

Schizophrenia

Dr. Fred Rose

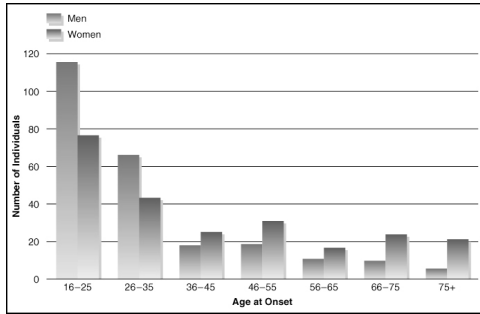
Nature of Schizophrenia and Psychosis: An Overview

- *Schizophrenia vs. Psychosis*
 - Psychosis – Cluster of disorders; hallucinations and/or loss of contact with reality
 - Schizophrenia – A type of psychosis
- *Affects 1 in 100 persons, \$65 Billion annually*
- *Historical Background*
 - Emil Kraepelin – 1896; Used the term dementia praecox, focused on onset and outcomes
 - Eugene Bleuler – 1911 he introduced the term “schizophrenia” or “splitting of the mind”

Prevalence of Schizophrenia

- *Prevalence of 1% worldwide*
 - 2 x Alzheimer’s
 - 5 x Multiple Sclerosis
 - 6 x Insulin-dependent Diabetes
 - 60 x Muscular Dystrophy
- *Schizophrenia Is Generally Chronic*
 - Moderate-to-severe lifelong impairment
 - Life expectancy is slightly less than average
- *Equal Gender Distribution*
 - Women - better long-term prognosis
 - Onset differs between men and women

Gender differences in onset of schizophrenia in a sample of 470 patients



Howard et al., 1993

Diagnosis: DSM IV

- **Symptoms (2 or more):**
 - Delusions (content)
 - Hallucinations
 - Disorganized speech (form)
 - Disorganized or catatonic behavior
 - Negative symptoms (flat affect etc.)
- **Social/Occupational Dysfunction**
- **Duration: 6-months (1 month of symptoms)**
- **Not caused by substances**
- **Not Schizoaffective/Mood Disorder**

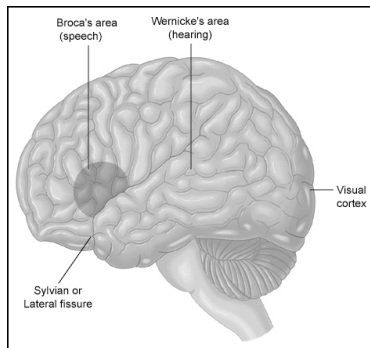
The "Positive" Symptoms

- **Active manifestations of abnormal behavior or distortions of normal behavior**
- **Delusions - 90%**
 - Somatic: "Snake living inside my abdomen"
 - Grandeur: "Chosen by God"
 - Persecution: "'They' are monitoring me"
 - Manifestations: Thought broadcasting, ideas of reference, thought withdrawal

The "Positive" Symptom Cluster

- **Hallucinations**
 - Sensory events without environmental input
 - Auditory are the most common (can be any sensory modality)
 - Normal volume, known, external, negative
 - Speech vs. auditory processing studies

Some major language areas of the cerebral cortex



The "Negative" Symptom Cluster

- **Absence or insufficiency of normal behavior**
- **Spectrum of Negative Symptoms**
 - Avolition (or apathy) – Inability to initiate and persist in activities
 - Alogia – A relative absence of speech
 - Anhedonia – Inability to experience pleasure or engage in pleasurable activities
 - Flat affect – Show little expressed emotion, but may still feel emotion

“Disorganized” Symptoms

- Severe and excess disruptions in:
- *Speech*
 - Cognitive slippage – Illogical and incoherent speech
 - Tangentiality – “Going off on a tangent” and not answering a question directly
 - Loose associations or derailment – Taking conversation in unrelated directions

“Disorganized” Speech

“I have also killed my ex-wife, [name], in a 2.5 to 3.0 hours sex bout in Devon Pennsylvania in 1976, while two Pitcairns were residing in my next room closet, hearing the event. Enclosed, please find my urology report, indicating that my male genitals, specifically my penis, are within normal size and that I’m capable of normal intercourse with any woman, signed by Dr. [name], a urologist and surgeon who performed a circumcision on me in 1982. Conclusions: I cannot be a nincompoop in a physical sense (unless Society would feed me chemicals for my picture in the nincompoop book).”

“Disorganized” Symptoms

- *Affect*
 - Inappropriate affect (e.g., crying when one should be laughing)
- *Behavior*
 - Disruption in goal directed behavior
 - Decline in routine daily functioning
 - Catatonia – Spectrum from wild agitation, waxy flexibility, to complete immobility

Symptoms of Schizophrenia

<i>Positive (Type I)</i>	<i>Negative (Type II)</i>	<i>Disorganized</i>
Thematic Delusions	Avolition (apathy)	Grossly Bizarre Behavior
Thematic Hallucinations	Alogia (Poverty of Speech/Content)	Incoherent hallucinations or delusions
Bizarre Behavior	Anhedonia	Disorganized Affect
	Flat Affect	Disorganized Speech
	Asociality	

Lenzenweger, Dworkin & Wethington (1991)

Subtypes of Schizophrenia

- ***Paranoid Type***
 - Intact cognitive skills and affect, and do not show disorganized behavior
 - Hallucinations and delusions thematic (e.g., grandeur or persecution)
- ***Disorganized Type***
 - Marked disruptions in speech, behavior, affect
 - Fragmented hallucinations and delusions
 - Develops early, tends to be chronic, lacks periods of remissions

Subtypes (cont.)

- ***Catatonic Type***
 - Unusual motor responses and odd mannerisms (e.g., echolalia, echopraxia)
 - ? Need for consistency
 - Tends to be severe and quite rare
- ***Undifferentiated Type***
 - Symptoms, but don't meet criteria for another type
- ***Residual Type***
 - One past episode of schizophrenia
 - Continue to display less extreme residual symptoms (e.g., odd beliefs)

Problems with Diagnosis

"Schizophrenia appears to be a disorder with no particular symptoms, no particular course, no particular outcome and which responds to no particular treatment" [Bentall, 1990]

- ***Heterogeneity of symptoms***
 - Symptoms change as the disorder develops
 - Schizophrenics 'slip back into reality'
- ***Treatment response varies***
- ***Is it a unitary disorder?***
- ***Is it distinct from normal experience?***

Other Psychotic Disorders

- ***Schizophreniform Disorder***
 - Schizophrenic symptoms for less than 6 months
 - Associated with good premorbid functioning; most resume normal lives
- ***Schizoaffective Disorder***
 - Symptoms of schizophrenia and a mood disorder
 - 10-year outcome better than Schizophrenia (Harrow et al., 2000)

Other Psychotic Disorders

- ***Delusional Disorder***
 - Delusions without other major schizophrenia symptoms
 - May show other negative symptoms
 - Type of delusions include erotomantic, grandiose, jealous, persecutory, and somatic
 - This condition is extremely rare

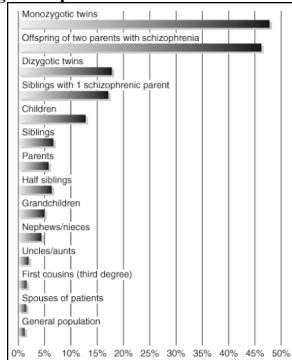
Additional Disorders with Psychotic Features

- **Brief Psychotic Disorder**
 - One or more positive symptoms of schizophrenia
 - Usually precipitated by extreme stress or trauma
 - Lasts < 1 month
- **Shared Psychotic Disorder**
 - Delusions from one person manifest in another person
 - Little is known about this condition
- **Schizotypal Personality Disorder**
 - May reflect a less severe form of schizophrenia

Genetic Influences

- **Family Studies**
 - Schizophrenia increases risk in other family members
- **Twin Studies**
 - Risk of schizophrenia in MZ twins ranges from 15% to 65%, with an average of 28% (Fuller-Torrey, 1994).
 - Risk of schizophrenia drops to 6% for dizygotic twins
- **Adoption Studies**
 - Risk remains high in adopted children with a biological parent suffering from schizophrenia

Risk of developing schizophrenia



Gottesman, 1991

Genetic Influences (cont.)

- *Summary of Genetic Research*
 - Risk of schizophrenia increases as a function of genetic relatedness
 - Multiple genes involved
 - One need not show symptoms of schizophrenia to pass on relevant genes
 - Schizophrenia has a strong genetic component, but genes alone are not enough

Etiology

- *The Dopamine Hypothesis*
 - Overactivity of dopamine (DA) neurons in the brain causes schizophrenia

The Dopamine Hypothesis

- *Support*
 - Drugs that block dopamine receptors reduce positive symptoms
 - Amphetamines, which increase dopamine, create positive symptoms
 - High number of D2 receptors in schizophrenic brains

The Dopamine Hypothesis

- **Problems**
 - Dopamine antagonists don't treat negative symptoms
 - Time lapse - immediately in brain but no improvement for 2 weeks
 - Parkinson's disease (but...)
 - Substantia-Nigra, Caudate-Putamen - PD
 - Ventral Tegmentum, Nucleus Accumbens, Septal area - Schiz.

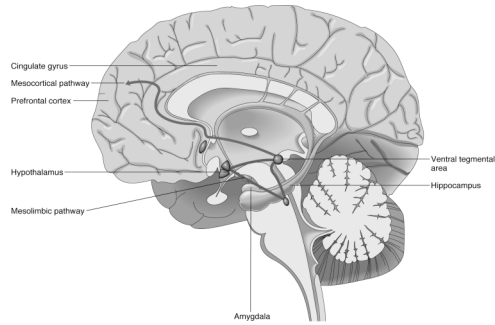
The Dopamine Hypothesis

- **Revised:**
 - **Overactivity** of dopamine neurons in the mesolimbic pathway may cause positive symptoms.
 - Antipsychotics which block dopamine receptors *lessen* positive symptoms
 - and...

The Dopamine Hypothesis

- **Revised:**
 - **Underactivity** of dopamine neurons in the mesocortical pathway in the prefrontal cortex may cause negative symptoms.
 - Antipsychotics have *little or no* effect on negative symptoms.

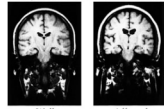
Dopamine Pathways



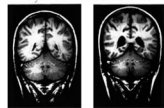
Other Brain Changes

MRI brain images of twins discordant for schizophrenia

35-year-old female identical twins

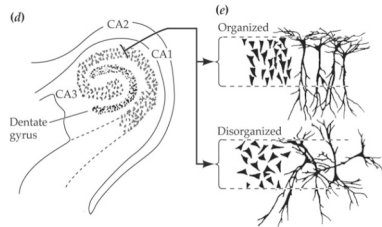


28-year-old male identical twins

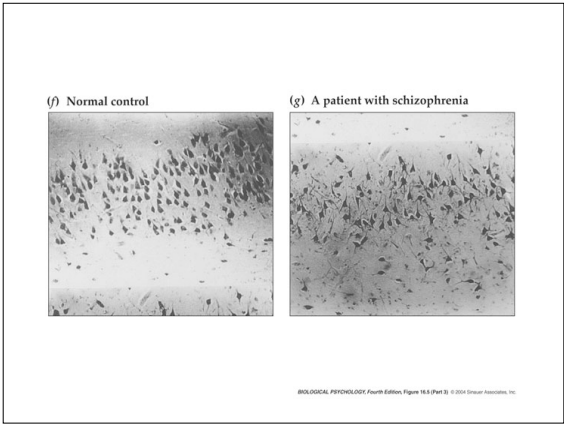


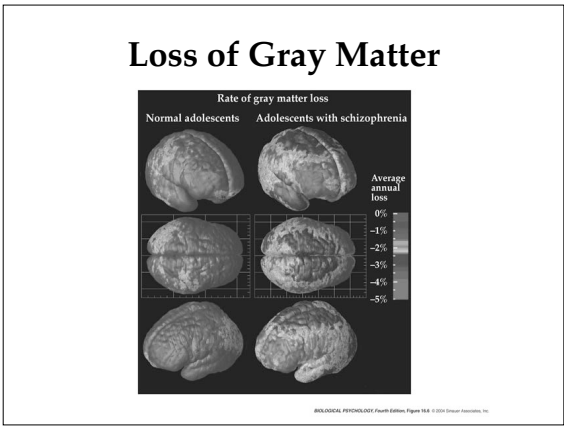
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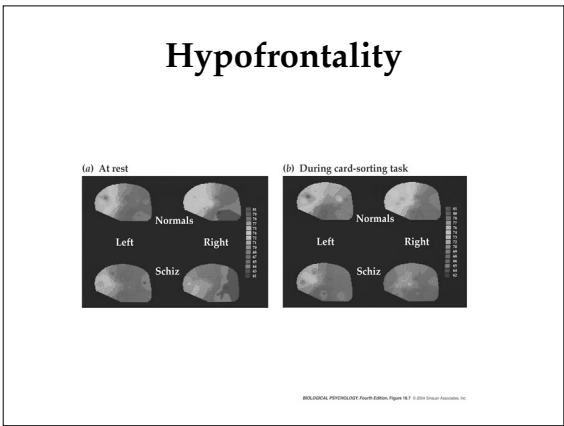
Cellular Organization

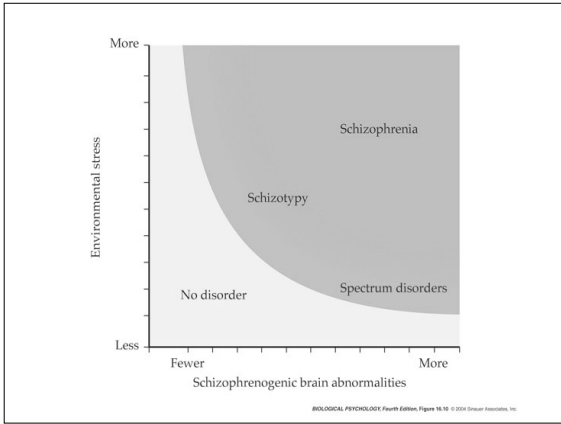


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Psychosocial Influences

- *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
- *The Role of Psychological Factors*
 - Likely exert only a minimal effect in producing schizophrenia

Gene-Environment Interaction

- Tienari et al. (1985, 1987); Tienari (1991, 1994)
 - Children of schizophrenic and “normal” mothers adopted out at birth)
 - Tracked family communication patterns

		Communication	
		Good	Poor
Schizo. Risk	High	LOWEST Impairment	High Impairment
	Low	No Impairment	No Impairment

Medical Treatment

- *Antipsychotic (Neuroleptic) Medications*
 - Dopamine agonists are often the first line of treatment for schizophrenia
 - Began in the 1950s
 - Most medications reduce or eliminate the positive symptoms of schizophrenia
 - Acute and permanent extrapyramidal and Parkinson-like side effects are common
 - Poor compliance with medication is common
 - Risperdal, Olanzapine are “atypical” neuroleptics with better side-effect profile than “Throrazine”

Psychosocial Treatment

- *Psychosocial Approaches: Overview and Goals*
 - Behavioral (i.e., token economies) on inpatient units
 - Community care programs
 - Social and living skills training
 - Behavioral family therapy
 - Vocational rehabilitation
- *Psychosocial Approaches Are Usually a Necessary Part of Treatment*

Summary

- *Schizophrenia Includes a Spectrum on Cognitive, Emotional, and Behavioral Dysfunctions*
 - Positive, negative, and disorganized symptom clusters
- *DSM-IV-TR Divides Schizophrenia Into Five Subtypes*
- *Other DSM-IV-TR Disorders Include Psychotic Features*
- *Genetic, Biological, and Environmental Causative Factors Have Been Implicated for Schizophrenia*
- *Successful Treatment Rarely Includes Complete Recovery*