Schizophrenia and other psychotic disorders

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Psychosis, schizophrenia

- Psychosis:

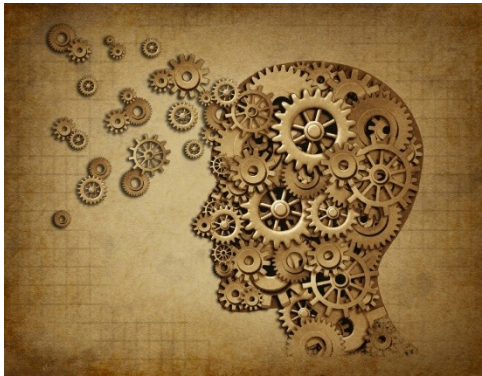
1. symptom, not illness

- halucinations, delusions, thought disorder

2. „psychoses“ = psychotic disorders (for example: schizophrenia, toxic psychosis, delusional disorder, acute polymorfic psychotic disorder, …)

- Schizophrenia:

- one of the psychoses, diagnosis



Definition of SCH

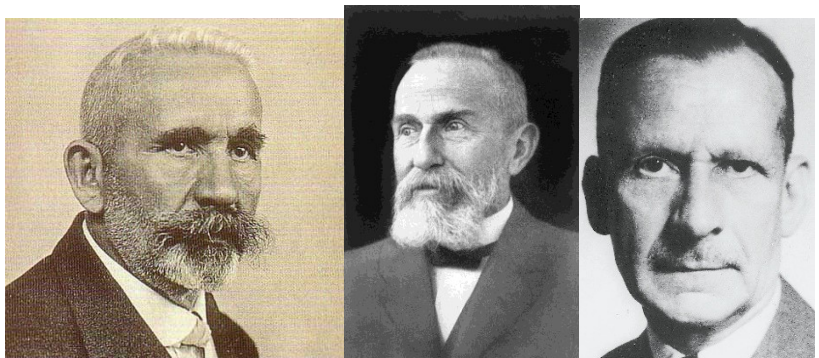
- The schizophrenic disorders are characterized in general by fundamental and characteristic distortions of thinking and perception, and affects that are inappropriate or blunted. Clear consciousness and intellectual capacity are usually maintained although certain cognitive deficits may evolve in the course of time.
- The most important psychopathological phenomena include
  - thought echo
  - thought insertion or withdrawal
  - thought broadcasting
  - delusional perception and delusions of control
  - hallucinatory voices commenting or discussing the patient in the third person
  - thought disorders
  - negative symptoms

Schizophrenia IS NOT

- Some laymen think that psychosis is „bifurcation“ of personality. That´s a false idea.
- Patients with schizophrenia can have postpsychotic changes of personality, can hear contradictory voices and can be ambivalent (all will be explained). But they don´t „live two different lives with two different personalities“.

History

- **Emil Kraepelin**: This illness develops relatively early in life, and its course is likely deteriorating and chronic; deterioration reminded dementia („Dementia praecox“), but was not followed by any organic changes of the brain, detectable at that time.
- **Eugen Bleuler**: He renamed Kraepelin’s dementia praecox as schizophrenia (1911); he recognized the cognitive impairment in this illness, which he named as a „splitting“ of mind.
- **Kurt Schneider**: He emphasized the role of psychotic symptoms, as hallucinations, delusions and gave them the privilege of „the first rank symptoms” even in the concept of the diagnosis of schizophrenia.



4 A (Bleuler) – „four“ A

- Bleuler maintained, that for the diagnosis of schizophrenia are most important the following four fundamental symptoms:
  - affective blunting
  - disturbance of association (fragmented thinking)
  - autism
  - ambivalence (fragmented emotional response)

- Bleuler thought, that they are „primary” for this diagnosis.

- The other known symptoms, hallucinations, delusions, which are appearing in schizophrenia very often also, he used to call as a “secondary symptoms”, because they could be seen in any other psychotic disease, which are caused by quite different factors — from intoxication to infection or other disease entities.

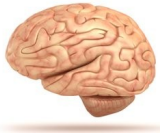
Schizophrenia - general information

- Is **heterogenous** disease – in symptoms, in course, in etiopatogenesis.
- Can disrupt almost any mental function – thinking, perception, emotions, behavior, cognitive functions; personality, …
- Usally begins in **early adultery**
- Is sometimes called „cancer of psychiatry“
- Many patients are invalidized, but 1/5 of patients have good prognosis

Symptoms

- Positive – „plus“, an excess or distortion or normal function

- Negative – „minus“, „lost“ functions



- Cognitive

- (Affective) – „secondary“, are not basic symptoms

Positive symptoms

- Halucinations
- Delusions
- Formal thought disorder
- Bizarre behaviour

Halucinations

Disturbance of **perception**

Auditory:

„hearing voices“, usual more, words or sentences, usually unplesant; commenting, imperative, giving advice; can be contradictory

Intrapsychical:

hearing own thoughts, thought broadcasting, thought insert, externalization, control

Tactile, olfactory – not so typical

Visual – not typical (typical for delirium, sometimes in toxic psychoses)

Delusions

- Disturbance of **thinking**/thought
- Delusion - a mistaken belief that is held with strong conviction
- 3 types:
- Macromanic – immortality, grandeur, inventory, erotomania, …
- Micromanic- nihilistic, autoaccusative, hypochondric, …
- **Paranoid – paranoid, persecutory, control, jealousy, dysmorfofobic, …**

Formal thought disorder

- Disorganized thinking (and speech, and behaviour)
- Organized (logical) – tangencial - disorganized

Example of disorganized thinking

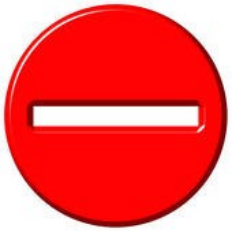
- Female patient, 28 years olf, hospitalized for the first time. Wrote many pages of text, we didn´t asked for it. She told the blue color are her thoughts, the red color are the voices of her dead father. Part of the text:

„give the cats, other rooks, and the firemen back; sirens, which are on where something is on fire; don´t be afraid, alarm“

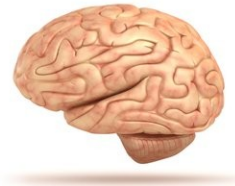
„You have tried to violate my friend, who is lying next to me, too, dissmiss and it..“

Negative symptoms

- **Alogie** – relative absence of thoughts and speech
- **Affective flattening** – little expressed emotion
- **Avoliation – apathy** – lack of initiation and persistence
- **Anhedonia** – asociality – lack of pleasure feeling
- **Attentional impairment**



Cognitive symptoms



- Impaired memory and attention

- Difficulty thinking through complicated processes, making sense of information

- Impaired ability to organize

- Poor decision-making

- Difficulty in interpreting social cues

Other symptoms

- Sleep distorsion
- Paralogia = pseudologia
- Catatonia
- Ambivalency (having simultaneous conflicting reactions, beliefs, or feelings towards some object)
- Anosognosia (they don´t accept they are ill)
- „Postpsychotic personality changes“ – they can become less active, more introversive, more hypochondrical, don´t have hobbies, feel stigmatized, are socially isolated, are not able to work, are not able to have close relationships

Symptoms

- No symptom is patognomic.
- One patient doesn´t necessarily have all groups of symptoms – positive, negative, cognitive.
- Positive symptoms are better treatable then negative and cognitive.

The Criteria of Diagnosis (ICD-10)

For the **diagnosis of schizophrenia** is necessary

- presence of one very clear symptom - from point a) to d)
- or the presence of the symptoms from at least two groups - from point e) to h)

for **one month or more**:

a) the hearing of own thoughts, the feelings of thought withdrawal, thought insertion, or thought broadcasting
b) the delusions of control, outside manipulation and influence, or the feelings of passivity, which are connected with the movements of the body or extremities, specific thoughts, acting or feelings, delusional perception
c) hallucinated voices, which are commenting permanently the behavior of the patient or they talk about him between themselves, or the other types of hallucinatory voices, coming from different parts of body
d) permanent delusions of different kind, which are inappropriate and unacceptable in given culture

The Criteria of Diagnosis

e) the lasting hallucination of every form

f) blocks or intrusion of thoughts into the flow of thinking and resulting incoherence and irrelevance of speach, or neologisms

g) catatonic behavior

h) „the negative symptoms", for instance the expressed apathy, poor speech, blunting and inappropriatness of emotional reactions

i) expressed and conspicuous qualitative changes in patient's behavior, the loss of interests, hobbies, aimlesness, inactivity, the loss of relations to others and social withdrawal

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- Diagnosis of acute schizophorm disorder (F23.2) – if the conditions for diagnosis of schizophrenia are fulfilled, but lasting less than one month
- Diagnosis of schizoaffective disorder (F25) - if the schizophrenic and affective symptoms are developing together at the same time

Types of schizophrenia

F20 Schizophrenia

F20.0 Paranoid schizophrenia

F20.1 Hebephrenic schizophrenia

F20.2 Catatonic schizophrenia

F20.3 Undifferentiated schizophrenia

F20.4 Post-schizophrenic depression

F20.5 Residual schizophrenia

F20.6 Simple schizophrenia

F20.8 Other schizophrenia

F20.9 Schizophrenia, unspecified

F20.0 Paranoid Schizophrenia

- is characterized mainly by **delusions of persecution**, feelings of passive or active **control**, feelings of intrusion, and sometimes by megalomanic tendencies also.
- The delusions are not usually systemized too much, without tight logical connections and are often combined with hallucinations of different senses, mostly with hearing voices.

Example of patient with paranoid schizophrenia

- 40 years old male patient, hospitalized few times, anosognostic.

„I want to write the complaint to the Center for human laws. I am doing nothing wrong to anyone. But „they“ are constantly disturbing me, annoying me. They don´t believe I am able to marry someone. They stare at me, I feel their sights. They yell at me, they are under the windows - at home, in the hospital, everywhere. They yell at me that I am dumb and ugly. „They“ are bad people, especially young women. They think I am a fool. I help Kájínek to be acquited, I like him. *(Kájínek is czech criminal, who had been jailed.)* I suffer from Kájinkophobia for many years. I suffer from many diseases caused by bad young women.“

psychopatology: vocal halucinations, persecutive delusions, ambivalency (to Kájínek – likes him and suffers from Kájínkophobia in the same time)

F20.1 Hebephrenic Schizophrenia

- is characterized by **disorganized thinking with blunted and inappropriate emotions**. The behavior is often bizarre. There could appear mannerisms, grimacing, inappropriate laugh and joking, pseudophilosophical brooding and sudden impulsive reactions without external stimulation. There is a tendency to social isolation.

- It often begins in adolescency.

- Usually the prognosis is poor because of the rapid development of "negative" symptoms, particularly flattening of affect and loss of volition.

- Denoted also as disorganized schizophrenia .

F20.2 Catatonic Schizophrenia

- is characterized mainly by **motoric activity**, which might be strongly **increased** (hypekinesis) or **decreased** (stupor), or automatic obedience and negativism.

  – productive form — which shows catatonic excitement, extreme and often aggressive activity.

    (rare symptoms: echopraxia, echolalia, echomimia)

  – stuporose form — characterized by general inhibition of patient's behavior or at least by retardation and slowness, followed often by mutism, negativism, flexibilitas cerea or by stupor.

TREATMENT: ECT, benzodiazepines, hypnotics, NOT antipsychotics (catatonia is hypodopaminergic situation)

movie

- Please watch the movie „catatonic and other symptoms“

F20.3 Undifferentiated Schizophrenia

- Psychotic conditions meeting the general diagnostic criteria for schizophrenia but not conforming to any of the subtypes in F20.0-F20.2 or exhibiting the features of more than one of them without a clear predominance of a particular set of diagnostic characteristics.

- This subgroup represents also the former diagnosis of atypical schizophrenia.

F20.4 Postschizophrenic Depression

- A depressive episode, which may be prolonged, arising in the aftermath of a schizophrenic illness. Some schizophrenic symptoms, either „positive“ or „negative“, must still be present but they no longer dominate the clinical picture.
- These depressive states are associated with an increased risk of suicide.

F20.5 Residual Schizophrenia

- A chronic stage in the development of schizophrenia with clear succession from the initial stage with one or more episodes characterized by general criteria of schizophrenia to the late stage with **long-lasting negative symptoms and deterioration** (not necessarily irreversible).

F20.6 Simple Schizophrenia

- Simple schizophrenia is characterized by early and slowly developing initial stage with growing **social isolation, withdrawal** („introvertization“)**, small activity, passivity, avolition and dependence on the others**.
- The patients are indifferent, without any initiative and volition. There is not expressed the presence of hallucinations and delusions.

Incidence, onset

- Schizophrenia occurs with regular frequency nearly everywhere in the world in 1 % of population.
- Begins mainly in young age (mostly around 16 to 25 years).
- Men usually earlier then women.
- Women: second peak of incidence – year 37 or 38.
- Onset after 40 is very unusual.

(Women – better prognosis, more „affective“ symptom, later onset then men, women are protected by estrogens.

The gender incidence is nearly the same - men 1,1 : women 1)

Schizophrenia in childhood

- Typical symptoms:

Disorganization

Disturbance of behaviour

Abnormal postures, movements

Cognitive dysfunction

Anxiety

Social disturbance

- Less typical, but possible symptoms:

Delusions, Hallucinations

- Prognosis depends on the type of schizphrenia, age of onset – the sooner onset, the worse prognosis.
- Onset of schizophrenia in childhood is rare.
- The diagnostic criteria for children are the same as for adults.

Course of Illness

- Course of schizophrenia:
  - continuous without temporary improvement
  - **episodic** with progressive or stable deficit
  - episodic with complete or incomplete remission

- Typical stages of schizophrenia:
  - prodromal phase
  - active phase
  - residual phase

Suicidality, lenght of life

- Approximately 5-6 % of SCH patients commite suicide.
- Schizophrenia shorten life of approximately 15 years.

Etiology of Schizophrenia

- The etiology and pathogenesis is **multifactorial**
- Nowadayys we know more and more, but not enough

  – internal factors – genetic, inborn, biochemical, immunological
  – external factors – trauma, infection of CNS, stress

Genetics of Schizophrenia

- Many psychiatric disorders are multifactorial (caused by the interaction of external and genetic factors) and from the genetic point of view very often polygenically determined.

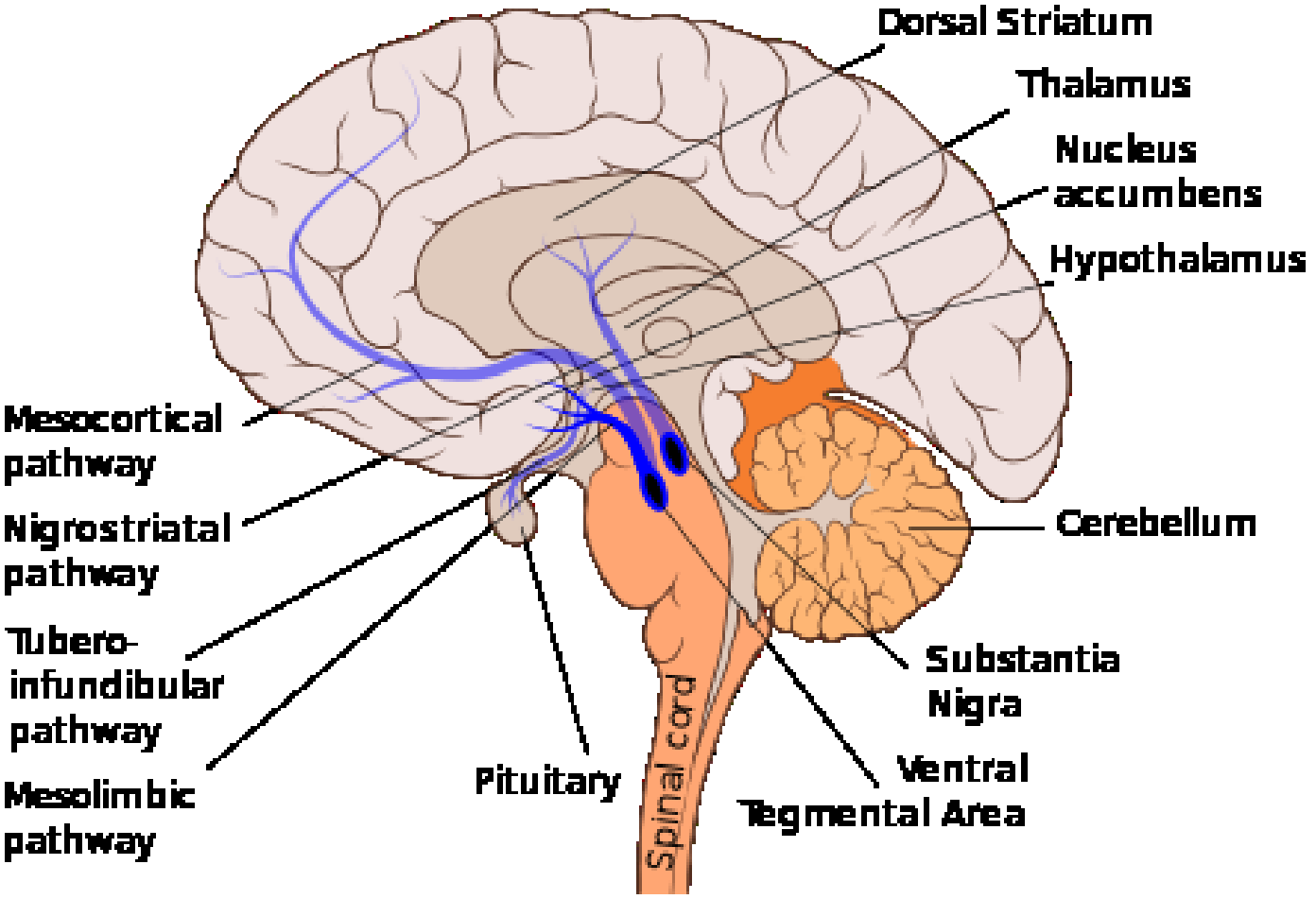
- Relative risk for schizophrenia is around:
  - 1% for normal population
  - 5.6% for parents
  - 10.1% for siblings
  - 12.8% for children

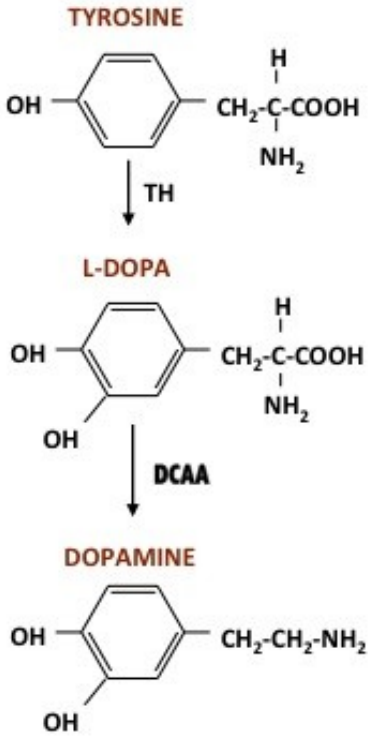
Dopamine Hypothesis

- The most influential and plausible are the hypotheses, based on the supposed **disorder of neurotransmission** in the brain, derived mainly from
  1. the **effects of antipsychotic** drugs that have in common the ability to **inhibit the dopaminergic system by blocking action of dopamine** in the brain
  2. **dopamine-releasing drugs** (amphetamine, mescaline, diethyl amide of lysergic acid - LSD) that **can induce state closely resembling paranoid schizophrenia**

- Classical dopamine hypothesis of schizophrenia: Psychotic symptoms are related to dopaminergic hyperactivity in the brain. **Hyperactivity of dopaminergic systems** during schizophrenia is result of **increased sensitivity and density of dopamine D2 receptors.**

Positive symptoms – hyperdopaminergic state in mesolimbic pathway
Negative symptoms – hypodopaminergic state in mesocortical area




TYROSINE
OH
H
CH2-C-COOH
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TH
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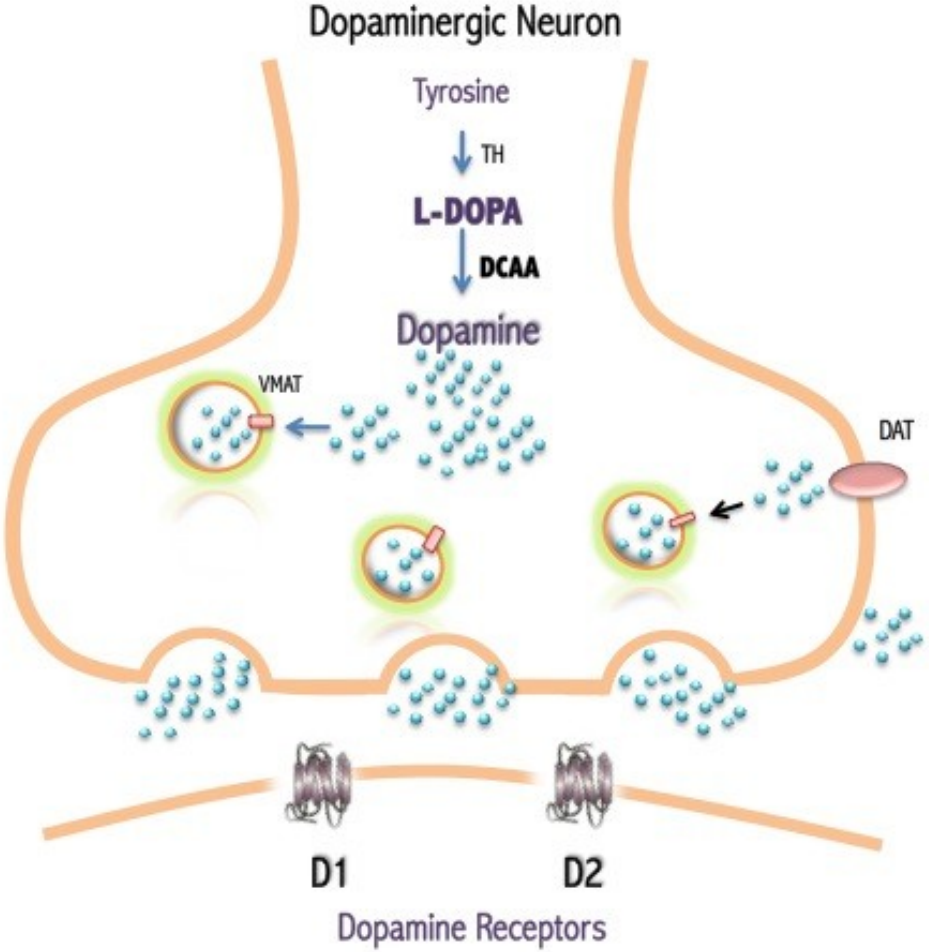
OH
H
CH2-C-COOH
NH2
OH
DCAA
DOPAMINE
OH
CH2-CH2-NH2
OH


Dopaminergic Neuron
Tyrosine
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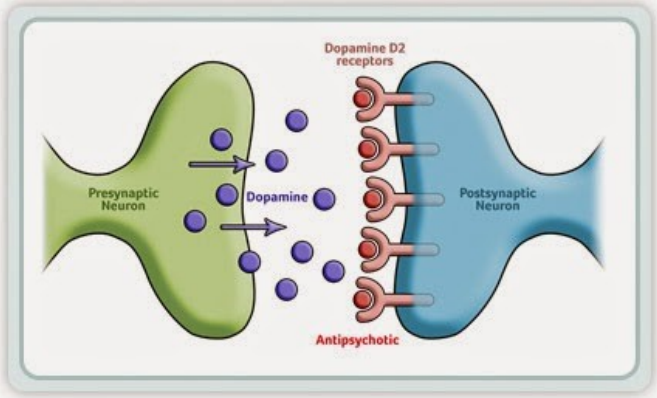
DAT
D1
D2
Dopamine Receptors


Dopamine D2 receptors
Presynaptic Neuron
Dopamine
Postsynaptic Neuron
Antipsychotic

Contemporary Models

- Dopamine hypothesis revisited: various neurotransmitter systems probably takes place in the etiology of schizophrenia (norepinephric, serotonergic, glutamatergic, some peptidergic systems); based on effects of atypical antipsychotics especially.

- Contemporary models of schizophrenia conceptualize it as a neurocognitive disorder, with the various signs and symptoms reflecting the downstream effects of a more fundamental cognitive deficit:
  - the symptoms of schizophrenia arise from "cognitive dysmetria" (Nancy C. Andreasen) (a dysfunction in cortical-subcortical-cerebellar circuitry)
  - concept of schizophrenia as a neurodevelopmental disorder (Daniel R. Weinberger)

Neurodevelopmental Model

- Neurodevelopmental model supposes in schizophrenia the presence of “silent lesion” in the brain, mostly in the parts, important for the development of integration (frontal, parietal and temporal), which is caused by different factors (genetic, inborn, infection, trauma...) during very early development of the brain in prenatal or early postnatal period of life.
- It does not interfere too much with the basic brain functioning in early years, but expresses itself in the time, when the subject is stressed by demands of growing needs for integration, during formative years in adolescence and young adulthood.

Abnormities in brain structure

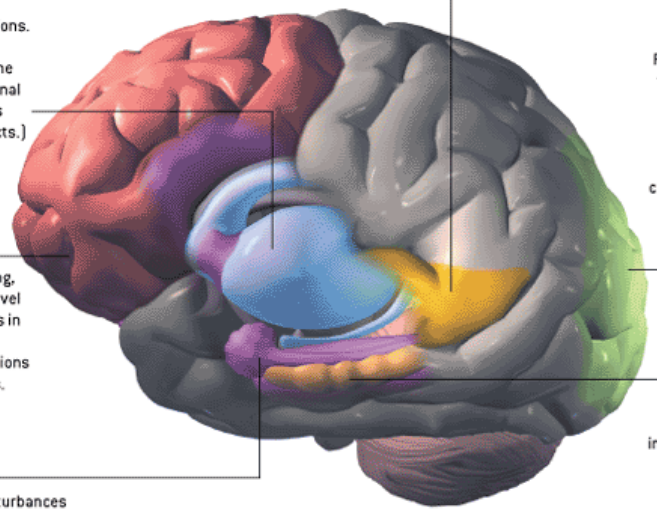
- Nonspecific, usually not visible on basic MRI
- cortical gray matter loss (i.e. superior temporal and inferior frontal regions)
- disrupted neural connectivity

THE BRAIN IN SCHIZOPHRENIA

MANY BRAIN REGIONS and systems operate abnormally in schizophrenia, including those highlighted below. Imbalances in the neurotransmitter dopamine were once thought to be the prime cause of schizophrenia. But new findings suggest that impoverished signaling by the more pervasive neurotransmitter glutamate—or, more specifically, by one of glutamate's key targets on neurons (the NMDA receptor)—better explains the wide range of symptoms in this disorder.

BASAL GANGLIA
Involved in movement and emotions and in integrating sensory information. Abnormal functioning in schizophrenia is thought to contribute to paranoia and hallucinations. (Excessive blockade of dopamine receptors in the basal ganglia by traditional antipsychotic medicines leads to motor side effects.)

AUDITORY SYSTEM
Enables humans to hear and understand speech. In schizophrenia, overactivity of the speech area (called Wernicke's area) can create auditory hallucinations—the illusion that internally generated thoughts are real voices coming from the outside.



OCCIPITAL LOBE
Processes information about the visual world. People with schizophrenia rarely have full-blown visual hallucinations, but disturbances in this area contribute to such difficulties as interpreting complex images, recognizing motion, and reading emotions on others' faces.

FRONTAL LOBE
Critical to problem solving, insight and other high-level reasoning. Perturbations in schizophrenia lead to difficulty in planning actions and organizing thoughts.

HIPPOCAMPUS
Mediates learning and memory formation, intertwined functions that are impaired in schizophrenia.

LIMBIC SYSTEM
Involved in emotion. Disturbances are thought to contribute to the agitation frequently seen in schizophrenia.

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Treatment of schizophrenia

- **Antipsychotics**
- Individual psychotherapy
- Family therapy
- Social skill training
- Supported employment etc
- ECT or rTMS in the minority of patient

(ECT – usually pharmacoresistant patients with affective symptoms, rTMS – vocal hallucinations, negative symptoms)

Antipsychotics

First generation	Second generation
- Typical, traditional - Cause more extrapyramidal and probably cardial side effects - Are effective to positive symptoms - Are less prescribed - We discovered and used earlier (late 60´s, 70´s) haloperidol, zuklopenthixol, melperone, chlopromazine, fluphenazine, chlorprothixen, levomepromazine, …	- Atypical, modern - Cause less extrapyramidal symptoms - Are effective to positive, probably to negative and cognitive symptoms - Are more prescribed - Usually are more expensive - We discovered (except clozapine) later risperidone, paliperidone, olanzapine, quetiapine, clozapine, amisulpride, aripiprazol, cariprazine

Is not easy to characterise all the first generation according to all the second one, because there are big differences (in usage, sife effects, effectivity..) among concrete antipsychotics in both groups.

First episode

- Usually they need hospitalization, only rarely can be treated outpatiently.
- Antipsychotics are immediately used – in the form of acute intramuscular injections or in peroral form. *(Examples of i.m. injections: olanzapine, haloperidol, zuklopenthixol)*
- We prefer monotherapy.
- First choice can use almost any (except clozapine) antipsychotic from the first or second generation, but we prefer second generation. (for example risperidon, olanzapin, amisulprid)
- We should consider side effects of the concrete medication, patient´s other diseases, …

First episode, other acute episode

- We can observe antipsychotic effect in at least 2 to 3 weeks.
- Sedative effect is obvious after few hours or days (usually we combine antipsychotics with anxiolytics in the beginning).
- The hospitalization usually takes 6 weeks.
- Sometimes the first antipsychotic is not effective, we shoud change it.
- Clozapine can be used like third antipsychotic, not the first one, not the second one. (Because it can cause agranulocytosis.)

First episode, other acute episode

- Some patients are converted to instramuscular long-lasting injections (LAI). The frequency of apllication is from 2 weeks to 1 month (depend on concrete medication).

Examples of LAI: paliperidon, olanzapin, aripiprazol, haloperidol, zuklopenthixol, fluphenazine

(Paliperidone exists in 3 months´form, it is usually used after 1 month form in outpatient care.)

How long should pharmacotherapy last?

- After first episode – 2 years
- After second episode – 5 years
- After third and other episodes, in patients with chronic course, in patients with repetitive suicidal behaviour – longer, usually the whole life

Some practical notes

- When the patient has symptoms of psychosis (not necessarily of schizophrenia, can be acute psychosis, concrete diagnosis is not so important), please don´t wait. Please handle psychiatric consult as soon as possible, the patient probably needs the hospitalization.

  (Also think about other diagnostical alternatives - is he intoxicated? Does he have any neurological symptoms?

- When the patient is treated for schizophrenia, attends psychiatry outpatiently and is stabile, there is no need to handle psychiatric consult („consilium“) just because of the diagnosis of schizophrenia when he is hospitalized in other department (internal, surgical etc.). But when you are not sure about his condition, behaviour, medication, suicidal thoughts, than of course handle the psychiatric consult.

F21 Schizotypal disorder

- eccentric behavior
- deviations of thinking and affectivity, which are similar to that occurring in schizophrenia,
- but without psychotic features and expressed symptoms of schizophrenia of any type.

F22.0 Delusional Disorder

- A disorder characterized by the development of one delusion or of the group of similar related delusions, which are persisting unusually long, very often for the whole life.
- Other psychopathological symptoms — intrusion of thoughts etc. are not present and are excluding this diagnosis.
- It begins usually in the middle age.
- Treated by usual antipsychotics.

F23 Acute and Transient Psychotic Disorders

- The criteria should be the following features:
  - acute beginning (to two weeks)
  - quickly changing “polymorphic symptoms” – emotivity, psychotics symptoms
  - typical schizophrenic symptoms are present or not
- Complete recovery usually occurs within a few months, often within a few weeks or even days.
- The disorder may or may not be associated with acute stress, defined as usually stressful events preceding the onset by one to two weeks.

F24 Induced Delusional Disorder

- A delusional disorder shared by two or more people with close emotional links. Only one of the people suffers from a genuine psychotic disorder; the delusions are induced in the other(s) and usually disappear when the people are separated.

F25 Schizoaffective Disorders

- Episodic disorders in which both affective and schizophrenic symptoms are prominent (during the same episode of the illness or at least during few days) but which do not justify a diagnosis of either schizophrenia or depressive or manic episodes.
- Patients suffering from periodic schizoaffective disorders, especially with manic symptoms, have often good prognosis with full remissions without any remaining defects.
- They are divided in different subgroups:
  - F25.0 Schizoaffective disorder, manic type
  - F25.1 Schizoaffective disorder, depressive type
  - F25.2 Schizoaffective disorder, mixed type
  - F25.8 Other schizoaffective disorders
  - F25.9 Schizoaffective disorder, unspecified

„Toxic psychoses“

- Usually caused by usage of marijuana or metamphetamine (the more frequent and longer use the higher probability)
- Negative and cognitive symptoms are not typical, but positive are
- Some patients can have visual hallucinations, which are not typical for schizophrenia
- Sometimes there is not easy to distinquish whether the substance was the trigger or the cause of psychosis
- Usually dissaper when the patient abstain
- Antipsychotics are usually used in acute phase, in some patients also in subsequent treatment

Thank you for your attention

There are some passages from my colleguages´presentations and some passages which had been googled in this presentation.