: all xanthines are capable of producing some degree of diuresis in humans (theophylline > caffeine)

Miscellaneous: xanthines shorten clotting time by increasing tissue prothrombin and factor V.
Adverse effects

- stimulate gastric secretions in patients with ulcer
- dehydration in children due to vomiting and transient diuretic action (theophylline)
- allergic reaction (aminophylline)
- psychic dependence (caffeine)
- high doses
- emesis, convulsion,
- lethal dose is about 10 g (about 100 cups of coffee) - induces arrhythmias
Therapeutic uses

**caffeine** + plus ergot alkaloid (ergotamine):
- used to treat migraine headaches

**theophylline**:
- prophylaxis for chronic asthma
- respiratory stimulant
- bronchodilator for relief of asthmatic symptoms
Psychomotor stimulants

- Drugs of primary importance
  - Amphetamine - prototype
  - Methamphetamine
  - Methylphenidate
Characteristics

- all compounds are absorbed well orally
- large portion of untransformed amphetamine is excreted unchanged in the urine
- acidifying the urine with ammonium chloride hastens its clearance, and thus reduces its reabsorption in the renal tubules.
- overdose: hyperreflexia, tremors and convulsions
- fatalities: hyperthermia rather than cardiovascular effects
Pharmacological actions

- The primary effects of an oral dose are:
  - Wakefulness, alertness, decrease fatigue
  - Mood elevation, increased ability to concentrate
  - An increase in motor and speech activity
- Amphetamines also diminish the awareness of fatigue - person may push exertion to the point of severe damage or even death.
- stimulate the respiratory center, especially when respiration is depressed by centrally acting drugs, (barbiturates and alcohol)
- amphetamine can reverse the marked sedation and behavioral retardation resulting from reserpine-like drug
- depresses appetite by their action on the lateral hypothalamus rather than an effect on metabolic rate
Mechanisms of action

- releases monoamines at synapses in the brain and spinal cord
- inhibits neuronal uptake of monoamine
Therapeutic uses

- methylphenidate
  - attention-deficit hyperactivity disorder (ADHD)
  - narcolepsy - amphetamine or methylphenidate

- fenfluramine
  - obesity – withdrawn due to cardiotoxicity /hypertension, cardiac fibrosis
Adverse effects

- **CNS**: euphoria, dizziness, tremor, irritability, insomnia, convulsion (at higher doses), hyperthermia and coma
- **CVS**: cardiac stimulation leads to headache, palpitations, cardiac arrhythmias, anginal pain
- **other**: weight loss, psychotic reaction which are often misdiagnosed as schizophrenia.
- **addiction** - including psychical dependence, tolerance and physical dependence.
Hallucinogens
Definitions

“Substances that create gross distortions in perception without causing loss of consciousness when administered in low doses.”

“Substances that alter sensory processing in the brain, causing perceptual disturbances, changes in thought processing, and depersonalization.”
Hallucinogens …

- Are found naturally in plants and can be produced synthetically.

- Resemble 1 of 4 neurotransmitters
  - Acetylcholine
  - Catecholamines (Norepinephrine & Dopamine)
  - Serotonin
Common Hallucinogenic Effects

1) Alterations in time and space perception
2) Changes in self-awareness
3) Increase sensitivity to textures, shapes, tastes, and sounds
4) Visual disturbances (i.e. flashes of light or kaleidoscope-like patterns)
5) Hallucinations
6) Feelings of enlightenment or spiritual awakening
Categories of Hallucinogens

1) Anticholinergic
2) Catecholamine-like
3) Serotonin-like
4) Psychedelic anesthetics
Anticholinergic Hallucinogens

- Attach to AhC (Impairs learning and memory as result)
- Found in Belladonna, Nightshade, Mandrake plants
- Effects: Dry mouth, ↓ sweating, dry skin, ↑ body temperature, blurred vision, ↑ heart rate, dilated pupils, drowsiness, ↓ attention.
- High Doses = Hallucinations, paralysis of respiratory system, coma, and death.
- Examples: scopolamine, mandrake, hyoscine, hyoscyamine, and atropine.
Catecholamine-Like Hallucinogens

Mescaline
Myristin
Elemicin

Synthetic Amphetamine Derivatives
**MDMA**

- **Street Names:** Adam, Ecstasy, X, E, XTC, Blue Kisses, E bombs, Happy Pill, Smurfs, Wafers, & others
- More psychedelic than MDMA
- Synthesized in 1912
- Schedule 1 Drug in 1985
- Effects similar to MDA

**Pharmacodynamics:**
Increases levels of Norepinephrine, dopamine, & serotonin released.
MDMA Effects

- **Hallucinogenic Effects**: distortions in time & perception.

- **Stimulant Effects**: Euphoria & hyperactivity, increase blood pressure & heart rate
MDMA…The Negative Effects

- **Psychological**: depression, severe anxiety, paranoia, and sleep disturbances.

- **Physical**: muscle tension, nausea, blurred vision, rapid eye movements,

- **High doses**: sharp increase in body temperature, muscle breakdown, and kidney & cardiovascular system failure.
  - These effects also happen at low doses in combination with intense exercise or activity.

- **Long-Term**: liver damage & brain damage.
  - Brain damage due to destruction of serotonin producing neurons = therefore problems regulating mood, pain, sleep, and aggression can result.
Serotonin-like Hallucinogens

- LSD
- Psilocybin
- Psilocin
- DMT
- Bufotenine
- Ololiuqui
- Harmine
Street names

Derived from ergot alkaloids of the rye fungus.

Colorless, odorless, bitter taste.

Most potent mood & perception altering drug (can cause effects at 25 μg = in weight to a few grains of salt).

Was used to treat alcoholism, paranoia, schizophrenia, and autism.
Pharmacodynamics

- Binds to 5-HT$_2$ serotonin receptors

- Effects due to disruption of raphe nuclei (pons/medulla), which filters incoming sensory stimuli, creating surge of sensory information and overload of brain circuits.

- Effects cerebral cortex (involved in mood, cognition, and perception) & locus ceruleus (receives sensory info)
Effects

- Dilation of pupils, dizziness, dreamy detached feelings, changes in time perception, color/smells/sounds intensified, increase heart rate & blood pressure, sweating, dry mouth, hallucinations.

- At **High** doses causes nausea, tremors, & confusion.

- Moods typically depends on mood prior to use, causing those to become intensified.

- However, moods can change quickly from euphoria to terror and panic.