Spring Semester 2018

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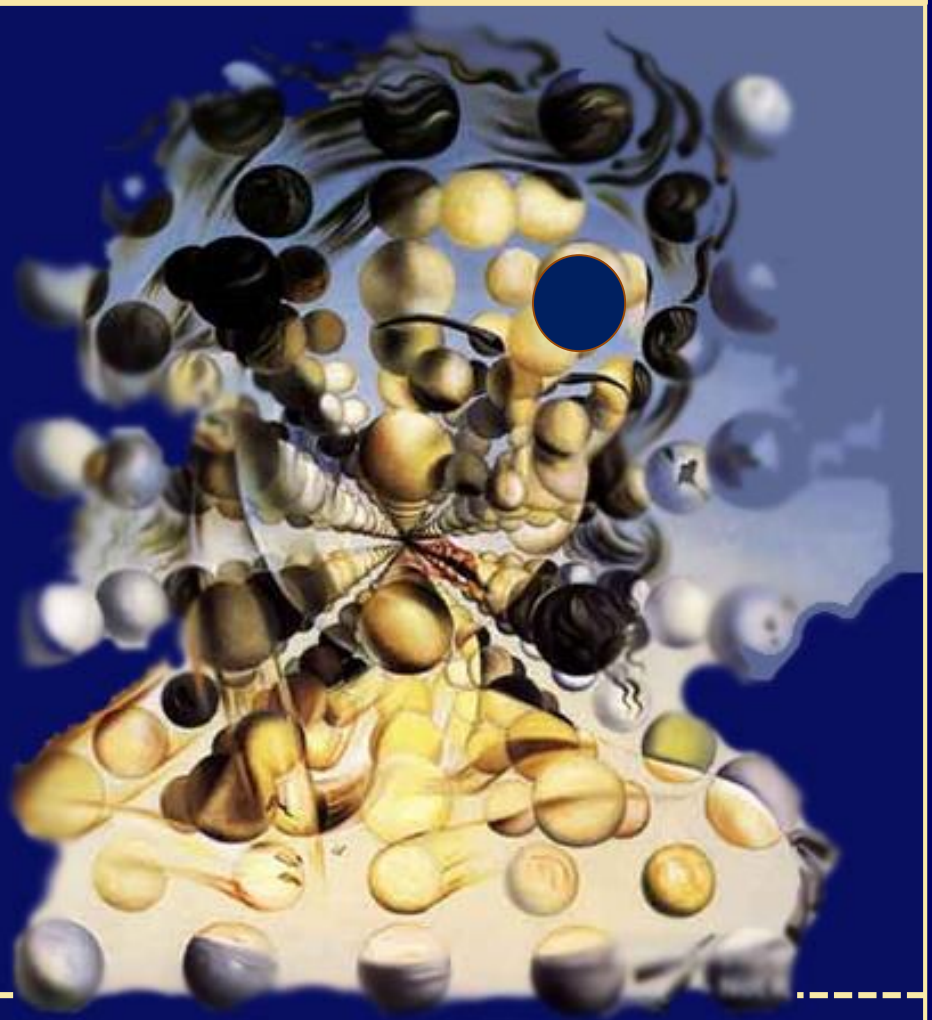


8. Schizophrenia

History

- Shakespeare (17th c.) et al. often use „madness“ as a common feature in their dramas, e.g. King Lear, Macbeth
- Pinel (1801): first scientific descriptions
- Morel (1850):
  ’démence‘ (loss of mind), ’précoce‘ (early, prematurely)
- Kraepelin (1899): dementia praecox
  - Catatonia (alternating immobilia)
  - Hebephrenia (silly emotionality)
  - Paranoia (delusions of grandeur/persecution)
- Bleuler (1908): Schizophrenia
  - Skhizein (Greek: split)
  - Phren (Greek: mind)

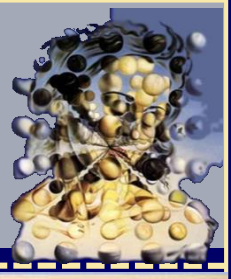
Classical Example (1)

The Genain quadruplets (born in 1930)

- Mother had schizophrenia, father alcohol dependece and OCD
- Difficult environment
  - Sadistic sexual harassment by their father
  - Father‘s patrols with a loaded gun
  - Genital mutilations by a surgeon
  - Mother: treated them as if they were two pairs (1) Nora and Myra (2) Iris and Hester
- *Nora* (firstborn)
  - „the best“ (IQ, cognitive development), preferred by parents
  - first to have a job (not for a long period, though), but never lived independently
  - first hospitalized at age 22, many hospitalizations

Classical Example (2)

The Genain quadruplets (born in the 30s)

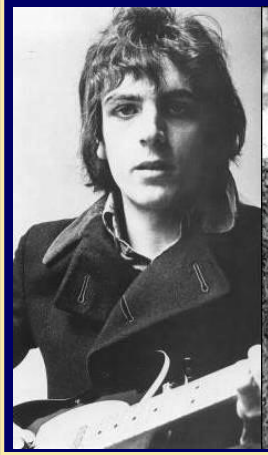


- *Iris (†2011)*
  - First hospitalized with age 22
  - 12 year in-patient in a hospital
  - No obvious brain disturbances
- *Myra*
  - No delusions and paranoia until her 40s
  - Married and has children
  - Not psychiatrically well, but could get off medication
  - Preferred by parents
- *Hester* (lastborn, *†2011*)
  - Lowest birth weight, slowest development
  - Removed from school, never held a job
  - Chronic nonremitting symptoms since age 18

Duncan (2013), doi:10.1016/j.schres.2013.06.011

Classical Examples (3)

- John Nash (mathematician, nobel prize winner)
- Mary Todd Lincoln (wife of Abraham Lincoln)
- Tom Harell (Jazz trumpetist)
- Syd Barrett (Pink Floyd; later called „psychedelic music“)





Terms (1) Positive symptoms

„pathological excesses“ (p. 469)

- *Delusion*

  Strongly defended false beliefs due to misinterpretations of biased perception of the world. E.g.: moderator of the TV show sends love messages to the patient within his show

- *Hallucination*

  Sensory experience without any external perceptual stimulus. E.g. hearing voices where there are none. (≠ illusion)

- *Disorganized thinking and speech*

  Disordered thought form; person does not follow the normal semantic and syntactic rules of verbal communications (loose associations, neologisms, clang)

- *Heightened perception:* perceived overstimulation

Terms (3) Negative symptoms

„pathological deficits“ (p. 474)

- *Affective flattening:* hardly any emotional reactions
- *Anhedonia:* lack of experiencing pleasure
- *Avolition:* apathy; inability to initiate or persist in activities
- *Alogia:* absence of speech

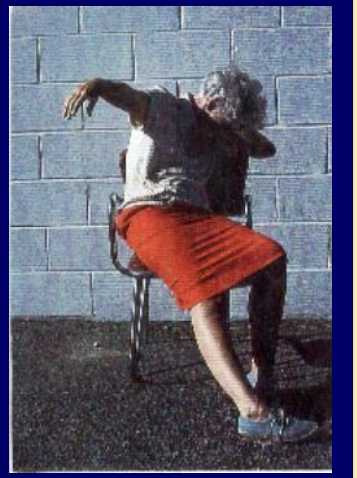
Terms (3)
Psychomotor symptoms

- *Disorganized behavior*

  No goal-directed activity (e.g. getting up and making breakfast) sometimes combined with inappropriate affect.

- *Catatonic behavior*

  Echolalia (repetition of words), echopraxia (constant repetition of movements), grimacing or absence of speech and all movements (stupor) with waxy flexibility.



Case example: Etta

„When you do the 25 of the clock, it means that you leave the house 25 after 1 to mail letters so that they can check on you....and they know where you‘re at. That is the eagle... If you don‘t do something they tell you, Jesus makes the shotgun sound, and then .... Not to answer the phone or doorbell....because you‘d get shot eagle.“

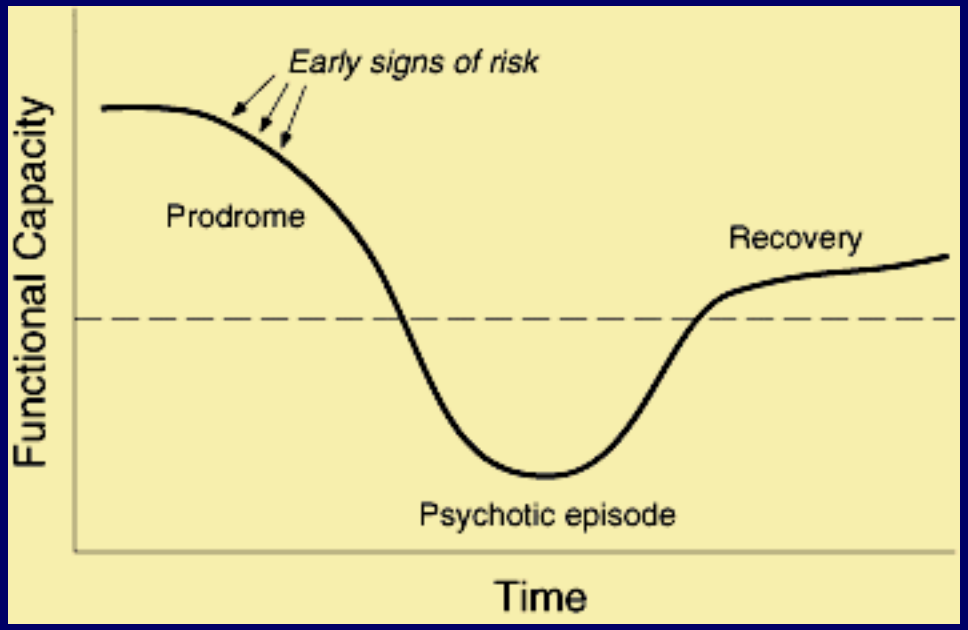
From: Barlow & Durand (1999), p. 409

Classification: Schizophrenia spectrum and other psychotic disorders (DSM-5)

- Delusional disorder
- Brief psychotic disorder
- Schizophreniform disorder (1 - <6 months)
- Schizophrenia
- Schizoaffective disorder
- Substance-/Medication induced psychotic disorder
- Psychotic disorder due to another medical condition
- Catatonia (as another separate condition)
- Other schizophrenia spectrum and psychotic disorder
- (Schizotypal personality disorder)

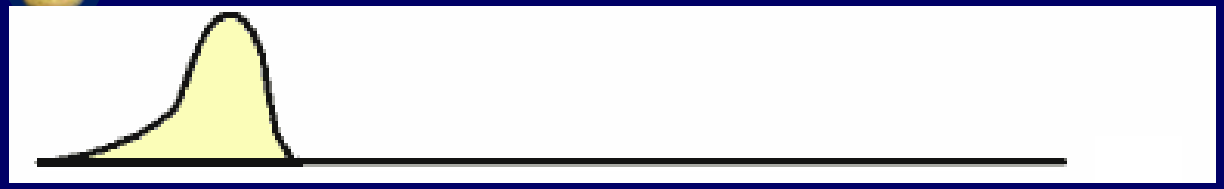
Typical Course (1)

chronic, insidious (68%)

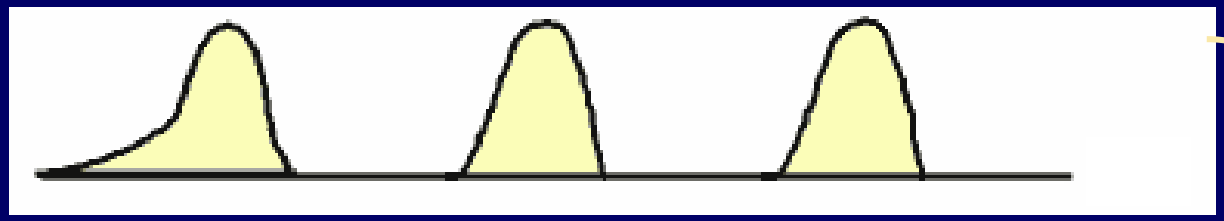


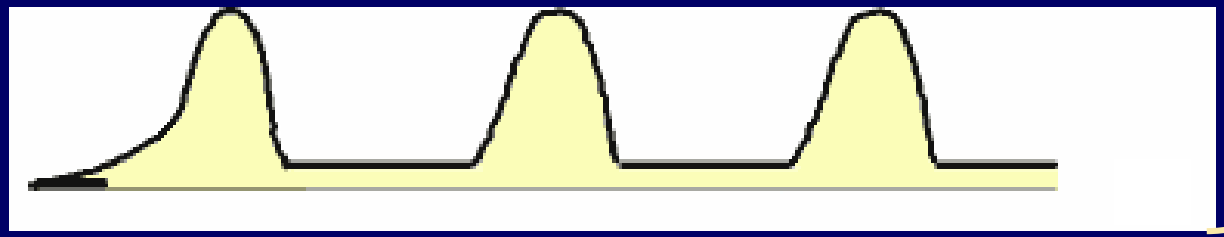
- *3-5 years before treatment:* depressive mood, lack of confidence, suicide attempts
- *1-3 years before treatment:* negative symptoms
- Then: dysfunctioning and psychosis

Typical Course (2)

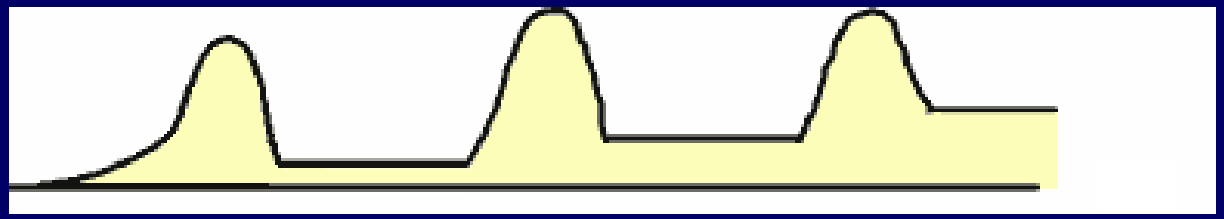


ca. 25% (21%)





ca. 50% (43%)



ca. 25% (36%)

Course (3)

Changes in perception

From:
Collection Prinzhorn, Heidelberg

Institutional life

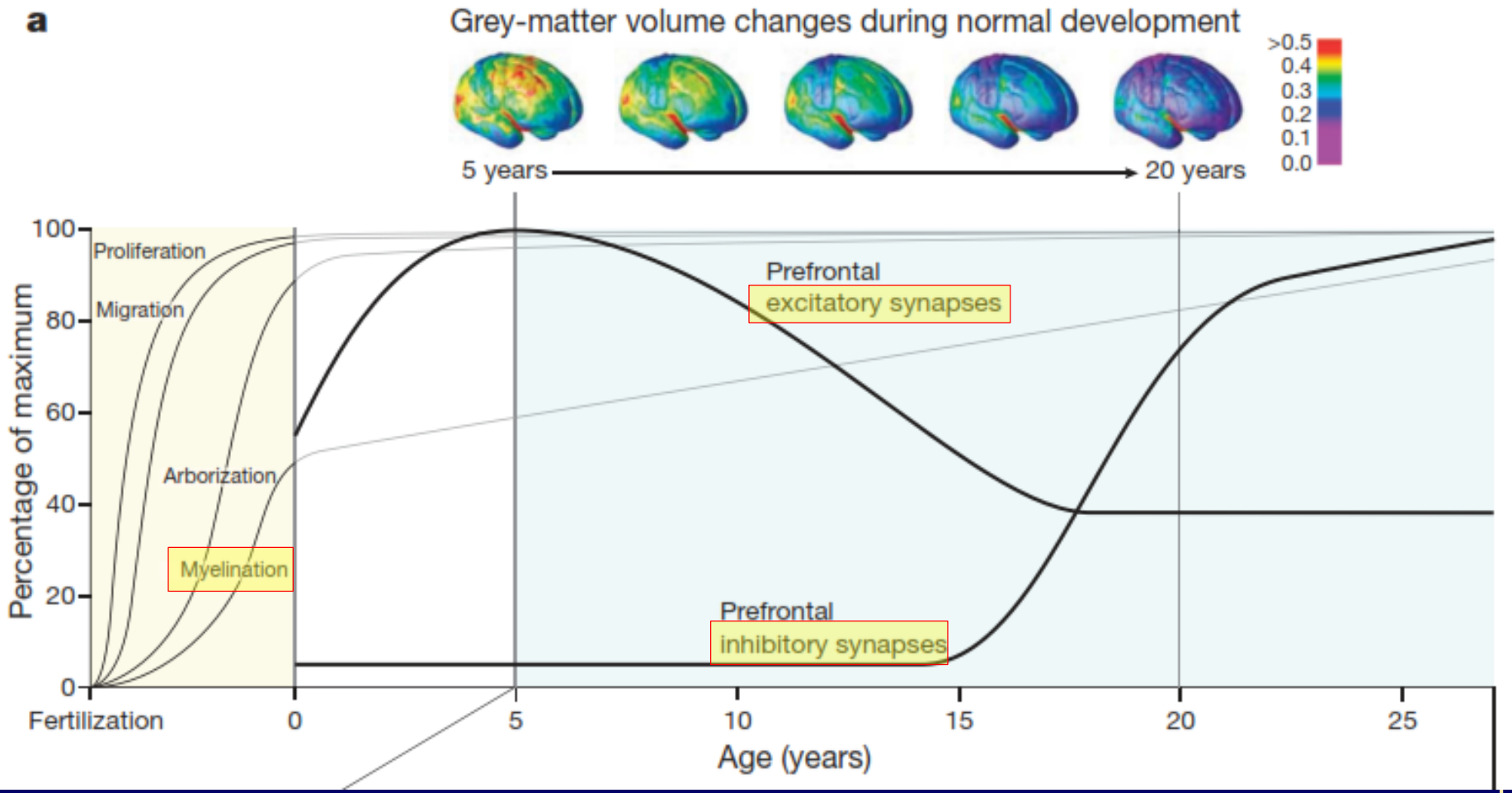
In a scene reminiscent of public mental hospitals in the United States during the first half of the twentieth century, these patients spend their days crowded together on a hospital ward in central Shanghai. Because of a shortage of therapists, only a small fraction of Chinese people with psychological disorders receive proper professional care today.

Epidemiology

- Life-time prevalence: around 0.5-1%
- If father at birth of child >45 years old: 3%
- Peak in women later than in men (men 20-24 years), women‘s second peak at age 45 (estrogen and menopause?)
- Schizophrenia in women seems less severe
- China (Phillips et al. 2009)
  - 1-month: 2%
  - Prevalence (women) = Prevalence (men)
  - Prevalence (urban areas) = Prevalence (rural areas)

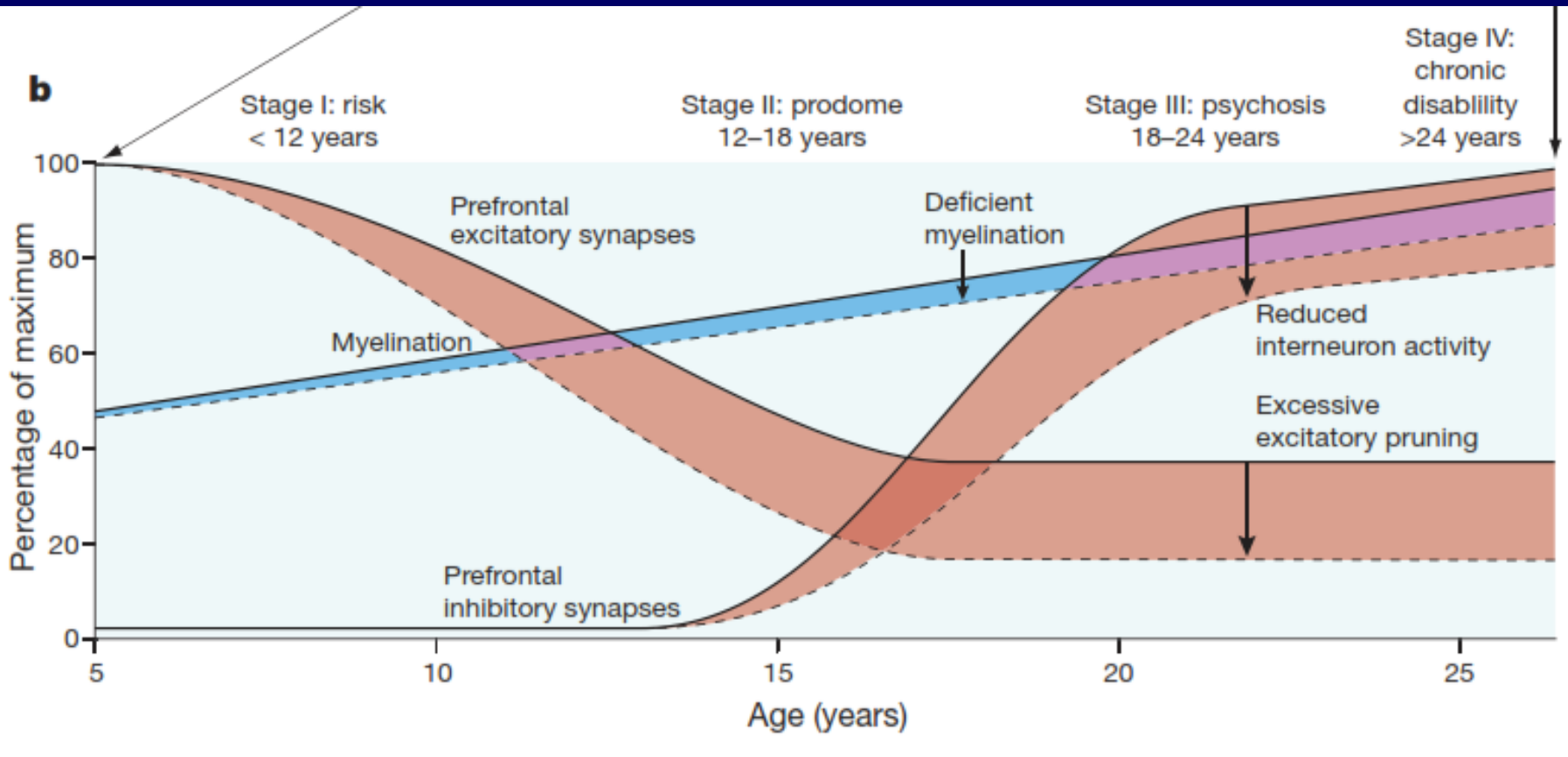
New biological explanation

Insel (2010) Normal development



Biological explanation

Insel (2010) Differences for patients with schizophrenia



Resulting stage model

Insel (2010)

Table 1 | Stages of schizophrenia

	Stage I	Stage II	Stage III	Stage IV
Features	Genetic vulnerability Environmental exposure	Cognitive, behavioural and social deficits Help-seeking	Abnormal thought and behaviour Relapsing–remitting course	Loss of function Medical complications Incarceration
Diagnosis	Genetic sequence Family history	SIPS Cognitive assessment Imaging	Clinical interview Loss of insight	Clinical interview Loss of function
Disability	None/mild cognitive deficit	Change in school and social function	Acute loss of function Acute family distress	Chronic disability Unemployment Homelessness
Intervention	Unknown	Cognitive training? Polyunsaturated fatty acids? Family support?	Medication Psychosocial interventions	Medication Psychosocial interventions Rehabilitation services

Stage I, pre-symptomatic risk; stage II, pre-psychotic prodrome; stage III, acute psychosis; stage IV, chronic illness.

Medical Treatment (1)

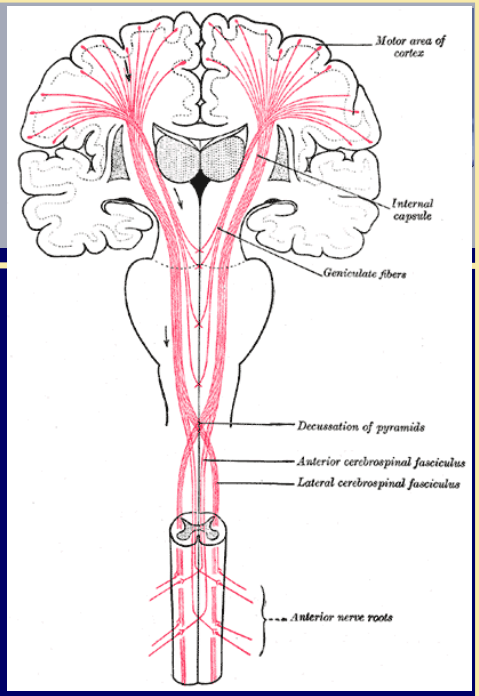
Most common drugs

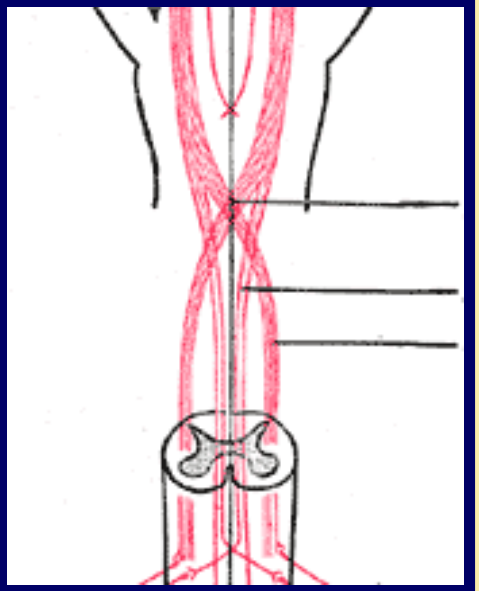
- Haloperidol, Chlorpromazine (high EPS)
- Clozapine, Risperidone (atypical; low EPS, but often suppresses white blood cell formation!)

Side effects

- Extrapyramidal symptoms (EPS)
  - Tardive dyskinesia: involuntary (!) tremor (face, extremities)
  - Muscle rigidity (extreme: „parkinsonism“)
  - Slowness of movement
  - Motor speech abnormalities
- Others

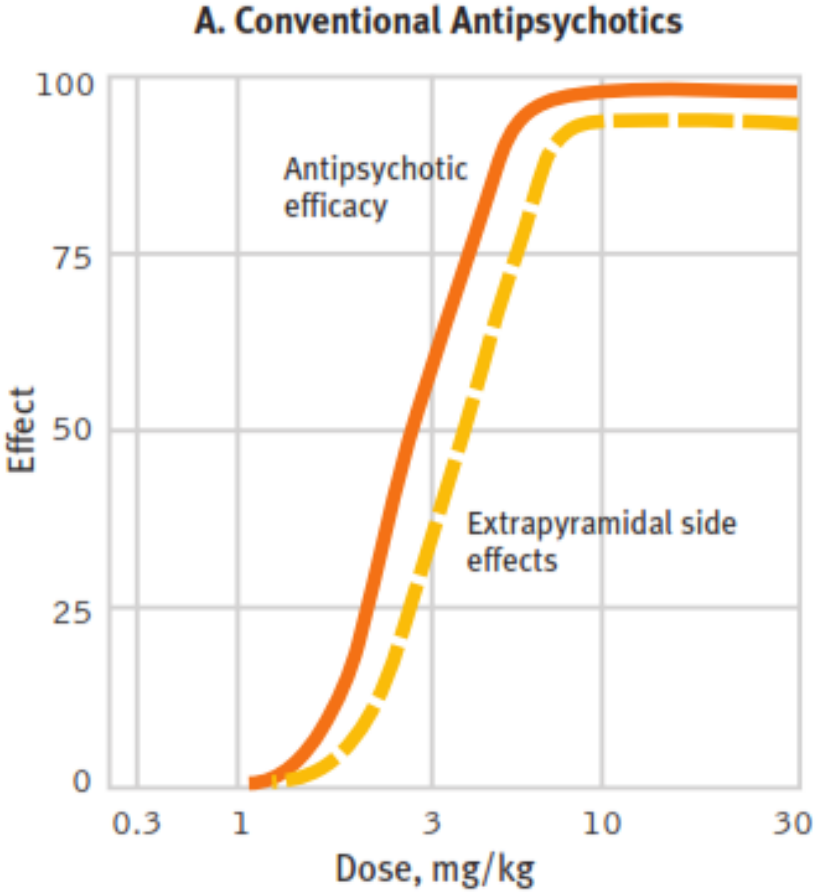
  Blurred vision, dry mouth, constipation, weight gain, decreased sex drive et al.

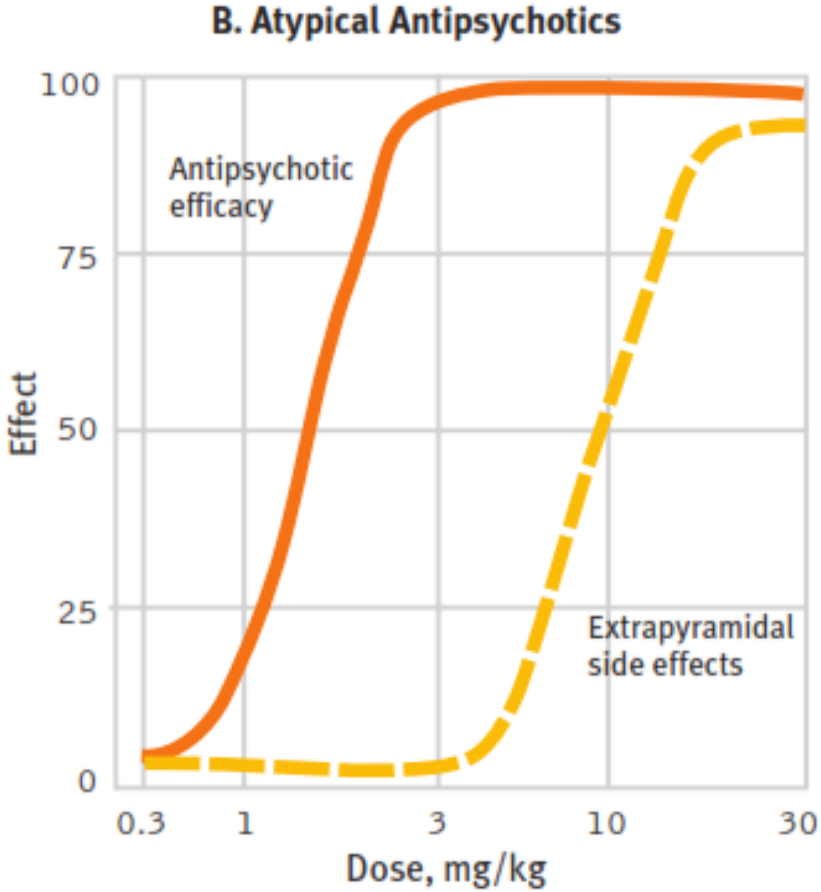




Medical Treatment (2)

Classical vs. Atypical drugs





Medical Treatment (3)

Effectiveness of drug treatment

- All drugs highly effective against positive symptoms
- Some atypical drugs also effective against negative symptoms
  But: Relapse rate around 40% within 1 year
- Severe side effects
- Patients often stop drug treatment
  (solution: depot injections)
- Medication can be reduced to a low level when early signs are recognized and reported

Electroconvulsive therapy

less effective than drug treatment, only used in cases where „nothing else works“

Psychological treatments

- Family therapy
  - *Goals*
    - Reduce the degree of expressed emotion
    - Make relatives have more realistic expectations, more tolerance
  - *Result:* reduces relapse rate
- Cognitive Behavior Therapy (CBT)
  - Stress management
    - Good results within 1-2years
    - Long-term effects questionable, but people have less problems than control groups
  - Belief modification
    - Goal: minimizes impact of hallucinations on people‘s everyday lives
    - Challenging hallucination leads to better understanding than distracting from them, including accepting existing but hindering biological signals
- Community services! (problem: coordination)

Homework

Listen to Eleanor Longden's TED talk:

http://www.ted.com/talks/eleanor_longden_the_voices_in_my_head

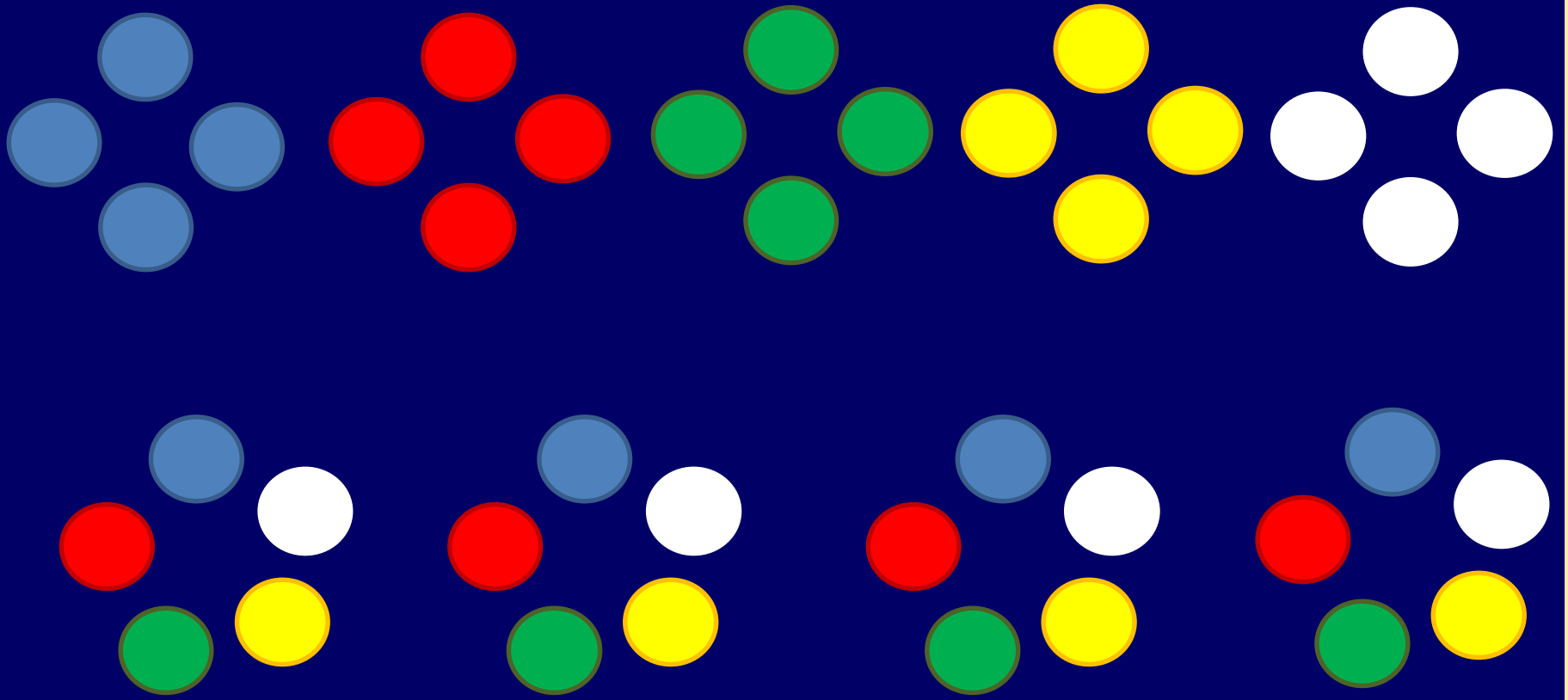
International Hearing Voices Network:

http://www.intervoiceonline.org/

Etiology – Group activity (1) Objectives

- To make you understand the complexity of etiology using schizophrenia as an example
- To be able to distinguish between a conclusion and the corresponding evidence
- To extract relevant information in limited time
- To organize a group efficiently while making sure that everyone understands the message

Etiology – Group activity (2)



Example

Since schizophrenia is more prevalent in high latitudes and cold climates, researchers have theorized vitamin D may be connected to the disorder.

The researchers reviewed the findings of 19 observational studies that assessed the link between vitamin D and schizophrenia. Combined, the studies looked at vitamin D levels and the mental health of 2,804 adult participants. The studies used blood tests to determine each participant's vitamin D levels.

The meta-analysis found that people with schizophrenia had significantly lower levels of vitamin D in the blood compared to the control groups. The average difference in vitamin D levels between schizophrenic patients and control participants was -5.91 ng/ml. People with vitamin D deficiency were 2.16 times more likely to have schizophrenia than those with sufficient vitamin D in their bloodstreams. In addition, 65 percent of the participants who had schizophrenia also were vitamin D deficient.

Etiology – Group activity (3)
Stage 1 (30 min)

- Get together in the group appointed to you.
- Get an overview over the material and make a plan how you will work in your group to make sure that all main ideas get extracted in time.
- Discuss and consolidate the results with your group-mates.
- Be sure that everybody understands the main idea of ALL topics within his or her group!
- You may use the table to help your memory.
- Every one has to feel able to summarize the results within 3-4 minutes!

Etiology – Group activity (4) Stage 2

- Change the groups so that each topic is represented in each of the new groups.
- Present your ideas in the specified order (Group 1-5): FOLLOW ME! I am doing the timing!
  - Group 1 starts on my sign and stops on my sign. If you have finished, permit questions.
  - Group 2 starts…
  - …
- Choose 1-2 open questions in your group and write them on a slid of paper.

Etiology – Group activity (5) Stage 3

- What is still missing in the consolidation? Discuss open questions.
- Reflect back on this group work.
- Write down one reminder to yourself what you will try out differently next time.

Your questions

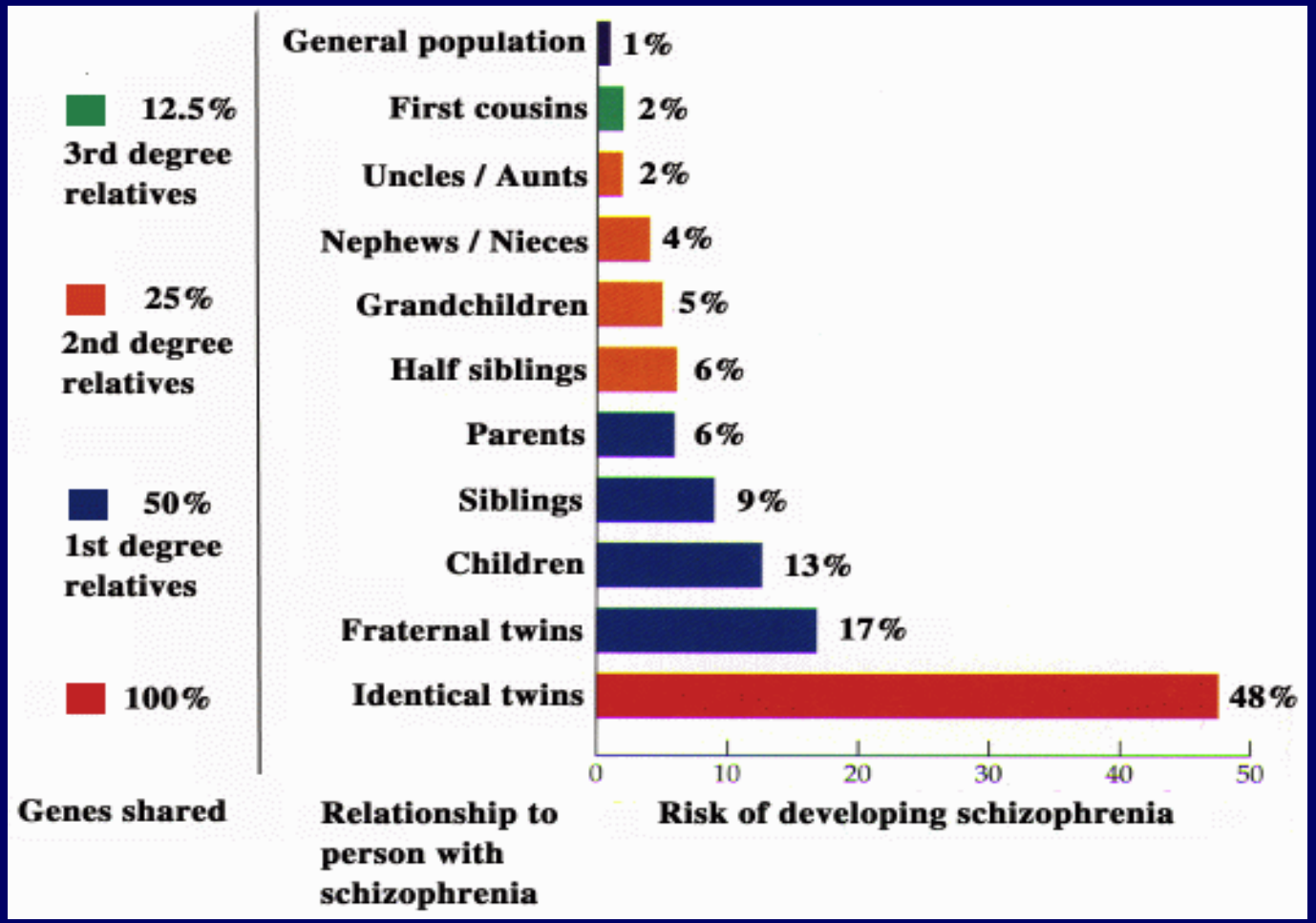
- What is the key factor?
  ("So many factors, some are not important!")
- How to come to causal relationships in brain imaging studies?
- Why is pressure on women increasing the risk of the infant?
- Is it ethical to cut a person's cortex?
- What are HEE?
- What can we do in the current environment?
  „If S. has a genetic basis, we cannot cure it perfectly?"

Etiology – Biological Features (1)

Genetical influences – twin studies

- Note: If schizophrenia is completely genetic, then the concordance rate for MZ twins must be 100%.
  - MZ twins concordance rate: 28-48%
  - DZ twins concordance rate: 6-15%
  - TORREY: reduction of shared genes from 100 to 50 percent leads to a reduction of the risk for schizophrenia of 80%!
  - 89% of schizophrenic patients have no family member with the disorder
- Conclusion
  - Genes play an important role
  - Genes alone cannot explain everything, e.g. why many MZ twin siblings of schizophrenia patients do *not* develop the disorder!

Prevalence rate based on degree of genetic relatedness



Etiology – Biological Features (2)

The dopamine hypothesis

- Based on findings
  - Drugs ↑ dopamine ⇒ hallucinations
  - Drugs ↓ dopamine ⇒ help against hallucinations
  - Dead schizophrenia patients had more dopamine receptors
  - Most helpful drugs work on D2 receptor
- Problem: alternative explanations possible
  - Findings based on treatment effects!
  - Most effective drug against schizophrenia works via serotonin system
  - Many patients do not profit from drug treatment
  - Negative symptoms not reduced by drug treatment

Neuronal transmission (1)

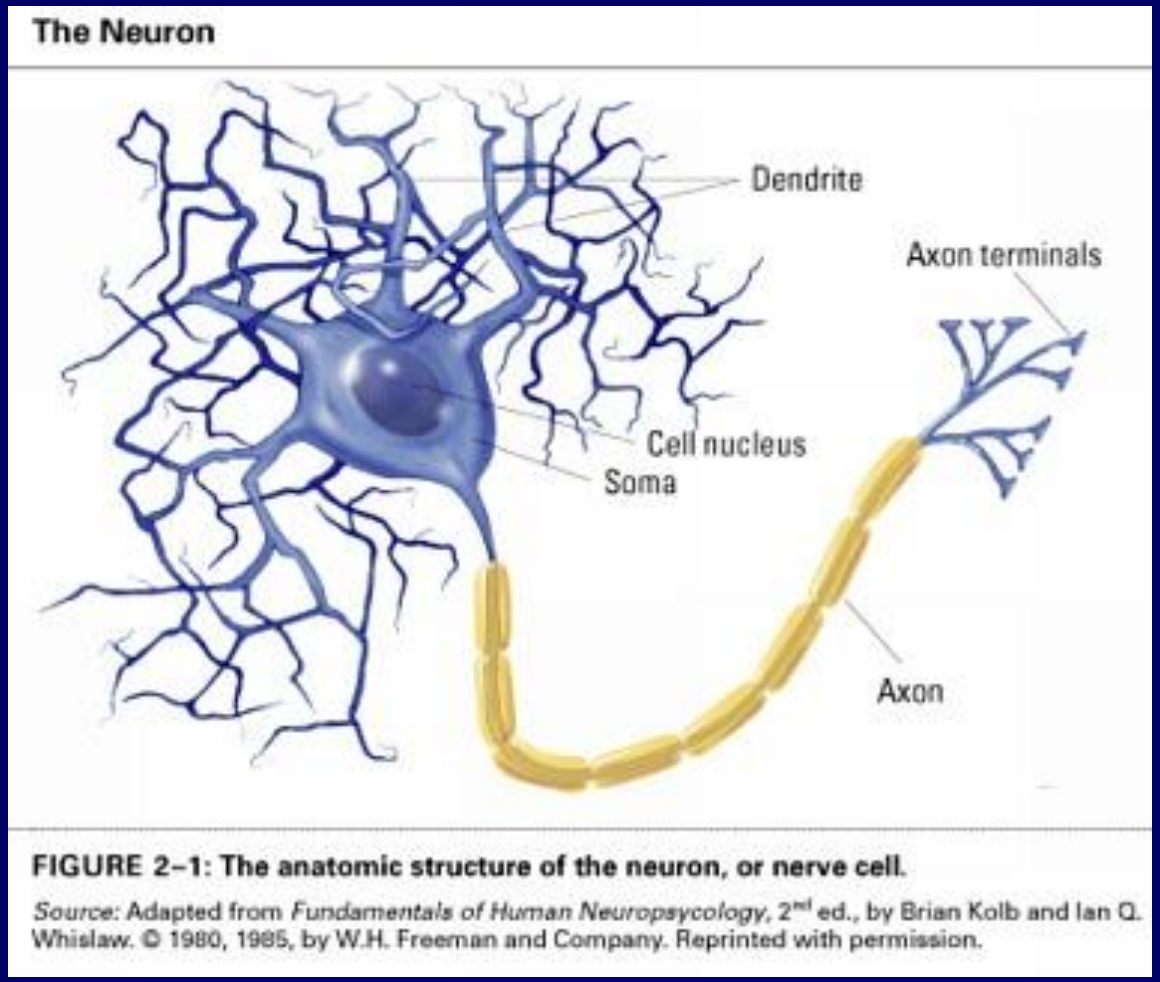


FIGURE 2–1: The anatomic structure of the neuron, or nerve cell.

Source: Adapted from *Fundamentals of Human Neuropsycology*, 2nd ed., by Brian Kolb and Ian Q. Whishaw. © 1980, 1985, by W.H. Freeman and Company. Reprinted with permission.

Neuronal transmission (2)

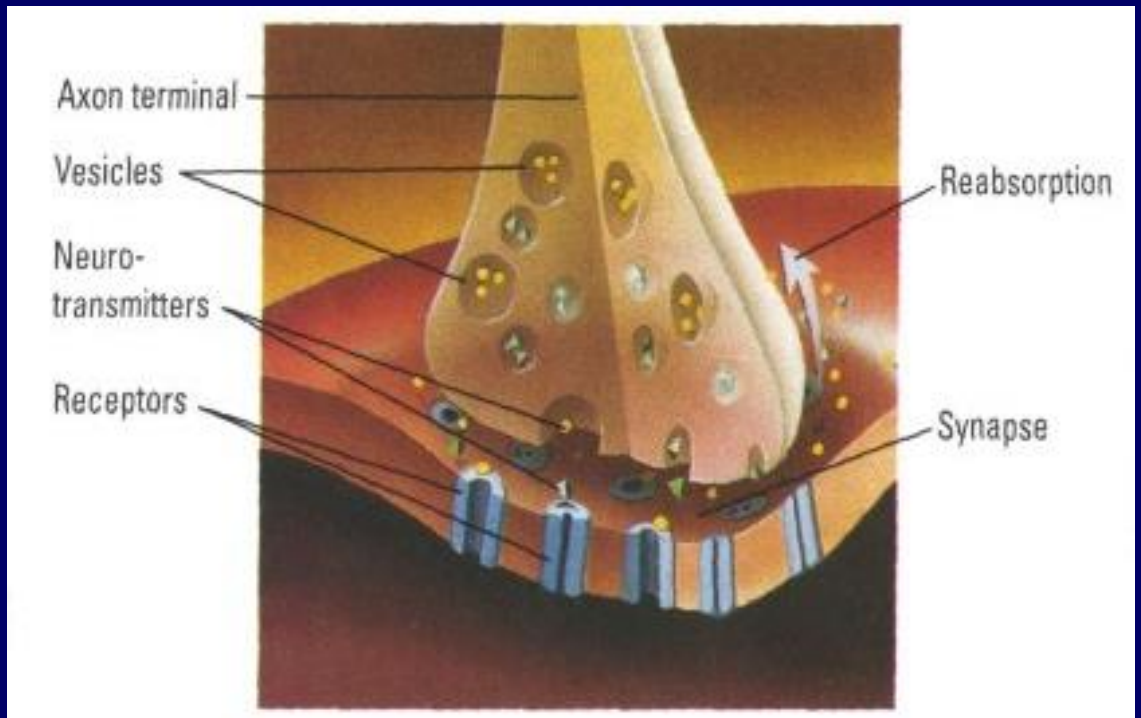


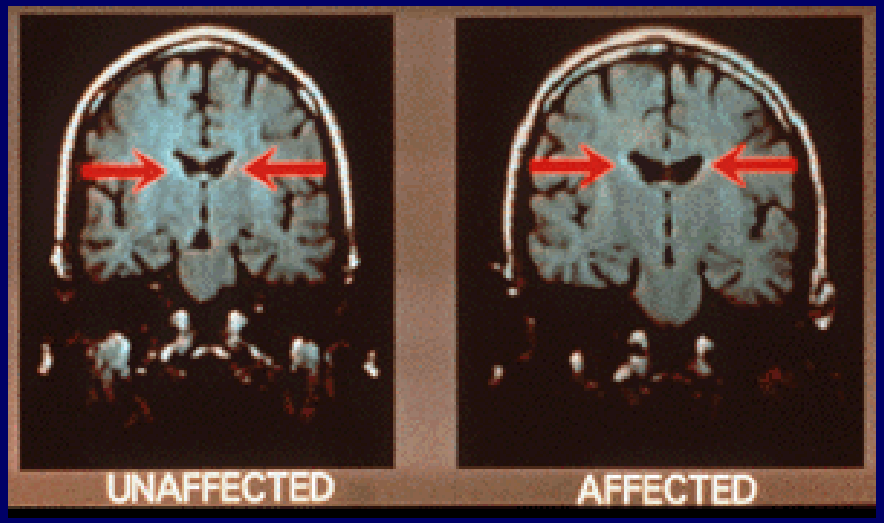
FIGURE 2–2: When an electrical nerve impulse reaches the end of a neuron, synaptic vesicles release neurotransmitters into the synapse. The chemical transmission between cells is complete when neurotransmitters travel to receptor sites on another neuron.

Source: Keith Kasnot, © National Geographic Image Collection.

Etiology – Biological Features (3)

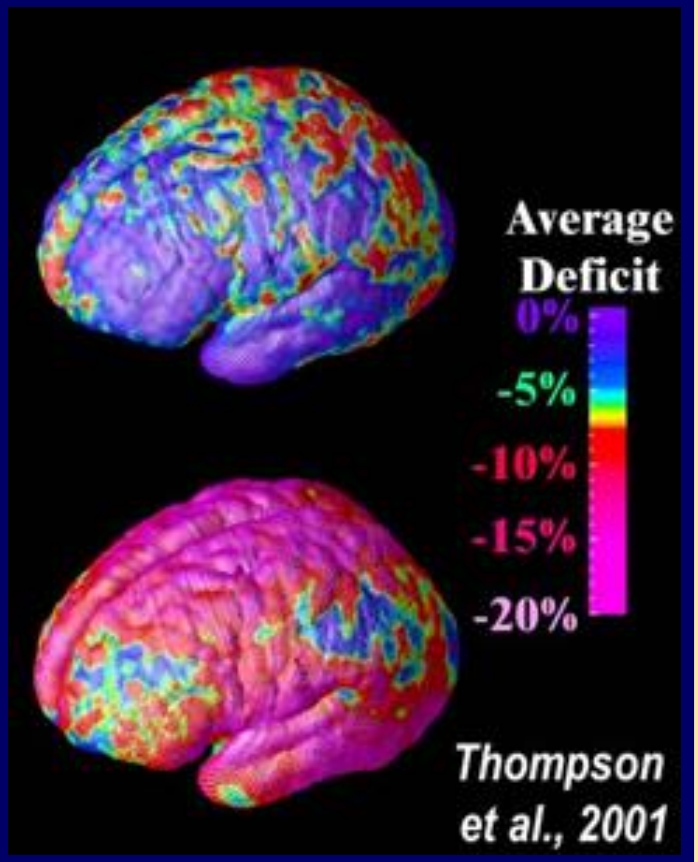
Further biological explanations

- Enlarged ventricles (but not always!)



- Loss of grey matter

  (here: after 5 years)



Etiology – Biological Features (4)

Possible reasons for biological findings

- Viral infection during pregnancy or as infant
- Dopamine excess
- Pre- and perinatal problems
- Substance abuse

Conclusion

Biological features play a role in the development of schizophrenia, but are not sufficient to explain everything.

Etiology – Psychosocial features (1)

Expressed Emotion (EE)

- Concept
  - Measure of the family environment
  - Criticism, hostility, emotional overinvolvement
- Relapse rate of patients suffering from schizophrenia in families $_{\text{(high EE)}}$ > families$_{\text{(low EE)}}$
- Mechanism: Higher stress rates?

Etiology – Psychosocial features (2)

Finnish adoption study (Tienary; Wahlberg)

- Started in the 1960s, following all adopted-away children of mothers with schizophrenia
- Adoptees of mothers with schizophrenia had a higher rate of the disorder, but:
- *More high-risk children in low communication deviance families remained healthy than low-risk children in high communication deviance families!*
- Communication deviance: measure of speech clarity and simplicity (i.e. „understandability“)

=> Indicates interaction models!

Homework (2)

- Open the risk factors section on this website:

  http://www.schizophreniaresearch.org.au/library/browse-library/risk-factors/

  Choose one risk factor listed there.

  What are the results? (cf. Factlist)

  What are the results based on? (cf. PRISMA checklist)

Final Comments

- Schizophrenia, although possibly more dependent on biological aspects than other disorders, can still not be explained by biological factors entirely.
- Hence:
  Treatment also has to focus on the different dimensions.
- Remaining problems
  - Do the different symptoms justify one category (schizophrenia)?
  - If not, are the current research results reliable?