Schizophrenia and assotiated disorders

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2006. 11. 15.

Possible manifestations of psychiatric disorders

Symptoms of experience

(hallucinations, delusions, anxiety)

Symptoms of behavior

Maladjusment of social adaptation

Decrease of productivity

Behavior suggest psychiatric disorder, if…

- It is not in accordance with social norms
- It is not in accordance with personal habits and motivations, and cannot be understood on the basis of previous personality traits

Persons to discover the illness in everyday life:

- parents
- spouse
- teachers
- colleauges
- GP (general practicioners)
- pharmacologists
- policemen
- lawers
- priests
- etc.

Psychosis:

loss of reality control

Psychoses according to etiology

- **Organic:** known somatic illness in the background
- **Exogenous:** known drug in the background
- **Reactive:** understood from special situations, psychic experiences
- **Endogenous**

„ENDOGENEOUS”:

- Non organic/somatic
- Non exogenous
- Non psychic

„inner” origin

Differential diagnosis of schizophrenia

„Functional”

Schizotypal disorder

Persistent delusional disorders

Schizoaffective disorders

Induced delusional disorder

Mania

Depressio

„Organic”

Drug/substance-induced psy

Epilepsy

Tumors

Stroke

Early dementia

Endocrine causes

Infections

Multiple sclerosis

Autoimmune disorder (SLE)

Metabolic disorders

Schizophrenia

„The psychopathology of schizophrenia is one of the most intriguing, since it permits a many-sided insight into the workings of the diseased as well as the healthy psyche”

Eugen Bleuler

No two cases are ever exactly the same

Benedict-Augustin Morel
(1809-1873)

First use **„premature dementia”**
(in the nineteenth century meaning of
incohaerence rather than low intelligence)

The first psychiatrist to classify psychotic
illnesses on the basis of outcome rather
than clinical presentation at a given moment

Diagnoses considered different, yet with similar courses of illness

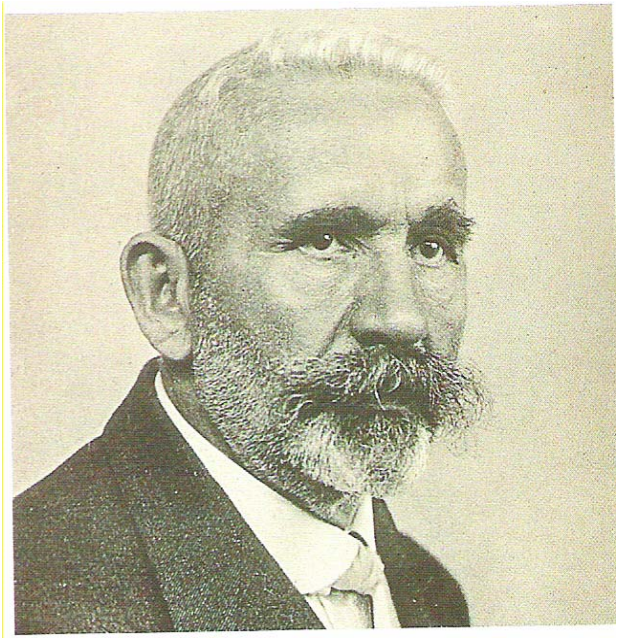
- Mendel: Paranoia (1884)
- Kahlbaum: Catatonia (1868-1874)
- Hecker: Hebephrenia (1871)

Emil Kraepelin (1856-1926)

dementia praecox (1893)

onset at a relatively early age

chronic and deteriorating course



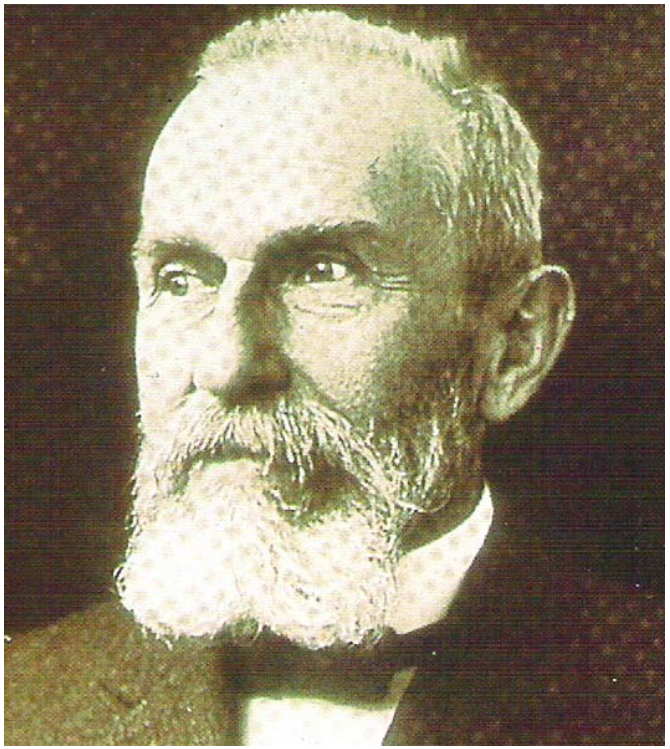
-to differentiate sch as an independent illness

-to establish disease on the basis of outcome/course

-separating from manic-depressive illness

Eugen Bleuler (1857-1939)

schizophrenia 1911



the reason of the cognitive impairment is the splitting of the psychic processes (behavior, emotion, thinking)

fundamental (basic) symptoms: four A's
affective blunting
disturbance of association
autism
ambivalence

accessory (additional) symptoms: delusions, hallucinations

Dementia Praecox or the Group of Schizophrenias
1911

Bleuler shifted the emphasis in schizophrenia from course and outcome to the **cross-sectional study of symptoms**, esssentially broadening the concept of the disease and give a more generous prognosis

Kurt Schneider (1887-1967)

not a separate disease, but a type of illness

first-rank psychotic symptoms

- Audible thoughts
- Voices heard arguing
- Voices heard commenting on one's actions
- The experience of influences playing on the body
- Thought withdrawal and other interferences with thought
- Delusional perception
- Feelings, impulses and volitional acts experienced as the work or influence of others

second-rank psychotic symptoms

Hallutinations
Flight of ideas
Distractedness
Perplexity
Out-of- body experiences
Emotional blunting
Compulsive behavior

Definition (DSM-IV-TR)

- characteristic positive and/or negative symptoms
- deterioration in social, occupational, and/or interpersonal relationship
- continuous signs of the disturbance for at least 6 months

- the disturbance is not due schizoaffective disorder, mood disorder with psychotic features, substance abuse and/or general medical condition

Subtypes of schizophrenia

- Catatonic type
- Disorganized type
- Paranoid type
- Residual type
- Undifferentiated type

Catatonic schizohrenia

- Catalepsy
- Stupor
- Hyperkinesiae
- Stereotypies
- Mannerisms
- Negativism
- Automatisms
- impulsivity

Hebephrenic/ Disorganized schizophrenia

- Incoherence
- Sever emotional disturbance
- Wild excitement alternating with tearfulness
- Vivid hallutinations
- Absurd, bizarr delusions, that are prolific, fleeting, and frequently concerned with ideas of omnipotence, sex change, cosmic identity and rebirth

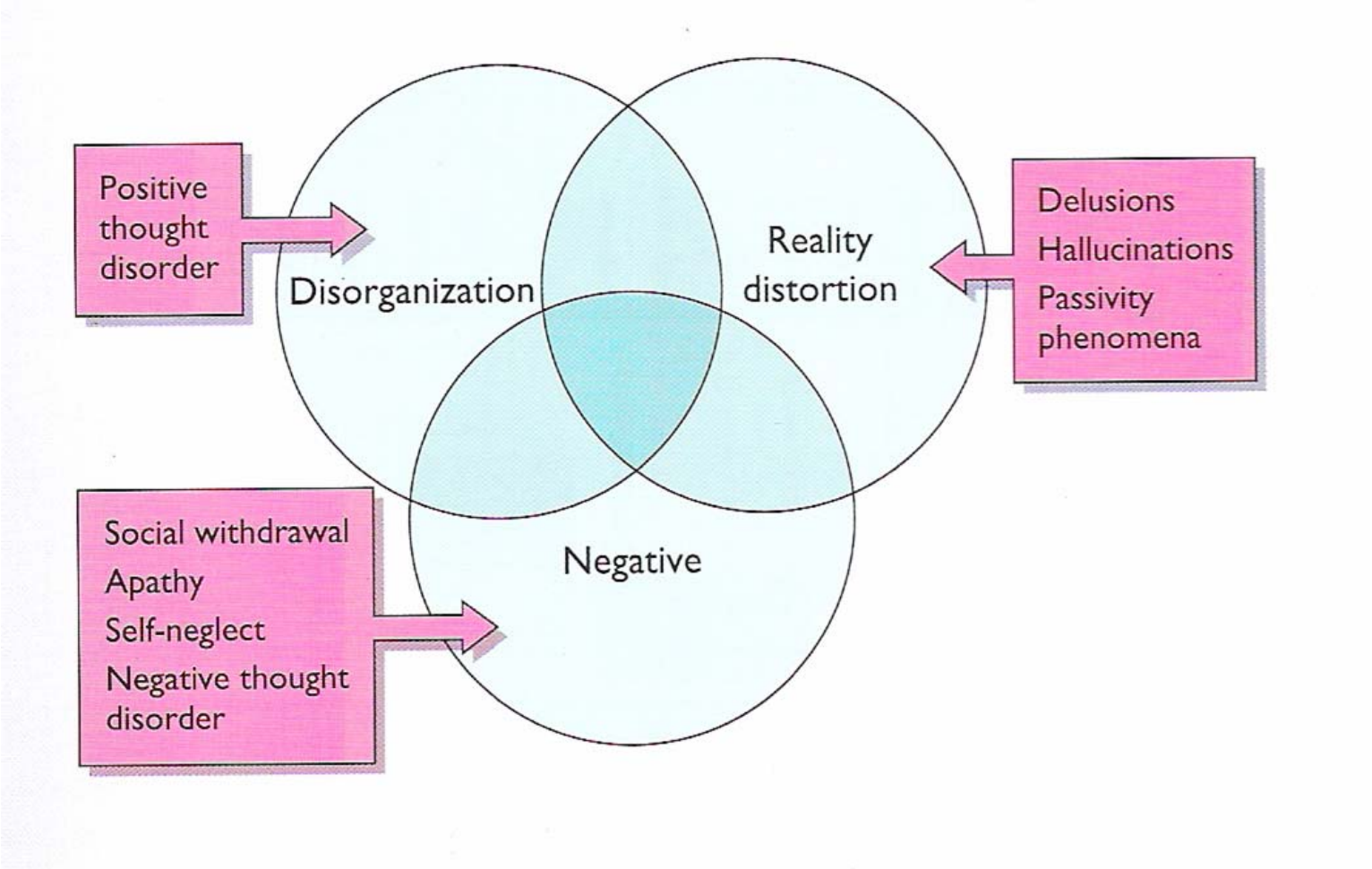
Paranoid schizophrenia

- Feeling, that external reality has changed and somehow become different
- Suspiciousness and ideas of dedication
- Ideas of references
- Hallucinations, especially of body sensations
- Delusions of persecutions or of grandiosity

Residual schizophrenia

- Interepisodic form
- The condition of being without gross psychotic symptoms following a psychotic schizophrenic episode

Syndromes of schizophrenia



Positive symptoms

- Formal thought disorder
- Disorganised behavior
- Inappropriate affect
- Delusions
- Hallucinations

Negative symptoms

- Poverty of speech
- Flattening of affect
- Anhedonia-asociality
- Avolition-apathy
- Attentional impairment

Affective symptoms

- anxiety
- dysthymia

Catatonic symptoms

These motor symptoms may occur in any form of schizophrenia, but are particularly associated with the catatonic subtype

- Ambitendence
- Echopraxia
- Stereotypies
- Negativism
- Posturing
- Waxy flexibility

The most frequent symptoms of acute phase

Symptom	Frequency (%)
Lack of insight	**97**
Auditory hallucinations	**74**
Ideas of reference	**70**
Suspiciousness	**66**
Flatness of affect	**66**
Second person hallucinations	**65**
Delusional mood	**64**
Delusion of persecution	**64**
Thought alienation	**52**
Thoughts spoken aloud	**50**

International Pilot Study of Schizophrenia 1970

Hallucinations

- False perceptions in the absence of a real external stimulus
- May involve any of the sensory modalities
- The most common are auditory hallucinations in the form of voices (60-70%)
- Visual hallucinations occur 10% (but:organic disorder!!!)
- Olfactory are more common in temporal lobe epilepsy
- Tactile hallutinations are more frequently than is reported by patients

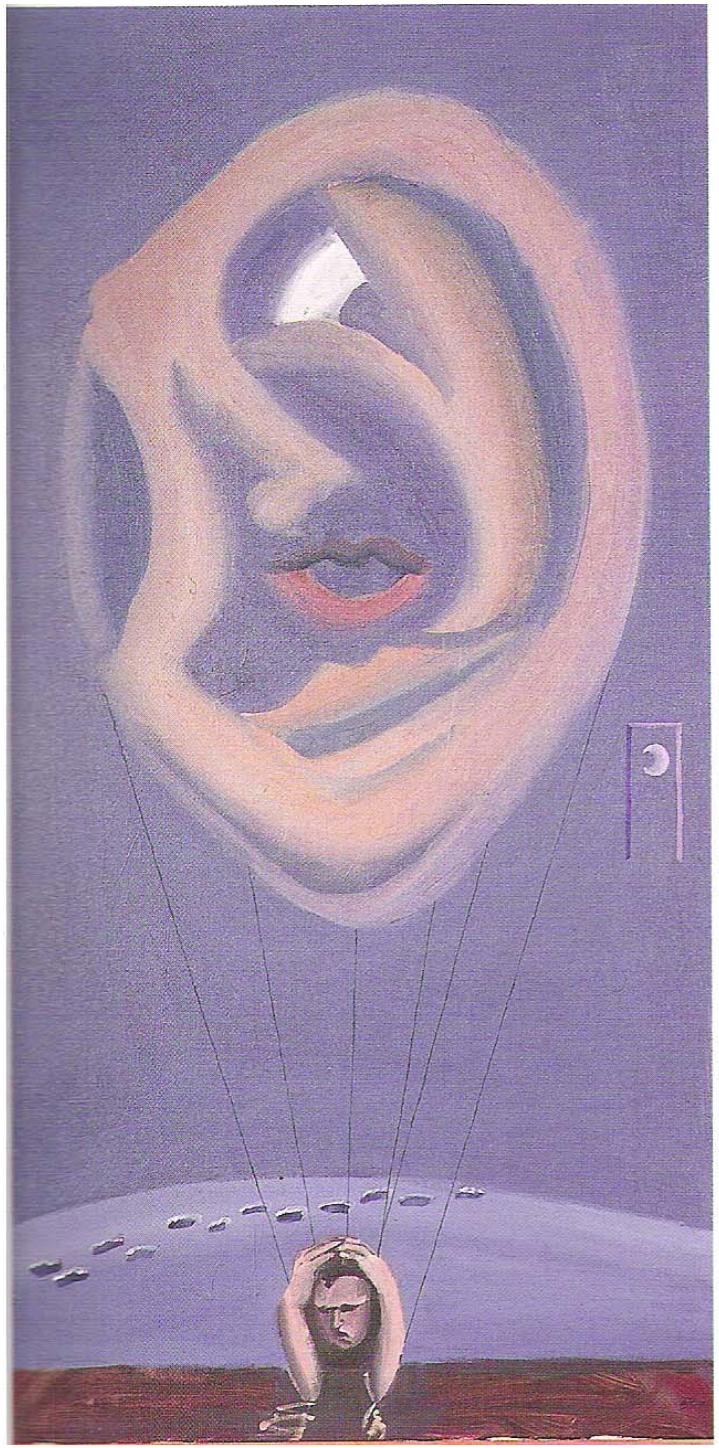


Figure 1.12 Grey self-portrait, by Bryan Charnley. This painting illustrates aspects of Charnley's psychotic symptoms, including that of hearing voices. Reproduced with kind permission of the Bethlem Royal Hospital Archives and Museum, Beckenham, Kent, UK

Epidemiology

- Schizophrenia occurs in all cultures
- Incidence is about 2-4 cases per 10 000 population per year
- Lifetime risk is 0,85-1%

Age and sex

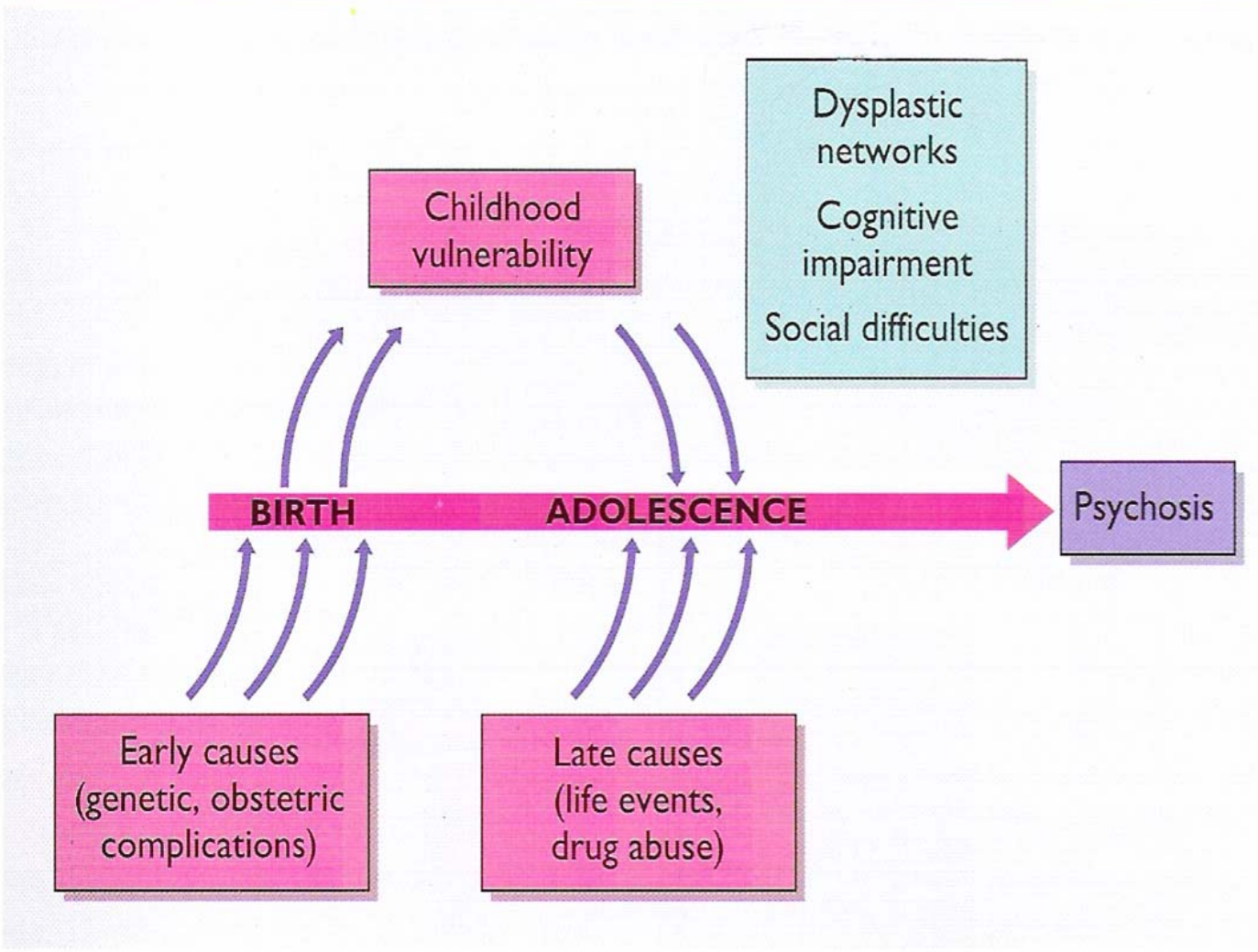
The peak incidence of onset is

15-25 years in men

and

25-35 years in women

THE DEVELOPMENTAL RISK FACTOR MODEL



Environmental influences

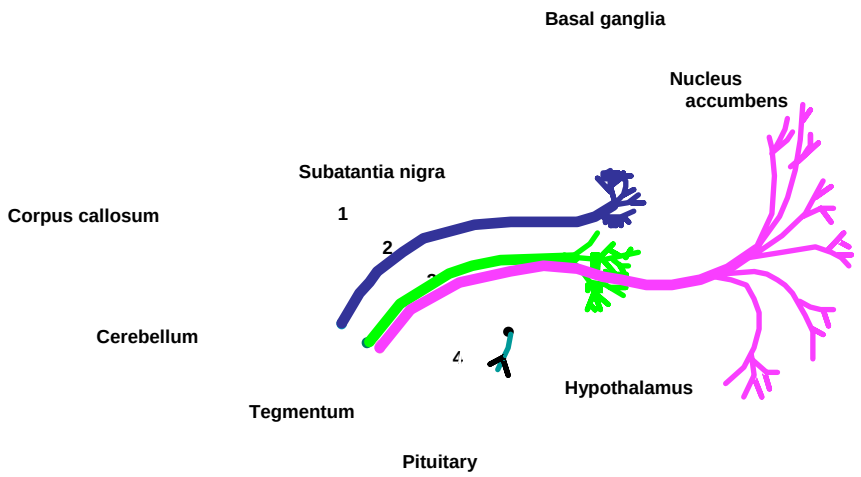
- Concordance in MZ twins is only about 50% !!!

- The rest of the variance must depend on the person’s environment

Lifetime expectancy of broadly defined schizophrenia in the relatives of schizophrenics

Relationship	Percentage schizophrenic
• Parent	5,6
• Sibling	10,1
• Sibling and one parent affected	16,7
• Children of one affected parents	12,8
• Children of two affected parents	46,3
• Uncles/aunts/nephews/nieces	2,8
• Grandchildren	3,7
• Unrelated	0,86

Dopaminergic pathways



Hales RE, Yudofsky SC. *Textbook of Neuropsychiatry*.
©1987 American Psychiatric Press.

The four major dopamine tracts:

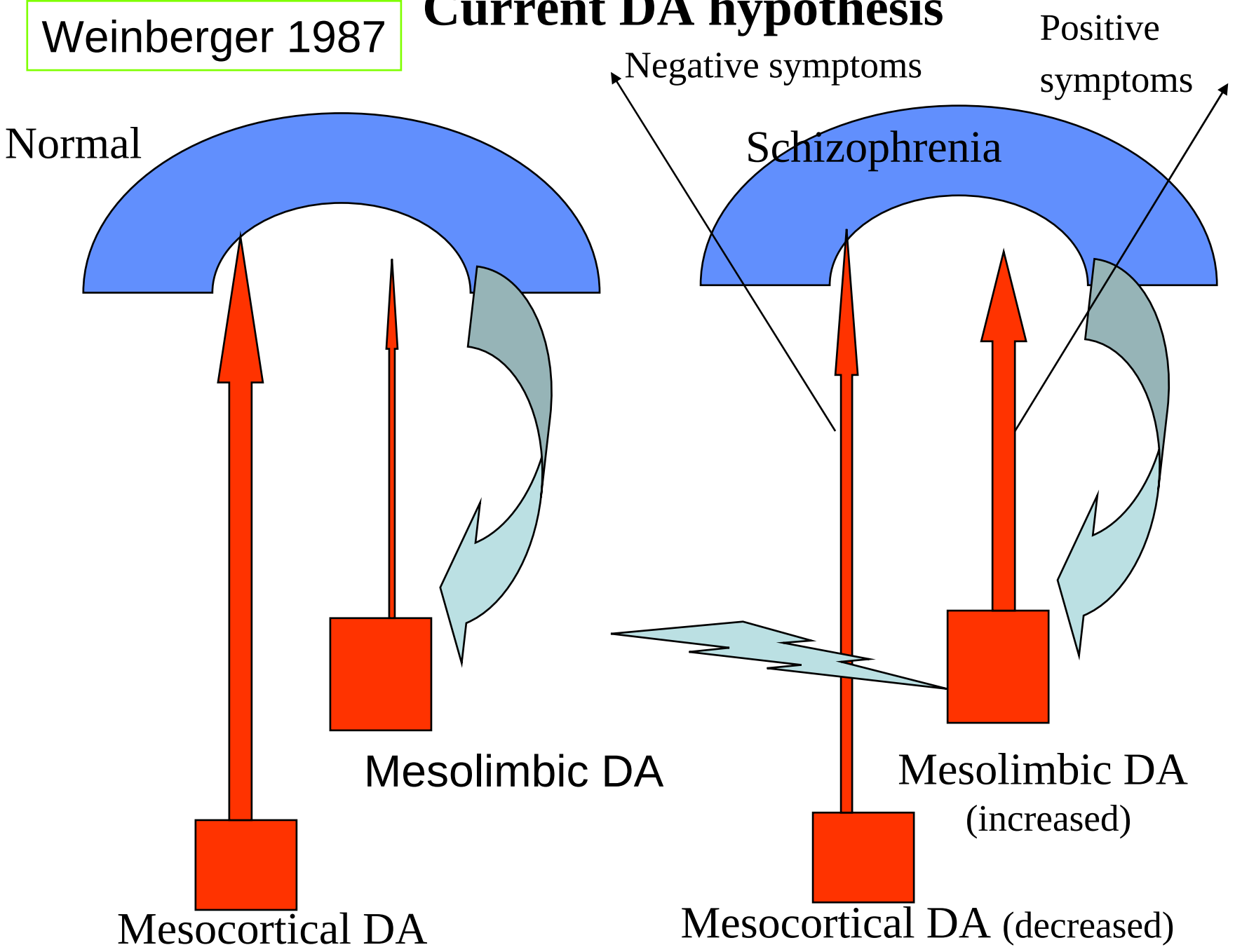
1) nigrostriatal
2) mesolimbic
3) mesocortical
4) tuberohypophyseal

mRNA Localization

D_1 and D_2: caudate/putamen
D_3: n. accumbens
D_4: cortex/hippocampus

Current DA hypothesis

Weinberger 1987



Outcome

After a first episode, all outcomes are possible

- Recover completly
- Relapsing and remitting course
- Severe progressive, disabling disorder with premature death (either from suicide or from a range of physical causes)

COURSE OF SCHIZOPHRENIA (THEORETICAL MODEL)

Table 1.1 Summary of long-term clinical outcome studies in schizophrenia.

Table reproduced with permission from Frangou S, Murray RM. *Schizophrenia*. London: Martin Dunitz, 1997

Study	Years of follow-up	Number of patients	Good clinical outcome (%)	Poor clinical outcome (%)	Social recovery (%)
Ciompi 1980[11,12]	37	289	27	42	39
Bleuler 1978[13]	23	208	20	24	51
Bland & Orne 1978[14]	14	90	26	37	65
Salokangas 1983[15]	8	161	26	24	69
Shepherd et al., 1989[16]	5	49	22	35	45

Treatment

Drug treatment strategy

- Acute treatment

- Maintenance treatment

Assesment of patient

- Diagnosis
- Evaluate risk of potential suicidal or antisocial behavior
- Evaluate possible consequences of delaying treatment
    - Poor treatment response and overall outcome
    - Rejection; difficult acceptance or reintegration into the community

Aims of treatment of acute psychosis

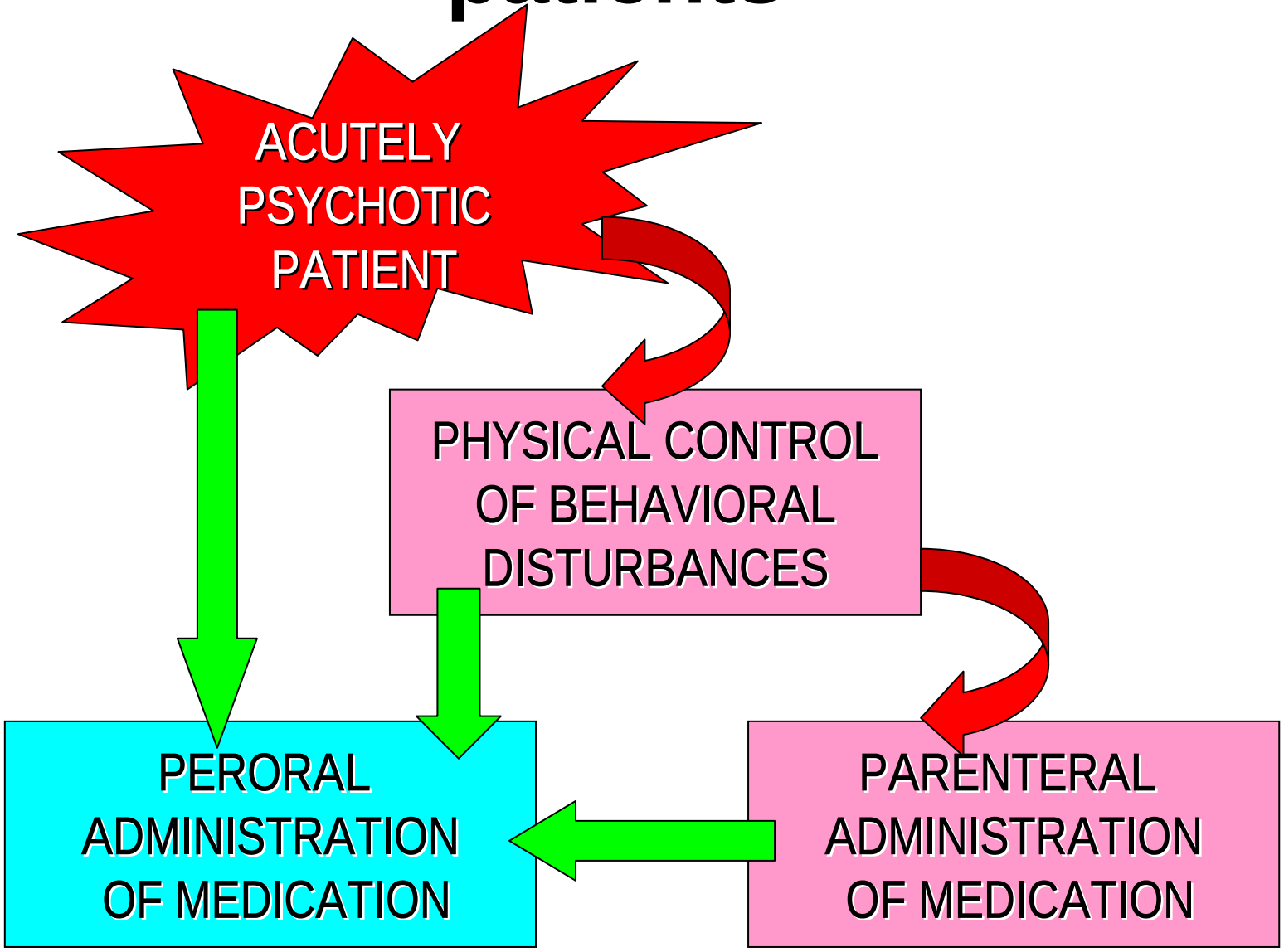
- to prevent harm and worsening of the pt’s state
- control disturbed behavior
- suppress symptoms
- rapid return to the best level of functioning
- develop an alliance with the patient and a close collaboration with the patient’s family
- short- and long-term treatment plans
- connect the patient with appropriate maintenance and follow-up care in the community
- adjust aims of treatment within a context of the community in which it takes place

Choice of treatment setting

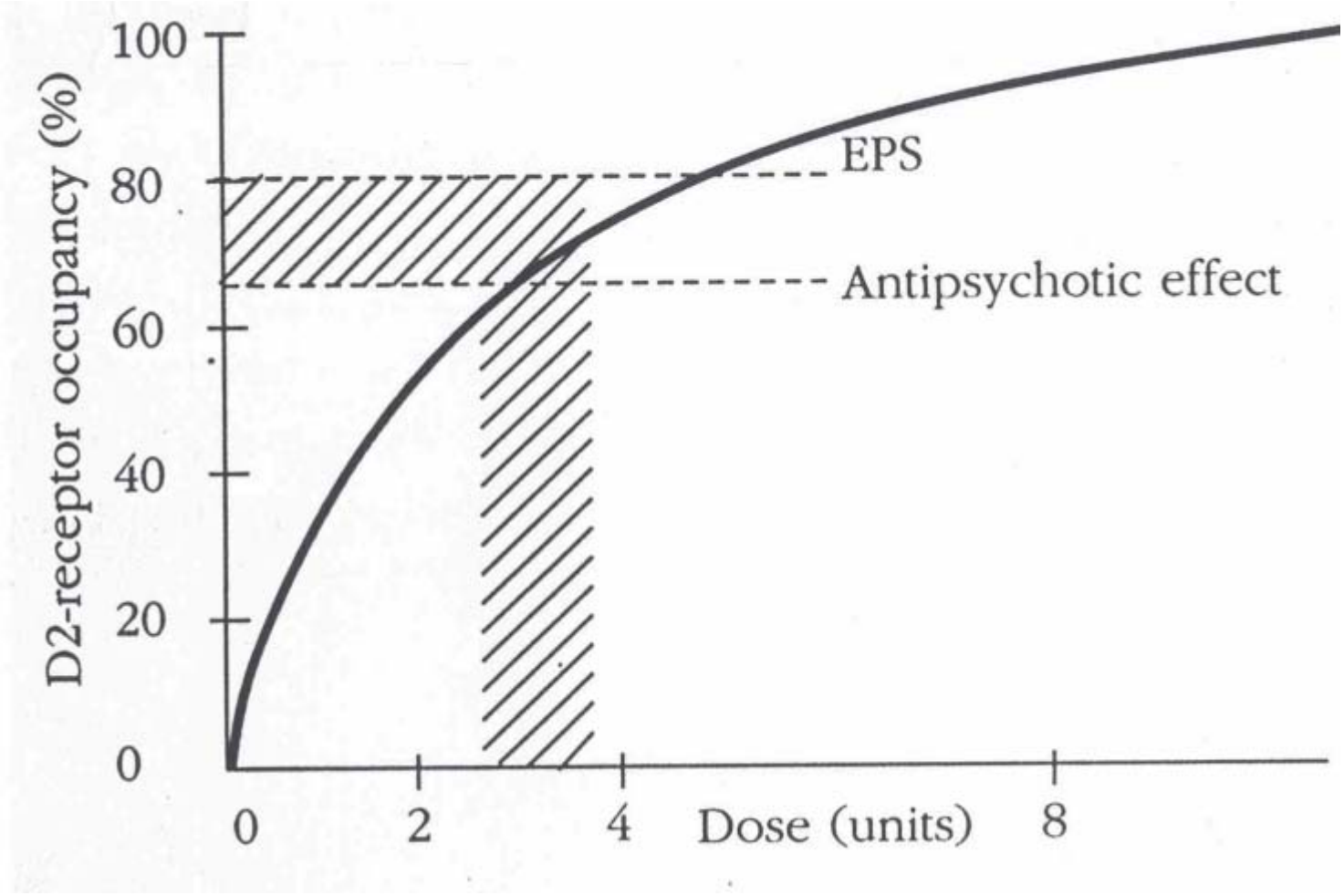
Depends on:

- severity of symptoms
- cooperation
- patient’s social situation and support
- need for specific therapy
- availability of various treatment options
- patient’s preferences

Management of acutely psychotic patients

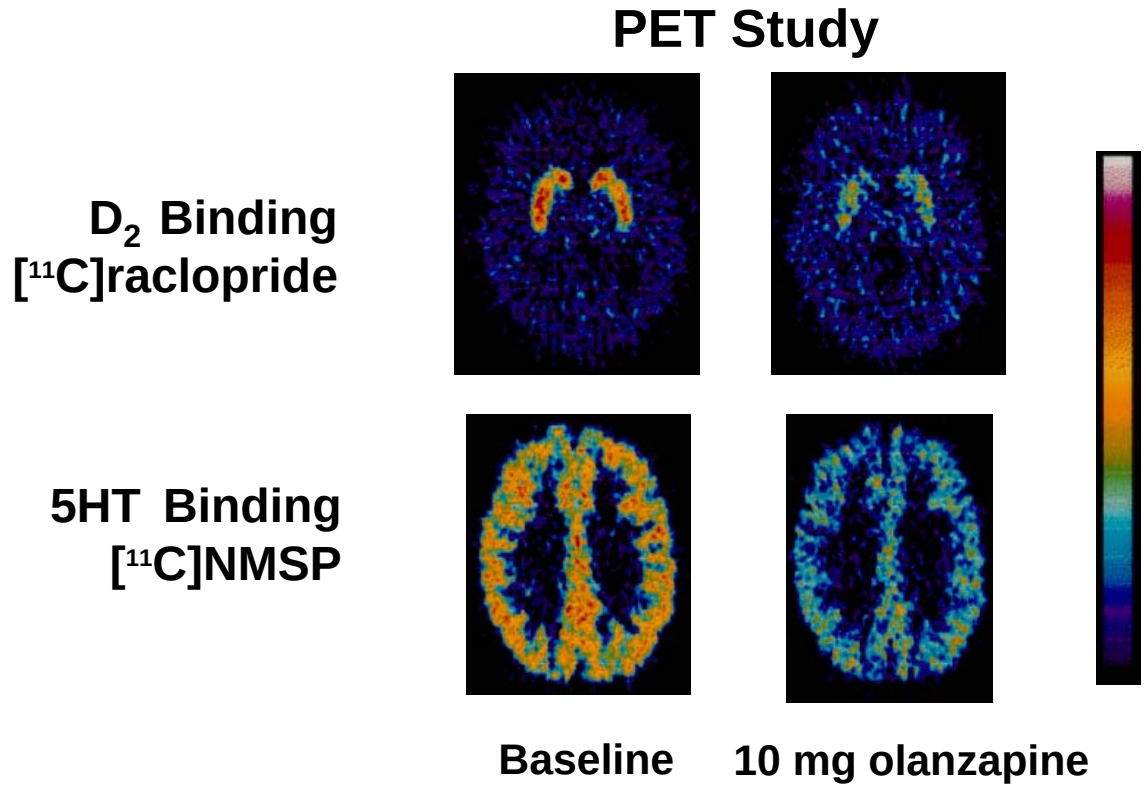


Relationship between the dose and D_2 receptor occupancy



Farde et al., 1992

Olanzapine: In Vivo Receptor Binding Affinity - 5-HT vs D_2



- Single 10 mg Olanzapine dose given
- Greater 5HT (84%) than D_2 (61%) occupancy approximates clozapine and suggests a low EPSE profile in contrast to other antipsychotic drugs

Nyberg et al 1996

Conventional antipsychotics

- Effective in control of positive symptoms and agitation
- Shorten duration of psychotic episode
- Reduce number of relapses
- Available in various drug forms (liquid, inject, depot inject.)

Conventional antipsychotics :

Side effects I.

- **Extrapyramidal side effects**

  acut dystonia

  akathisia

  rigidity

  tremor

  tardiv dyskinesia

Conventional antipsychotics :

Side effects II.

- **Anticholinergic effects:**
  - dry mouth, blurred vision, constipation, tachycardia, urinary retention, cognitive impairments, confusion, delirium
- **Antihistaminic effects:**
  - sedation, weight gain
- **Antiadrenergic effects:**
  - orthostatic hypotension

Conventional antipsychotics :

Side effects III.

- Allergy
- Photosensitivity
- Hepatic impairments (elevation of liver enzymes, jaundice)
- Pigmentary retinopathies; corneal opacities
- Leucopenia and agranulocytosis
- Pulmonary embolism
- QT prolongation
- Sudden death
- Seizures
- Neuroleptic-induced deficit syndrome?

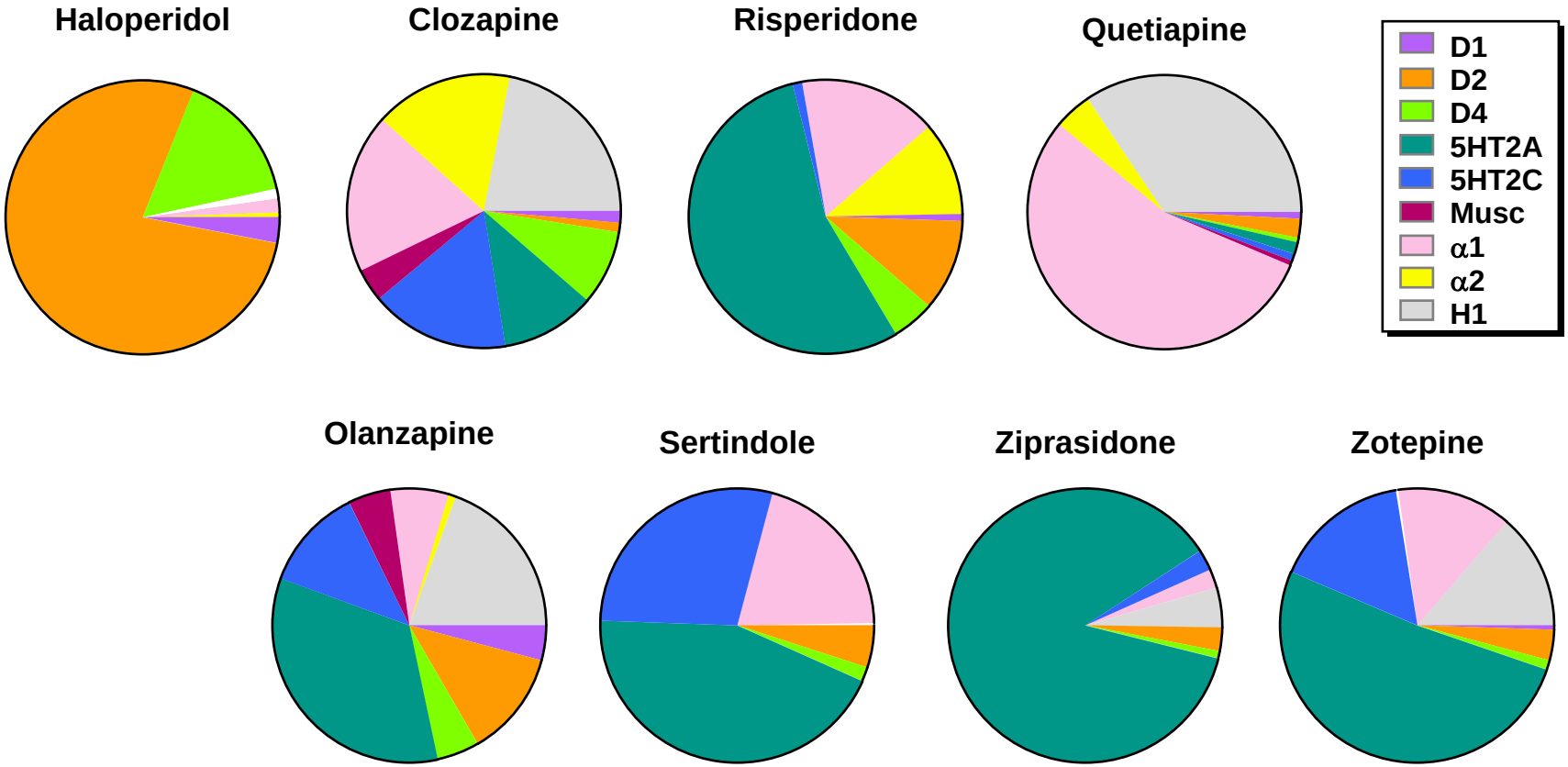
Conventional antipsychotics :
Limitations

- Less efficient in treatment of negative, affective, and cognitive symptoms
- Less effective in prophylaxis and control of relapses
- High number of non-responders and residual states
- High incidence of side effects
- High non-compliance rate

Second generation antipsychotics

- **Amisulpirid (Amitrex)**
- **Aripiprazol (Abilify)**
- **Clozapine („gold standard”) (Leponex)**
- **Olanzapine (Zyprexa)**
- **Quetiapine (Seroquel)**
- **Risperidone (Risperdal)**
- **Ziprasidone (Zeldox)**

Receptor selectivity vs multineurotransmitter activity



Data From Bymaster et al., 1996 & Schotte et al., 1996

2nd generation antipsychotics: most frequent side effects

- Sedation (H1, alpha1)
- Orthostatic hypotension (alpha2)
- Anticholinergic effects (M)
- Weight gain (H1)
- ECG abnormalities - prolongation QTc
- Seizures
- EPS and hyperprolactinaemia
- Agranulocytosis
- Hypersalivation

Summary

- Second generation antipsychotics (SA) improve positive and negative symptoms in acute psychosis; they may also affect affective symptoms and cognitive impairment

- SA are better tolerated with less problematic side effects than conventional antipsychotics (CA)

- Second generation antipsychotics should be among the first-line options in treatment of acute psychotic disorders

Treatments are most effective
when they are used in combination:

-pharmacotherapy
-psychotherapy
-psychosocial treatment/ family
 and social support

Psychosocial treatments

- Cognitive behavioural therapy
- Family interventions
- Psychoeducation
- Social skills training