



Schizophrenia and other psychotic disorders

Beatrix Mersich M.D., Ph.D.

Semmelweis University Department of
Psychiatry and Psychotherapy



Outline

Schizophrenia

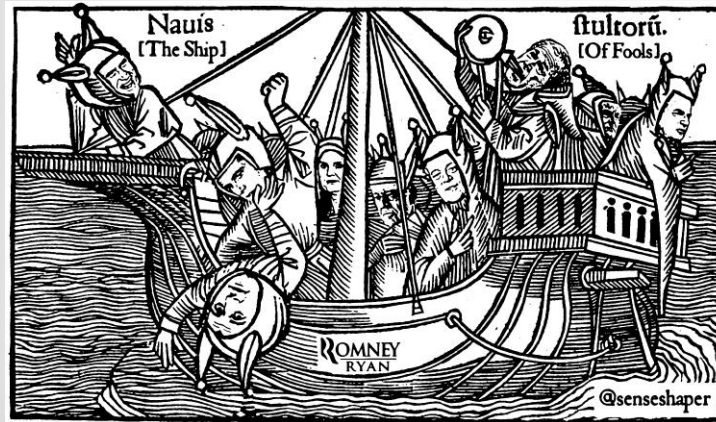
- History
- Terminology
- Symptoms - Diagnosis
- Epidemiology
- Etiology
- Pathophysiology
- Treatment

Other psychotic disorders



Schizophrenia – history 1

Before the XIXth century: irrational behaviour was explained mostly by religious beliefs. Treatment was isolation ~ ship of fools

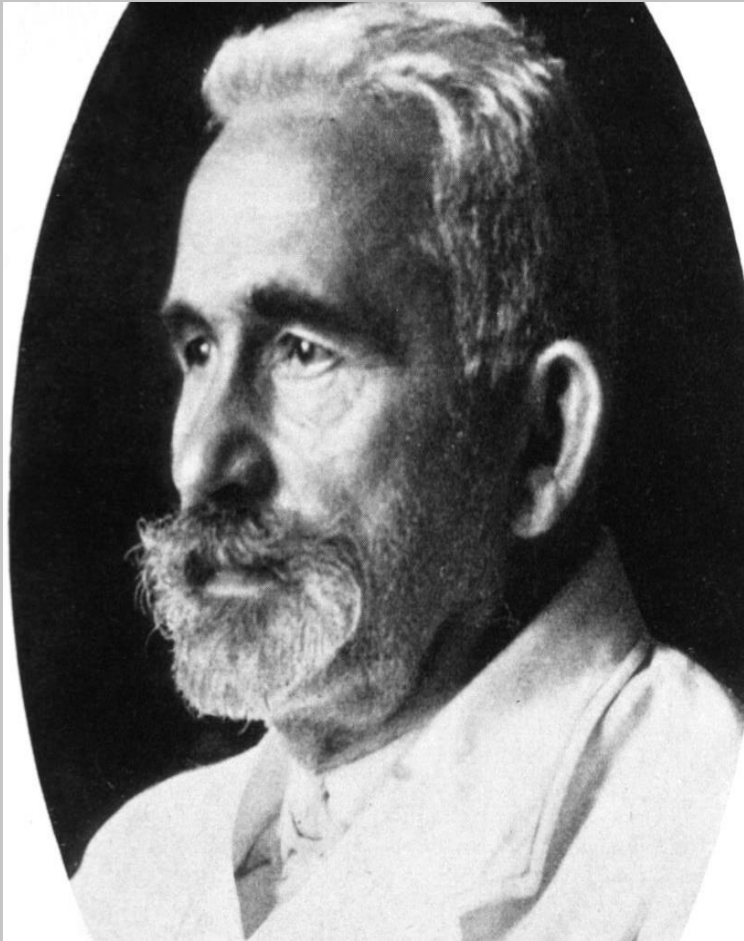


Emil Kraepelin (1856-1926) german psychiatrist: „**dementia praecox**” – loss of cognitive functions at young age

Distinguished from mood disorders

Eugen Bleuler (1857-1939) swiss psychiatrist : the separation of function between personality, thinking, memory, and perception

the word comes from the greek roots *schizein* ("to split") and *phrēn, phren-* ("mind,,) ~ **schizophrenia** ~ **splitting of the mind**



Emil Kraepelin – 1896
„dementia praecox”



Eugen Bleuler – 1911
„schizophrenia”

Schizophrenia – history 2

- **Kurt Schneider** (1887-1967) german psychiatrist: **first rank symptoms**: delusions of being controlled by an external force, the belief that thoughts are being inserted into or withdrawn from one's conscious mind, the belief that one's thoughts are being broadcast to other people, hearing hallucinatory voices that comment on one's thoughts ~ see. recent classifications
- **Andreasen /Crow (~1970)**: Positive and negative symptoms

Terminology

Psychosis ≠ Schizophrenia!

Psychosis is a mental **condition**.

Schizophrenia is a mental **disorder** (illness).

Psychosis is a break of connection with reality.

And then what is schizophrenia?

How to diagnose schizophrenia?

DIAGNOSING SCHIZOPHRENIA FROM THE DSM-5

- **Criterion A (Active- phase symptoms):** Two or more of the following, each present for a significant portion of time during a 1-month period. One of these **MUST** be (1), (2), or (3).
 - 1. Delusions
 - 2. Hallucinations
 - 3. Disorganized speech (e.g., frequent derailment or incoherence)
 - 4. Grossly disorganized or catatonic behavior
 - 5. Negative symptoms (i.e., diminished emotional expression or avolition)



Schizophrenia - diagnosis

- Symptoms must be present for **6 months**
- **Active for 1 month**
- Symptoms causing **functional decline** (occupational, social life, partnership etc)
- The condition is not better explained by other mental disorder

- Diagnosis of schizophrenia is made by psychiatric INTERVIEWS (patients and heteroanamnesis!) + OBSERVATION of patient's behaviour
- lab tests (blood, urine), CT/MRI
- psychometric tests: SCID-I, PANSS

Symptoms of psychosis

- Great variety of symptoms
- Several grouping
- Positive/negative/catatonic/cognitive



Positive Symptoms in schizophrenia

An **excess or distortion of normal** functions, such as:

- Hallucinations (perception without stimulus)
- Delusions (false beliefs)
- Desorganised speech and behaviour
- Hostility

Negative symptoms in schizophrenia

Diminution or loss of normal functions

- Emotional withdrawal
- Blunted affect
- Poor rapport
- Lack of spontaneity
- Social withdrawal



Catatonic symptoms

Psychomotor system abnormalities, such as:

- Bizarre posture/ movements
- Waxy flexibility, cristallisation
- Psychomotor agitation/retardation
- Stupor = complete immobility
- Mutism

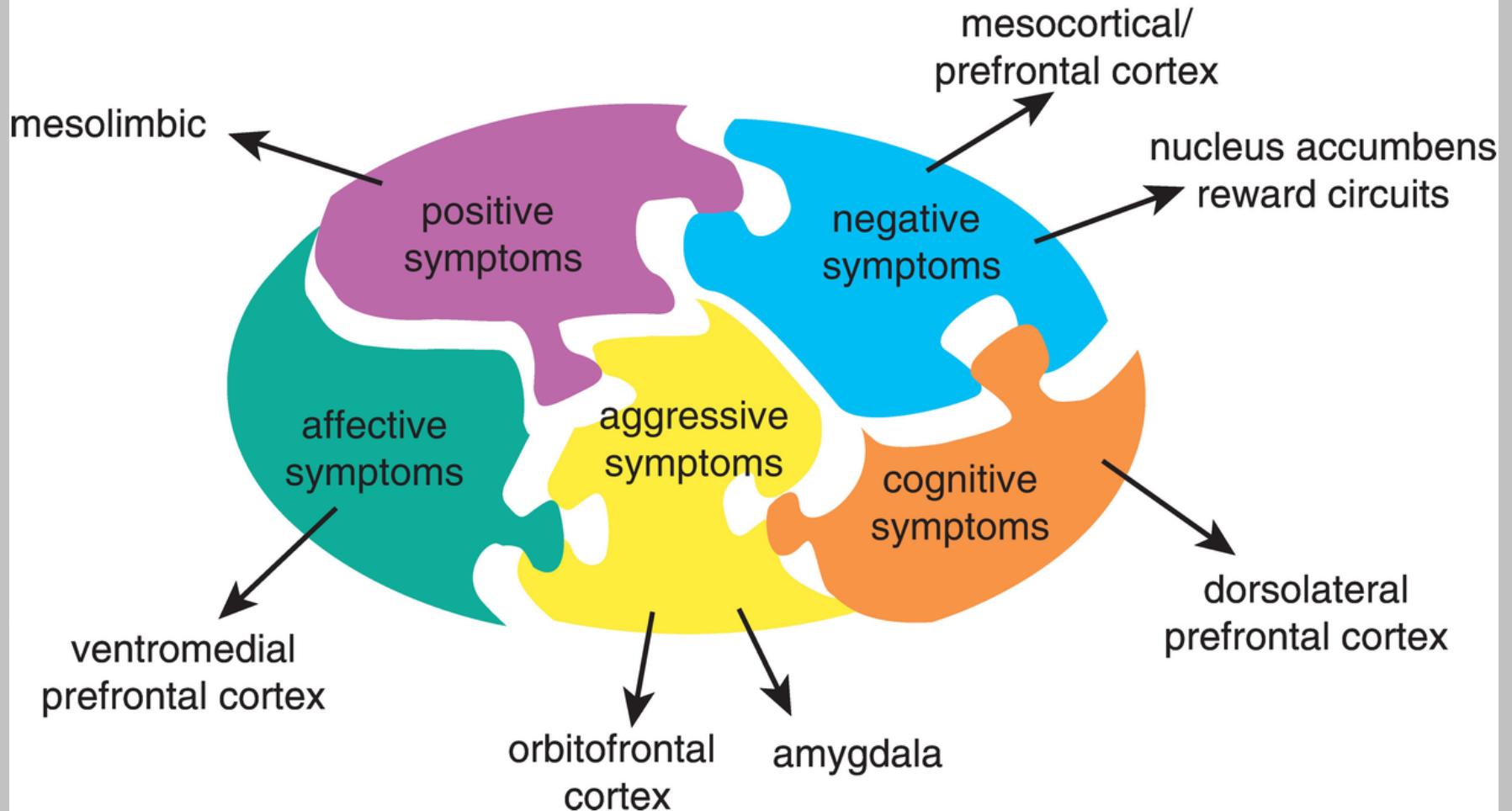


Cognitive symptoms

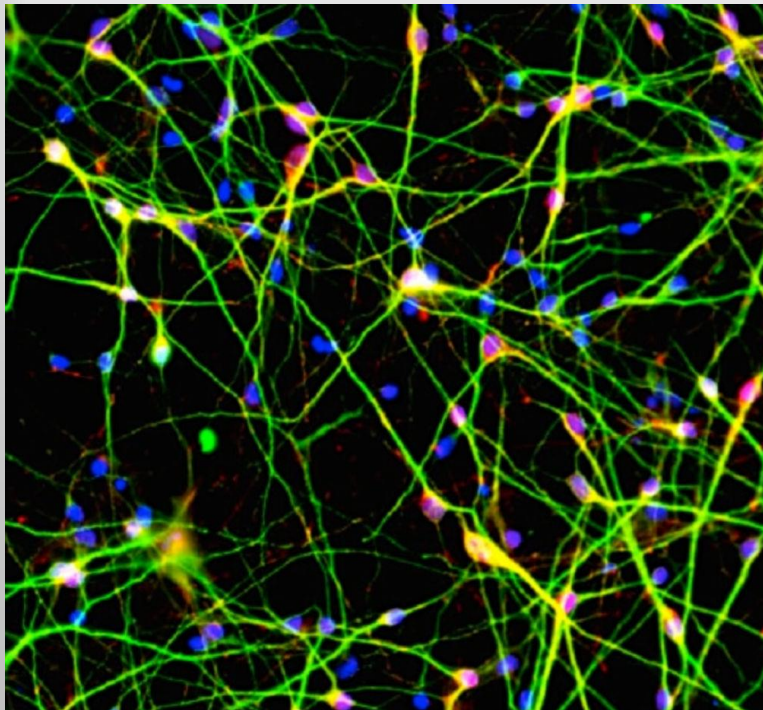
- Lack of concentration
- Memory (working memory) problems
- Executive function deficit
- Loss of abstract thinking



Match Each Symptom to Hypothetically Malfunctioning Brain Circuits



Causes of schizophrenia



Epidemiology

- Incidence consistent worldwide
 - 1% general population
 - 10% siblings , parents / offspring, dizygotic twins
 - 50% monozygotic twins
- Environmental factors implicated
 - Prenatal stress - infection, famine, war, death of spouse
 - Season of birth - winter > summer
 - Urban setting > rural setting
- Age of onset
 - Men 17 - 27, Women 17 - 37
 - Childhood onset extremely rare: 1 in 10,000-100,000
- Outcome
 - 10% good - optimistic
 - 80% remission(緩和) without full recovery
 - 10% no remission

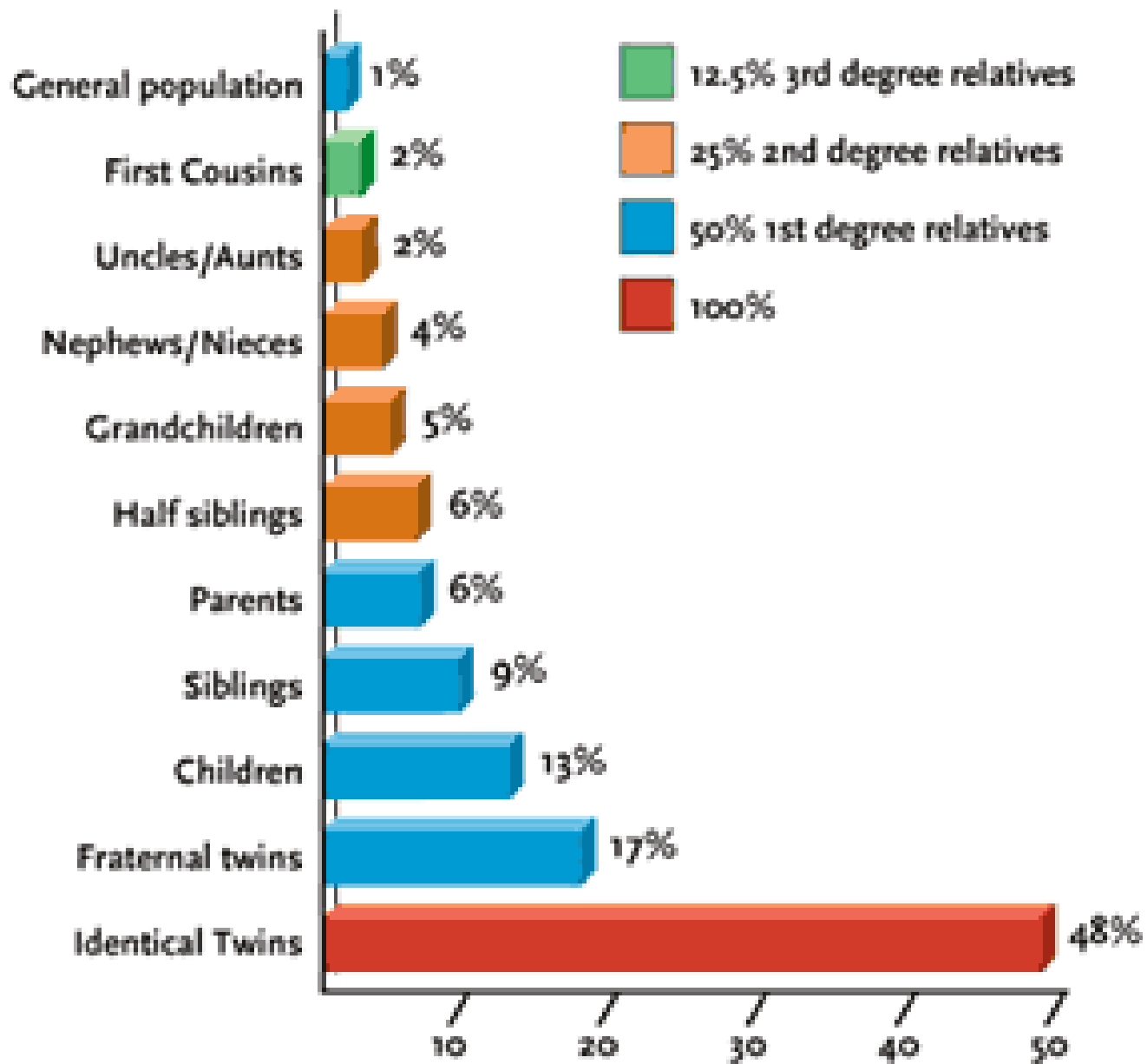
Causes of schizophrenia

Multifactorial etiology!:

- Genetic
- Neurodevelopmental
- Epigenetic (environment, psychosocial interactions, substance abuse)
- Cognitive model

Causes of schizophrenia- genetics

- Family Studies
 - Other family members are at increased risk of schizophrenia
- Twin Studies
 - Risk of schizophrenia in monozygotic twins is 48%
 - Risk of schizophrenia drops to 17% for fraternal (dizygotic) twins
- Adoption Studies
 - Risk of schizophrenia remains high in adopted children with a biological parent suffering from schizophrenia



<http://www.the-scientist.com/?articles.view/articleNo/15199/title/The-Infection-Connection-in-Schizophrenia>/Adapted from image by I.I. Gottesman ©2001

Candidate genes

- D2 receptor gene
- COMT gene
- NRG1, DISC1, TCF4, MIR137, NRGN, NRXN1-genes, etc...
- Multigenic inheritance!



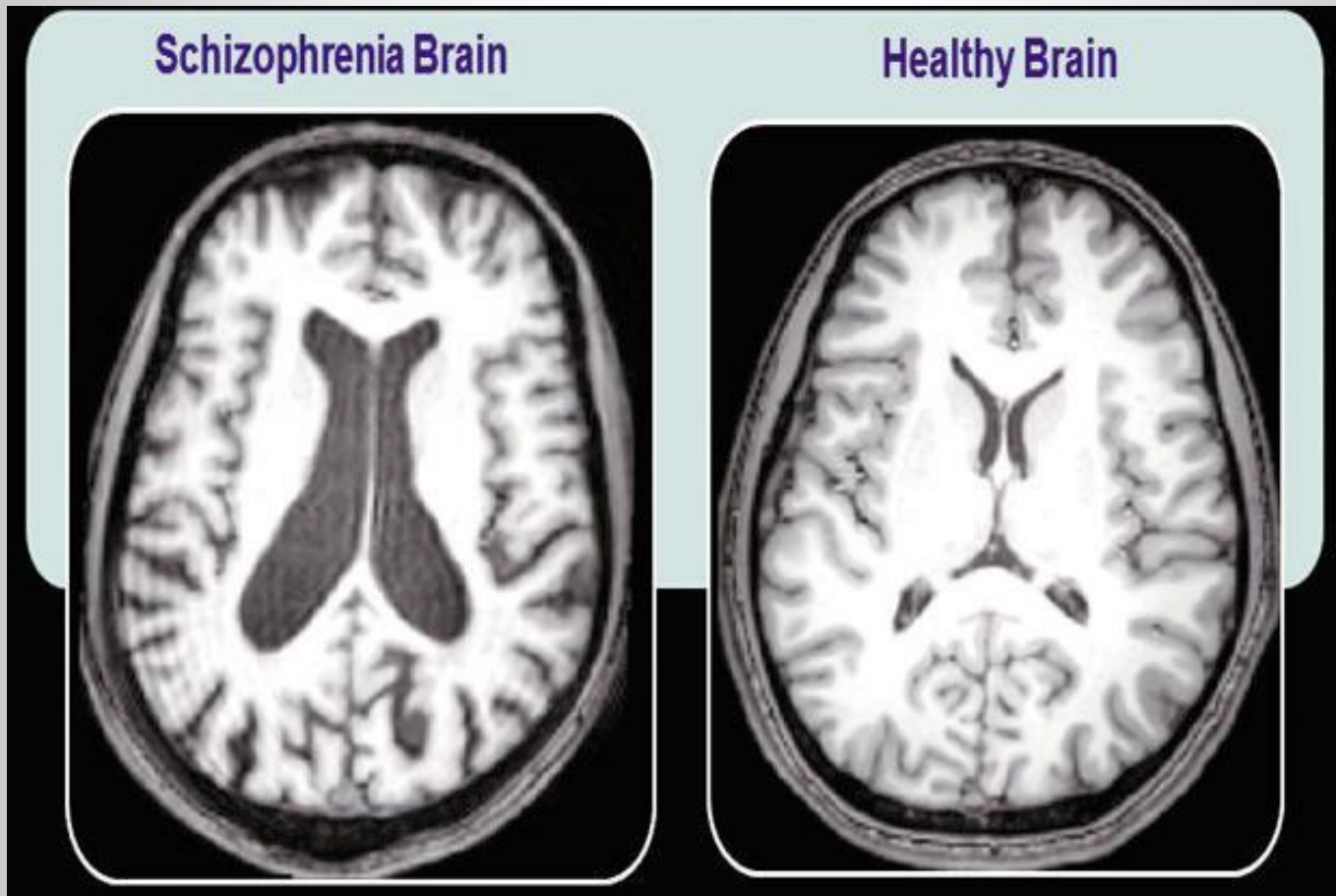
Causes of schizophrenia - neurodevelopmental model

- Schizophrenia is a „silent lesion” in the brain: disconnection or abnormal connection between frontal, temporal and parietal lobe
- Caused by different factors (genetic, inborn, infections, trauma, etc..)
- In very early developmental period (prenatal and early postnatal)
- Leading to brain structural and functional abnormalities

Neurodevelopmental model

	Link to schizophrenia	Strength of evidence
Prenatal or perinatal risk factors		
Obstetric complications	↑	++
Low birthweight	↑	++
In-utero infection	↑	++
Developmental trajectory		
Motor delay	↑	++
Social alterations	↑	++
Cognitive impairments	↑	++
Brain structural alterations		
Ventricular enlargement	↑	++
Grey matter reductions	↑	++
White matter disruption	↑	+

Structural and functional abnormalities in the brain



- Enlarged ventricles and reduced tissue volume
- Hypofrontality – Less active frontal lobes (a major dopamine pathway)

Epigenetics: Psychological and Social Influences

The Role of Stress

- May activate underlying vulnerability and/or increase risk of relapse

Family Interactions

- Families of people with schizophrenia show ineffective communication patterns
- High expressed emotion in the family is associated with relapse

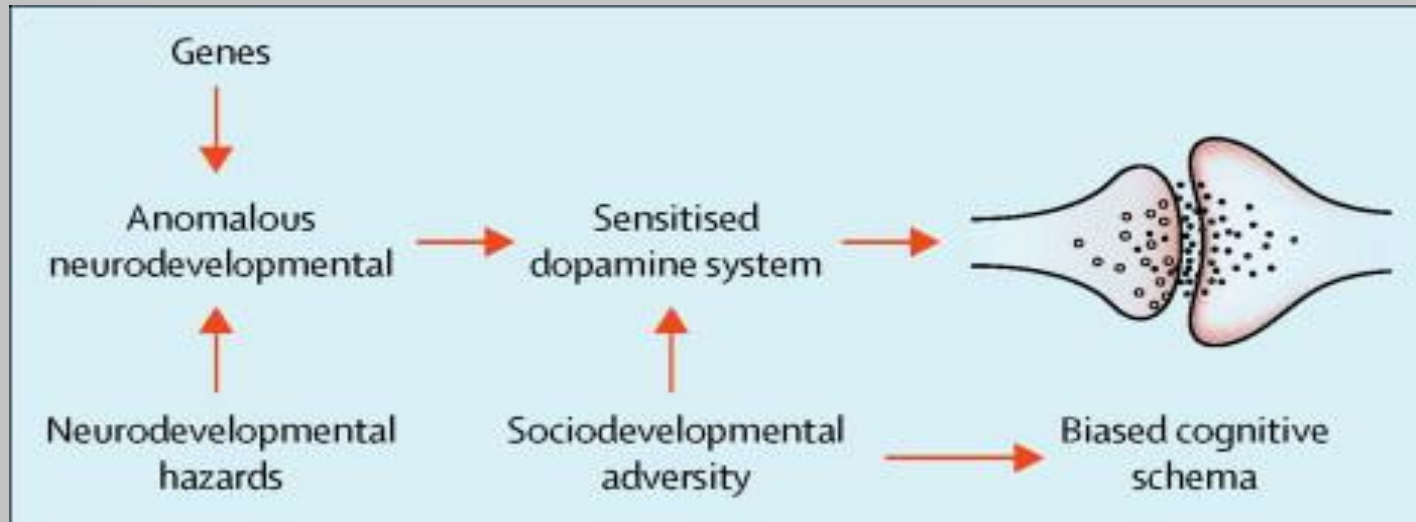
Substance abuse (cannabis etc..)

- May activate underlying vulnerability and/or increase risk of relapse

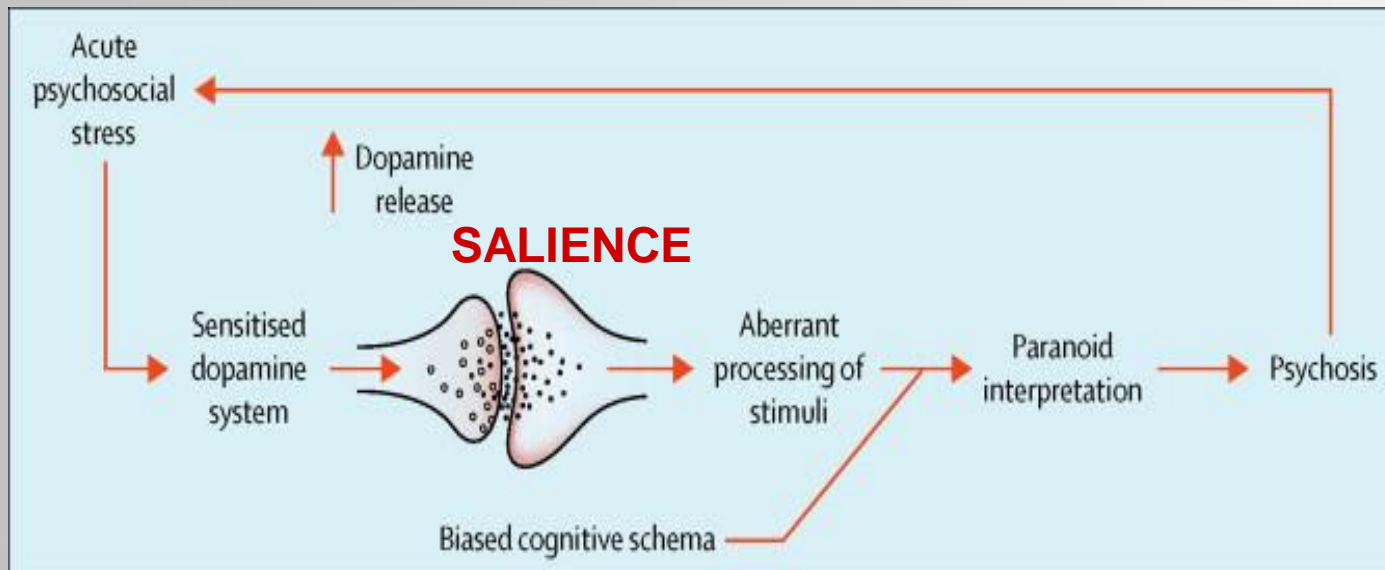
Causes of schizophrenia- Cognitive model

- Normal brain filters among stimuli
- Sch brain is unable to filter –”**abberant salience**”- even neutral stimuli can lead to inappropriate perceptions, thughts and behaviour
- Impairment in working memory (prefrontal cortex) and problem solving

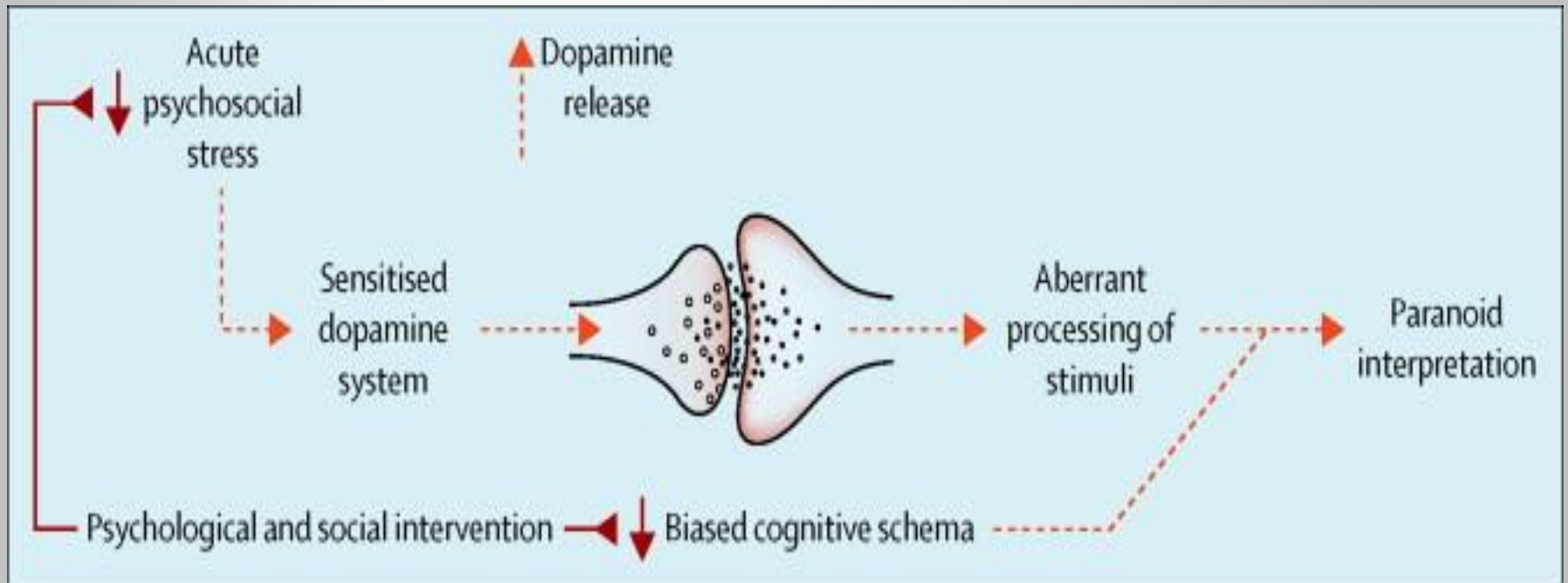
The effect of neurodevelopmental and sociodevelopmental risk factors for psychosis on the dopamine system and cognitive schema



Model of the onset of psychosis showing the interaction between acute stress, dopamine dysfunction, and biased cognitive schema



Sites at which psychosocial interventions could act to prevent psychosis



General Model

Etiology: Multiple convergent factors
(e.g., DNA, gene expression, viruses, toxins, nutrition, birth injury, psychological experiences)



Pathophysiology: Brain development from conception to early adulthood
(e.g., neuron formation, migration, synaptogenesis, pruning, apoptosis, activity dependent changes)



Anatomic and functional disruption in neural connectivity and communication



Impairment in a fundamental cognitive process



Phenomenology: Impairment in one or more second-order cognitive processes
(e.g., attention, memory, language, emotion)



Phenomenology: Symptoms of schizophrenia
(e.g., hallucinations, delusions, negative symptoms, disorganized speech)

Genetic vulnerability

Identified genes, such as neuregulin 1, dysbindin, and possibly COMT

- **Prenatal environment:**

Obstetric complications
Viral exposure
Maternal stress and malnutrition

- **Childhood environment:**

Child-rearing
Child abuse
Head injury

- **Later life environment:**

Drug abuse
Migration/ethnicity
Urbanicity
Social adversity/life events

- *Vulnerability for psychosis evident in markers of neurodevelopmental abnormality*

- *Childhood antecedents evident as a result of vulnerability interact with environment*

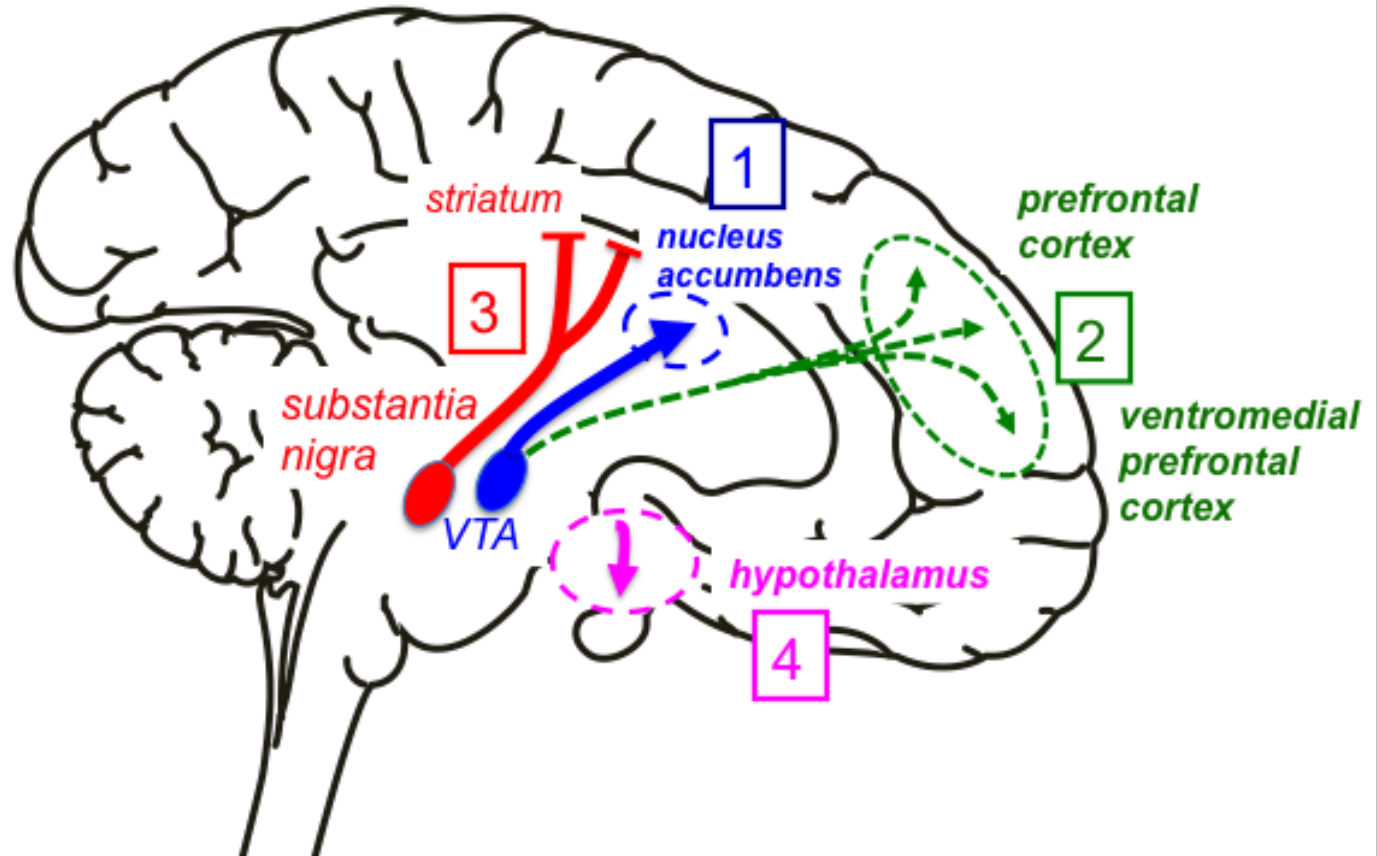
- *Interacts with maturational brain changes during adolescence*

Onset of schizophrenia

Neurotransmitters in schizophrenia- dopamine

- Drugs that increase dopamine (agonists), result in schizophrenic-like behavior
- Drugs that decrease dopamine (antagonists), reduce schizophrenic-like behavior

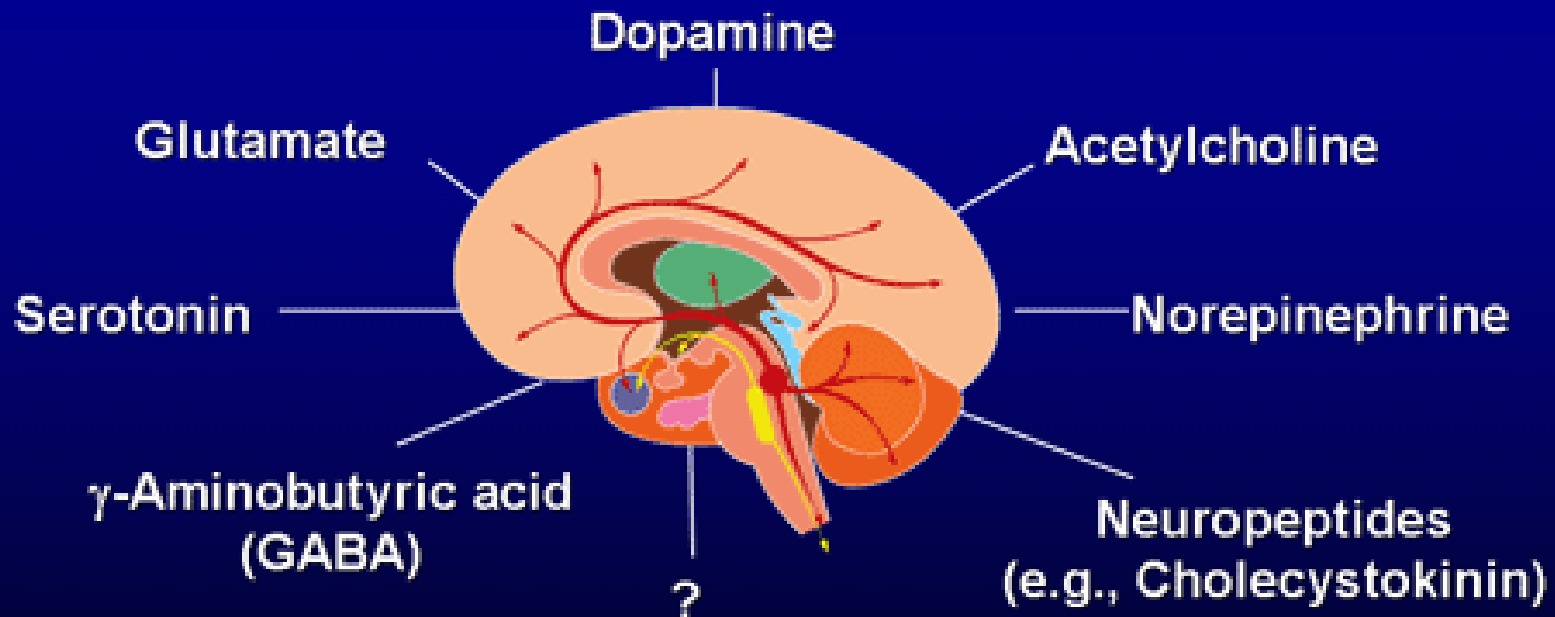
Four Dopamine Pathways & Schizophrenia



- 1) Mesolimbic (SCZ - increase in DA causes positive symptoms)
- 2) Mesocortical (SCZ – DA hypoactivity: negative & cognitive & affective symptoms)
- 3) Nigrostriatal (Drugs - EPS & TD drug side effects)
- 4) Tuberohypophyseal (Drugs - hyperprolactinemia side effects)

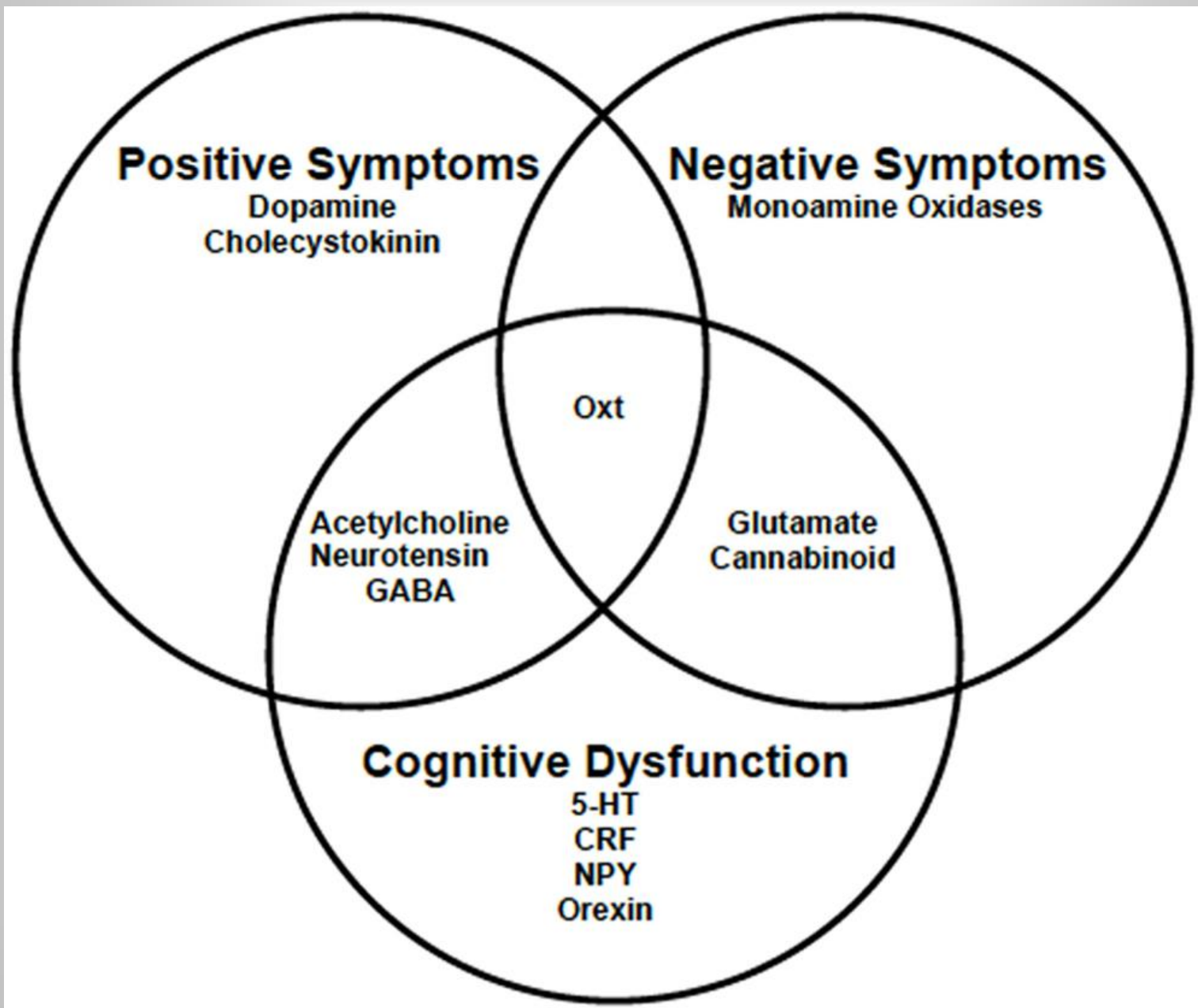
Neurotransmitters in schizophrenia

Neurotransmitter Systems Implicated in Schizophrenia

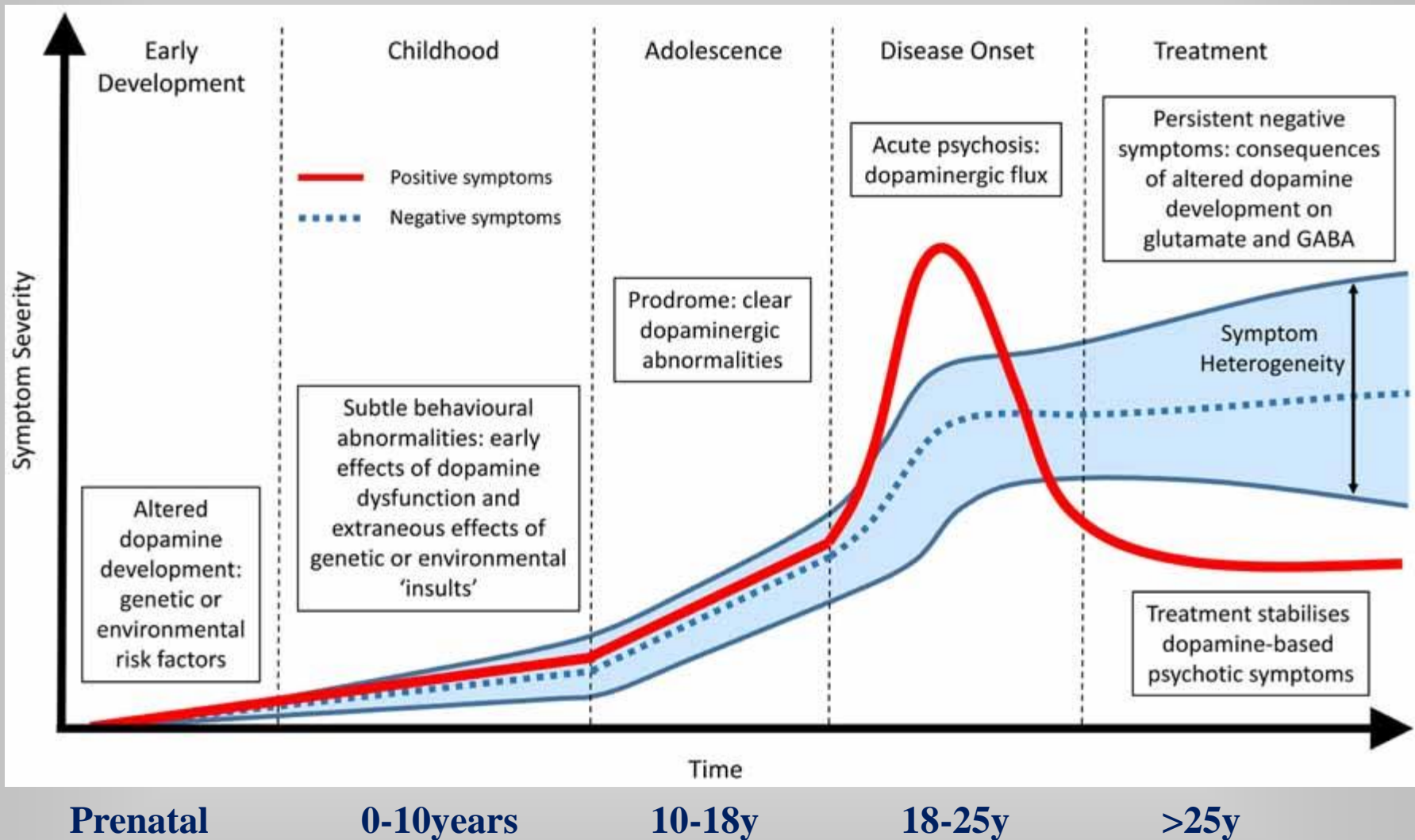


Schizophrenia Probably Involves Multiple Neurotransmitter System Abnormalities^{1, 2}

¹Goff et al. (2001), *Med Clin North Am* 85:663-689; ²Casey, Zorn (2001), *J Clin Psychiatry* 62(suppl 7):4-10

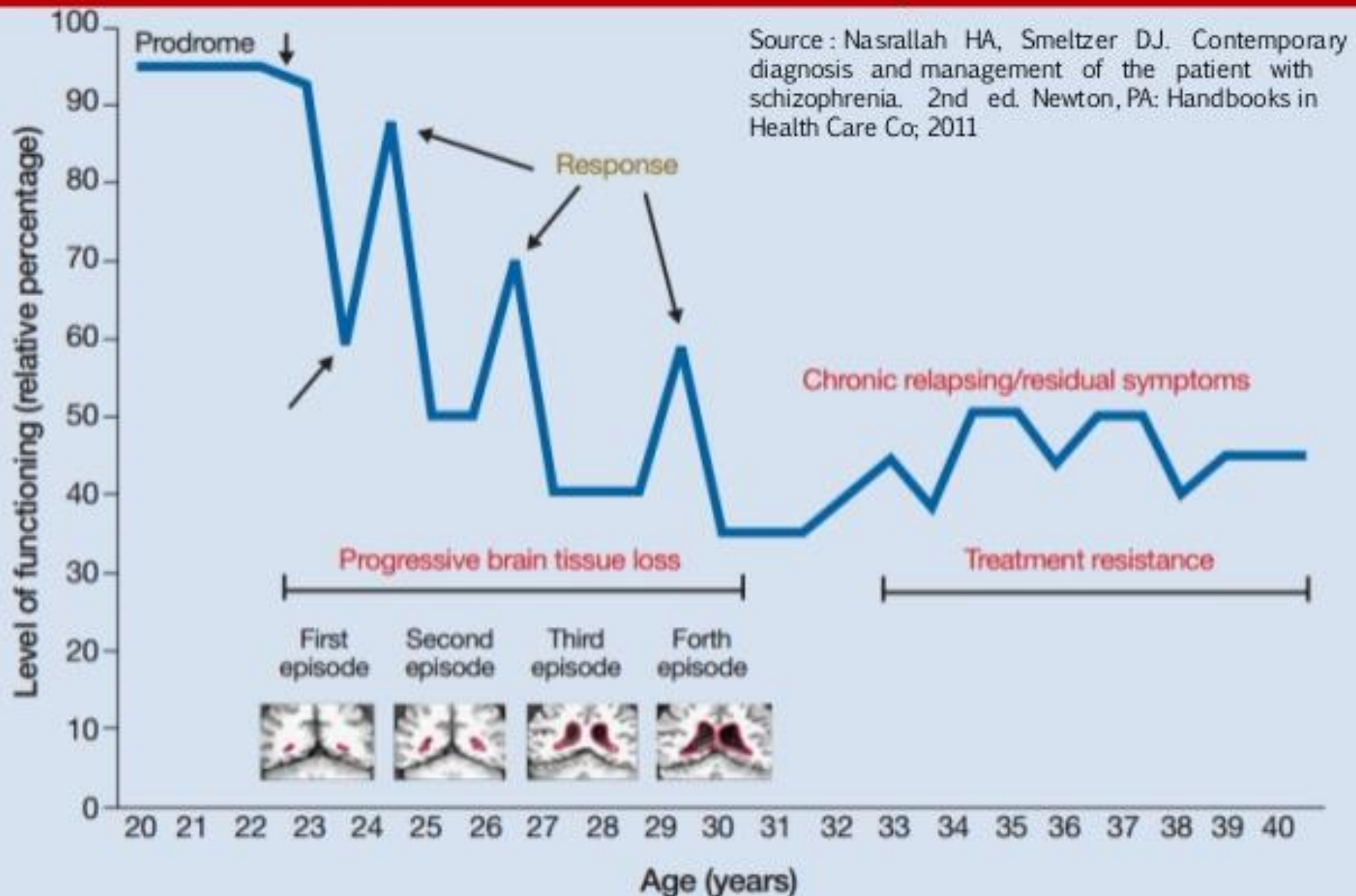


Course of schizophrenia



COURSE OF ILLNESS IN SCHIZOPHRENIA

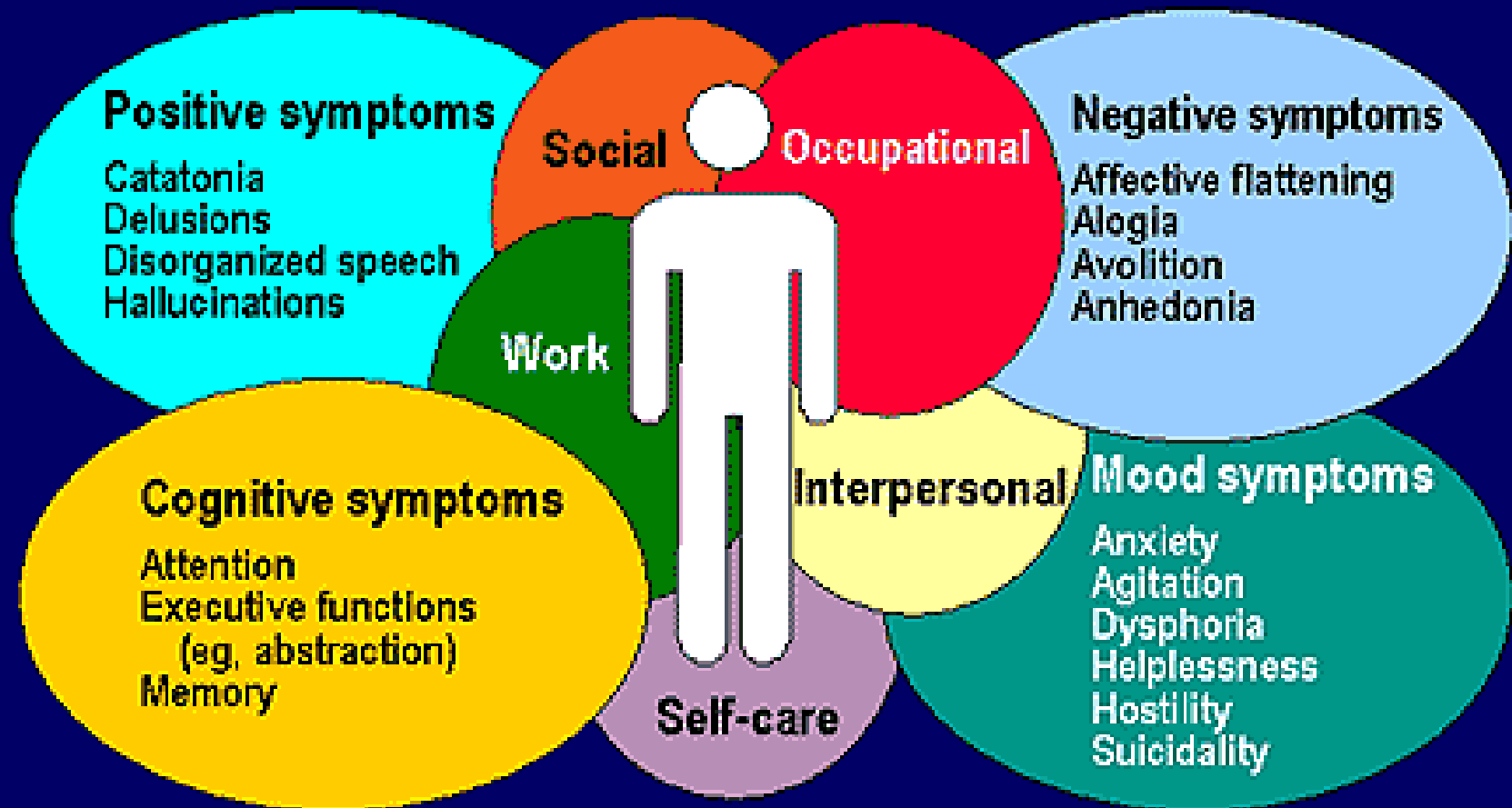
After the first episode in schizophrenia, there is progressive deterioration, loss in brain tissue, and treatment resistance with repetitive RELAPSES





Louis Wain - a schizophrenic painter known for his cat pictures. These ones show his deteriorating mental health over time.

The Impact of Schizophrenia on Overall Functioning



Treatment of schizophrenia 1

Pharmacological

Antipsychotics: main act: D2 antagonist

Pill, solution or short time acting im.injection

- 1st generation or typical: i.e haloperidol, tiapride
- 2nd generations or atypical: i.e.: riperidone, olanzapine, quetiapine, clozapine, amisulpirid, aripiprazol (D2 parcial agonist)

Side effects:

- extrapiramidal (dystonia, akathisia, tremor, tardive dyskinesia)
- weight gain, sexual dysfunction, sedation, hypotonia, obstipation, accomodation problem (vision)
- **Depot injections:** acting for 2-4weeks, im. inj. :olanzapine, riperidone, paliperidone, aripiprazol, haloperidol

Treatment of schizophrenia 2

Psychoeducation : patient and family!



Schizophrenia group therapy.

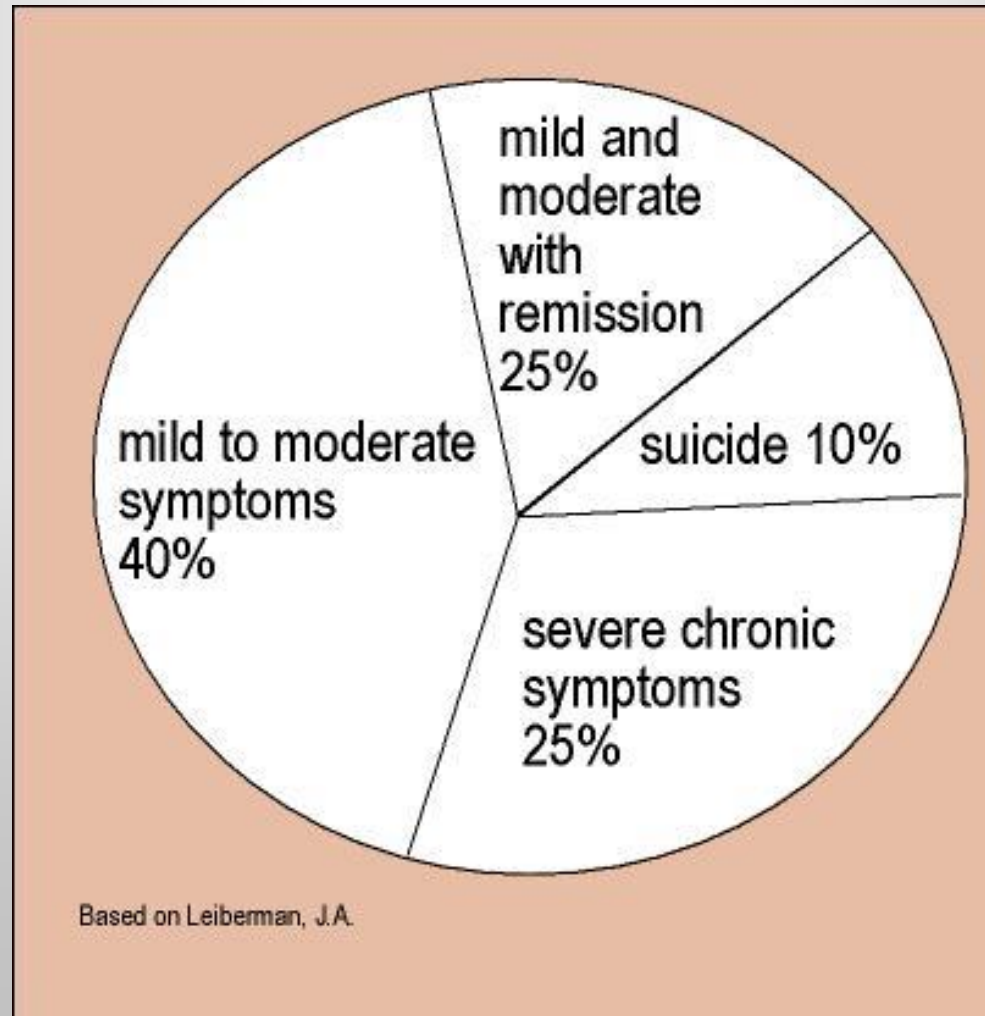
Treatment of schizophrenia 3

Psychotherapy:

- supportive care in the acute phase;
- cognitive-behaviour therapy after the first episode and early stages;
- social skill training
- family intervention
- community psychiatry
- day hospital



Outcome of schizophrenia



Prognosis

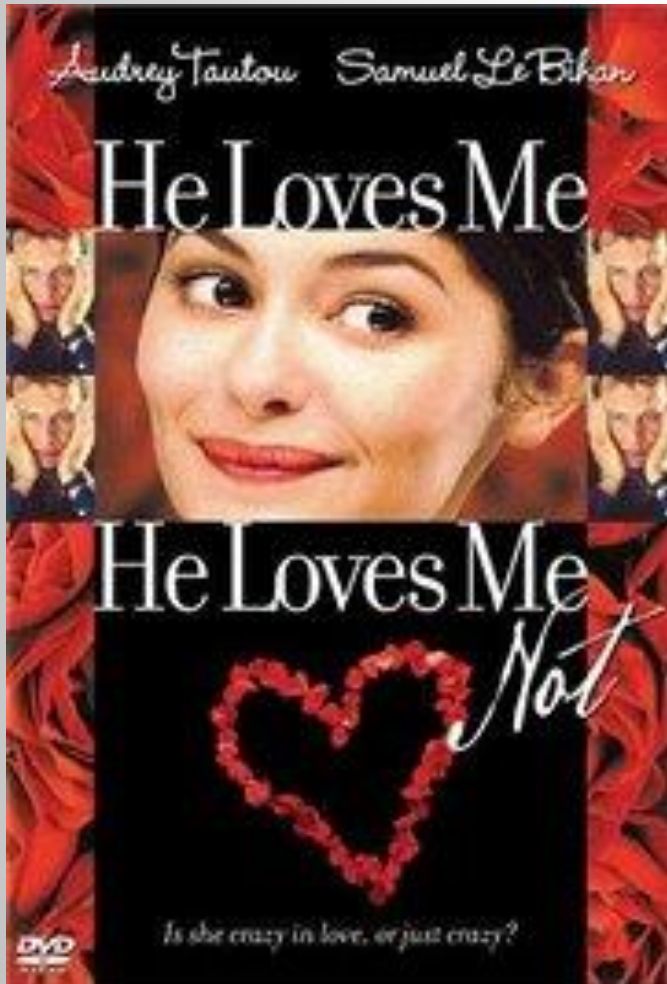
Good prognosis

- Old age of onset
- Female
- Married
- No family history
- Good premorbid personality
- High IQ
- Precipitants
- Positive symptoms
- Treatment compliance
- Good support
- Acute onset
- Presence of mood component

Poor prognosis

- Young age of onset
- Male
- Unmarried
- Family history
- Personality problems
- Low IQ
- No obvious precipitants
- Negative symptoms
- Poor treatment compliance
- Low support
- Insidious onset
- No mood component

Other psychotic disorders



De Clerembault Syndrome
(erotomantic delusion)



Othello Syndrome
(delusion of jealousy)

ICD 10 categories of psychotic disorders

- Schizophrenia
- Schizotypal Disorder
- Persistent Delusional Disorders
- Acute and Transient Psychotic Disorders Induced
Delusional Disorder
- Schizoaffective Disorders
- Other Non-organic Psychotic Disorders

DSM 5 categories of psychotic disorders

- Schizophrenia
- Brief Psychotic Disorder
- Schizophreniform Disorder
- Schizoaffective Disorder
- Delusional Disorder
- Shared Psychotic Disorder
- Psychotic Disorder due to a General Medical Condition
- Substance-induced Psychotic Disorder
Psychotic Disorder Not Otherwise Specified

Brief psychotic disorder

- Symptoms for at least 1 day, no more than 1 month
- Can have postpartum onset

Schizophreniform disorder

- Symptoms for at least 1 month but less than 6 months

Schizoaffective disorder

- Uninterrupted period of illness
- Major Depressive Episode
- Manic Episode or a Major Depressive Episode,
- Manic Episode or a Mixed episode with concurrent psychotic symptoms
- In the same period, there have been 2 weeks of delusions/hallucinations without mood symptoms
Bipolar type, Depressive type

Delusional disorder I .

- Well-systematized, encapsulated, non-bizarre delusions
- lasting for at least 1 month
- involving situations that occur in real life (non bizarre)
- Well-preserved personality
- Absence of hallucinations
- No mental deterioration
- Erotomanic, grandiose, jealous, persecutory, somatic

SHARED PSYCHOTIC DISORDER „Folie à deux”

- Person develops delusion based on a relationship with a psychotic individual
- Uncommon
- Treatment: Separation
- Treat ill individual with medications/counselling

PSYCHOTIC DISORDERS DUE TO GENERAL MEDICAL CONDITION I

Neurological conditions:

- Stroke
- Epilepsy (temporal lobe)
- Huntington's/Pick's disease
- Alzheimer's disease
- Multi-infarct dementia
- Leukoencephalopathies
- Multiple sclerosis (rare)
- Migraine headaches (rare)

PSYCHOTIC DISORDERS DUE TO GENERAL MEDICAL CONDITION II

- Ionic/endocrine imbalances
- Hyperthyroidism Hypercortisolism
- Cushing's syndrome/disease
- **Corticosteroids/anabolic steroid use/abuse**
- Auto-immune disorders
- Porphyria
- Iron storage diseases
- Copper storage disease (Wilson)
- Trauma
- Infections
- Vitamin deficiency

OTHER MENTAL DISORDERS WHICH PRESENT WITH PSYCHOSIS

- **Mood disorder with psychotic features** (common in severe mood disorders)
- **Dementia with psychotic features** (delusional disorders and hallucinations are quite common)

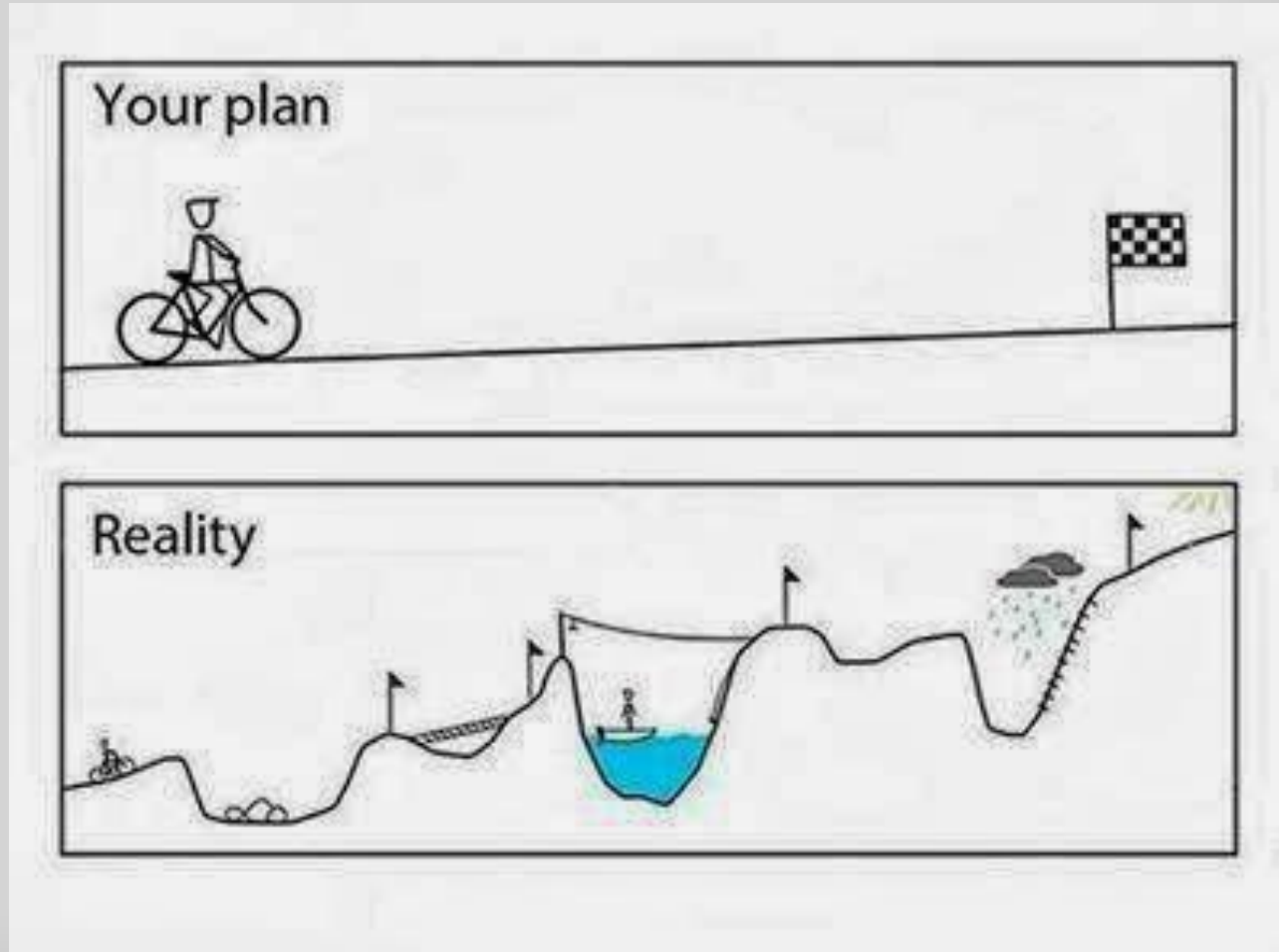
Substance induced psychosis

- Alcohol
- Barbiturates
- Stimulants (Amphetamines)
- Marijuana
- Hallucinogens (L S D)
- Cocaine
- Anticholinergic
- Designer drugs
- Etc...



Thank you for your attention!

Reality testing is sometimes difficult...



<http://semmelweis.hu/pszichiatria/oktatas/gradualis-kepzes/english-education/lectures-in-downloadable-format-pdf>