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# **Overview of Clinical Symptoms and Medication Treatment in Early Psychosis**

**Christian Kohler, M.D.**



All psychotic disorders are referenced to schizophrenia

Diagnostic and Statistical Manual of Mental Disorders DSM-V (2013)

A. Characteristic Symptoms ( $\geq 2$ )  $\geq 1$  month

- delusions
- hallucinations
- disorganized speech
- disorganized behavior
- negative symptoms

B. Social/Occupational Dysfunction during A

C. Duration: prodrome/acute/residual symptoms  $\geq 6$  months



## Health Costs

- 65 Billion USD (2002 estimate) (Aggarwal et al, *J Clin Psych* 2005)
- 3% of all health expenditures (Knapp et al, *Schiz Bull* 2004)
- 22% of all mental health costs (Theida et al, *Psych Serv* 2003)

20-30 % live independently

<20% work 20 hours per week or more

Life expectancy: 20% lower than average



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## Prevalence of Schizophrenia

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### Lifetime Prevalence

ranges between 0.5% (rural regions) - 2.5% (urban settings)

across US ~4 Mill

Phila area ~50 000

similar to epilepsy, more than DAT and Parkinsonism

similar rates across different cultures

WHO study incl. US, South America, Japan, India, Africa and Europe

2 yr outcome better in developing countries

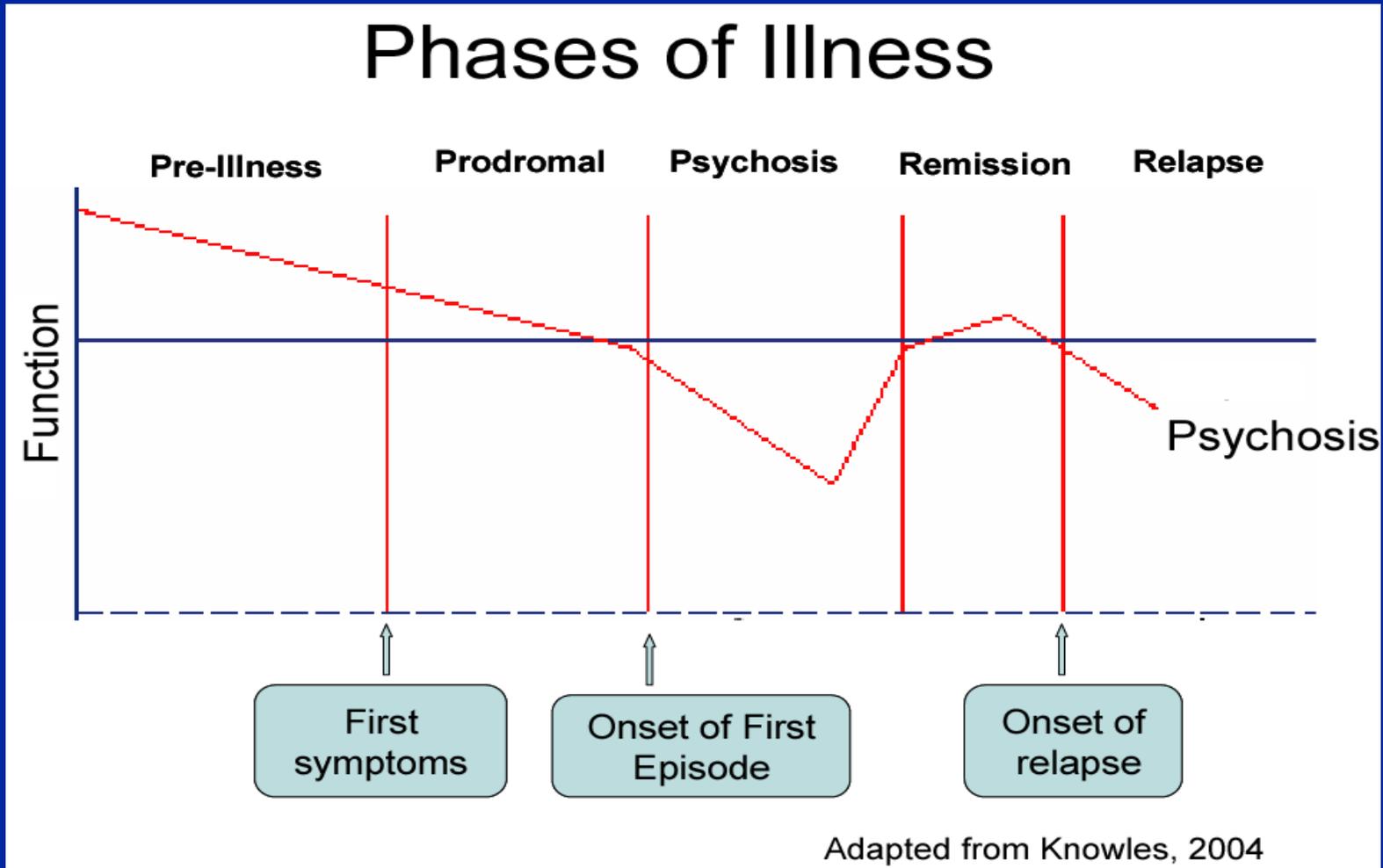


## Course/Outcome with Treatment

- complete, prolonged recovery of psychosis with minimal/ no negative sx's
- partial recovery of psychosis or recurrent psychotic episodes
- no significant recovery of psychosis

## Prognosticators for better outcome

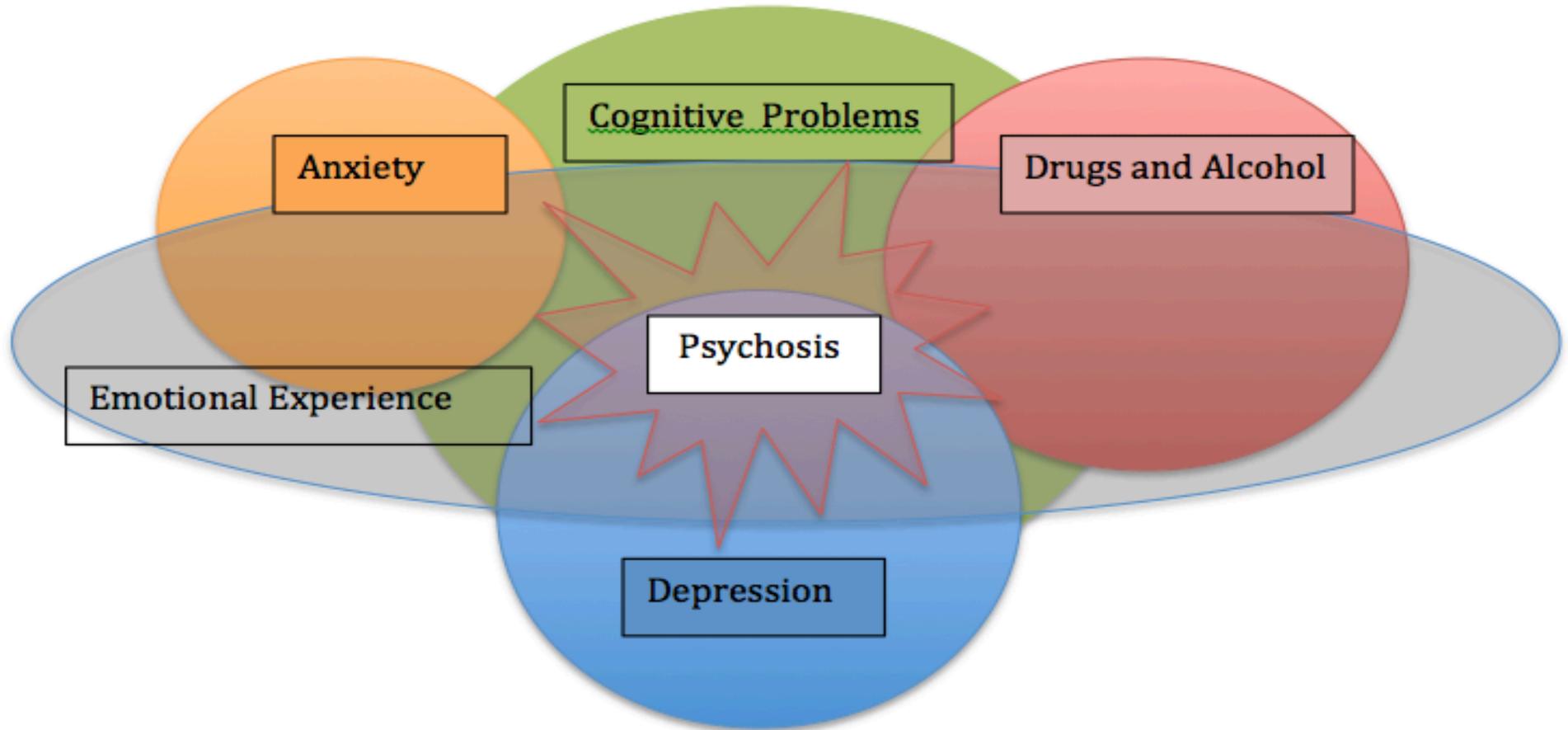
- later and abrupt onset
- level of premorbid functioning
- brief duration of untreated psychosis
- prominent affective symptoms or disorganized behavior
- paucity of negative symptoms





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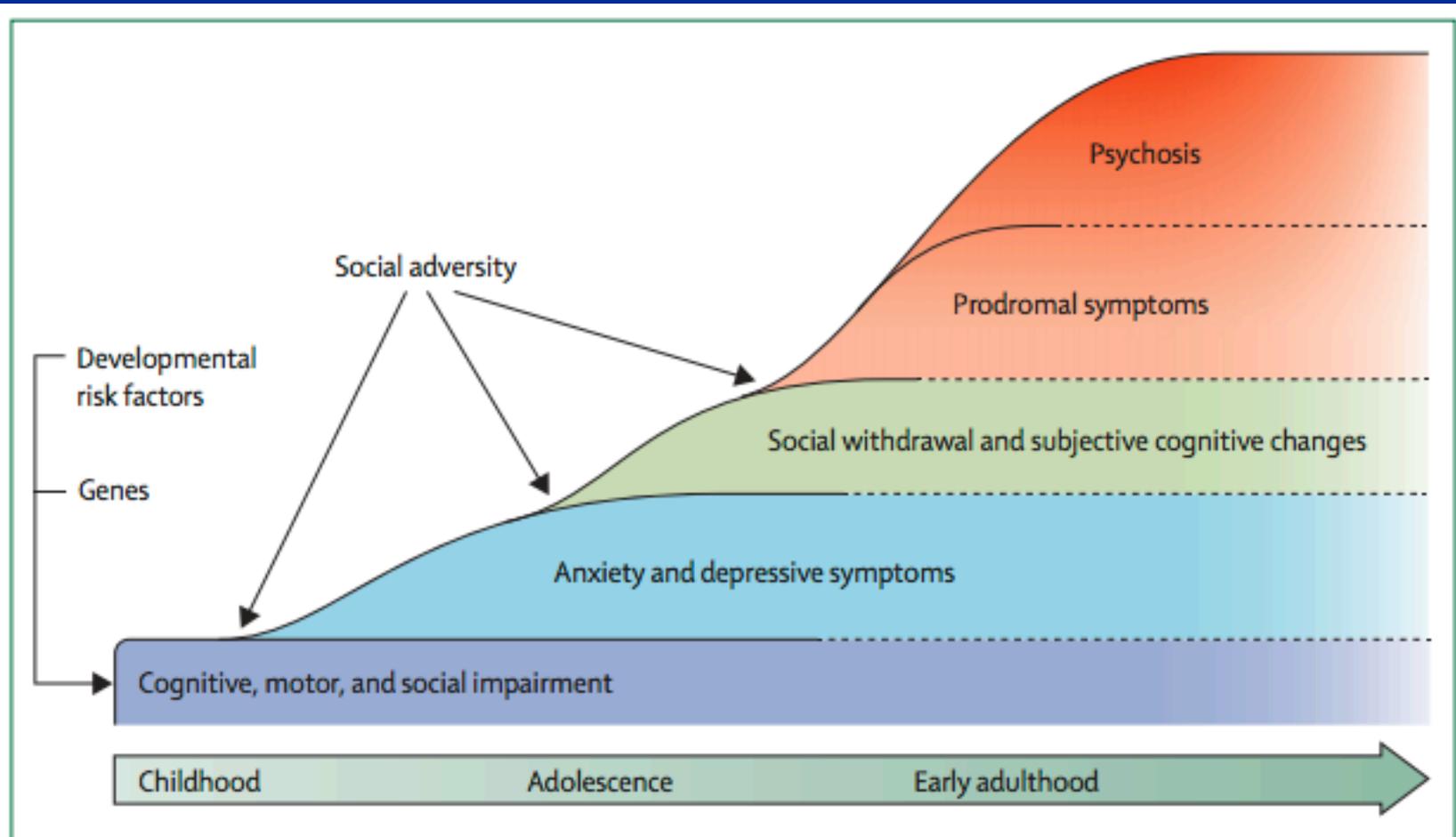


Figure 1: The trajectory to schizophrenia showing the evolution of symptoms and the main risk factors



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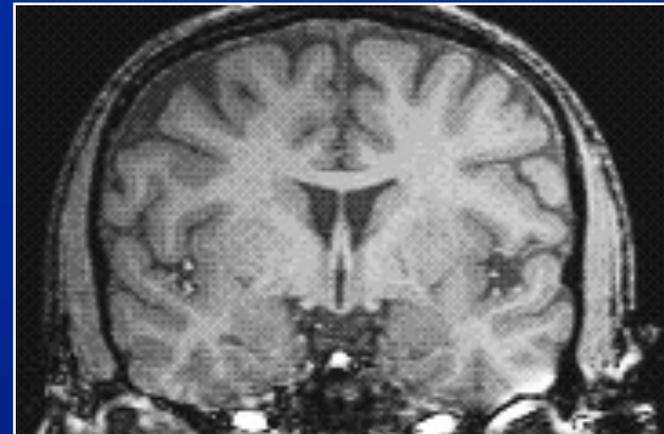
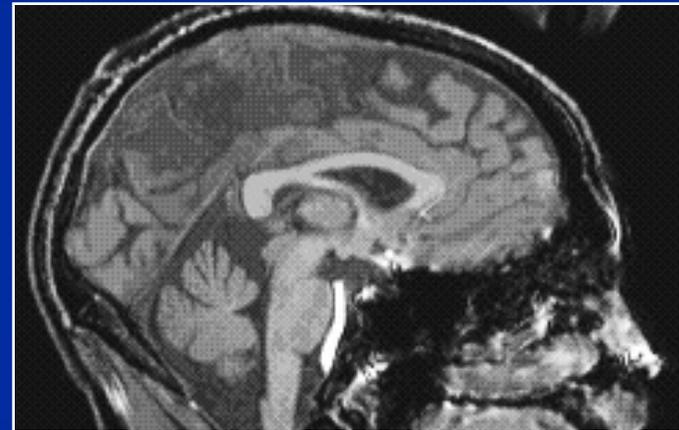
## Neurobiology and Genetics

### Neurobiology and Genetics:

- pervasive disorder affecting most brain regions without gross alteration in brain structure

### Limbic areas of the brain

- cingulate gyrus
- amygdala
- hippocampus
- prefrontal areas



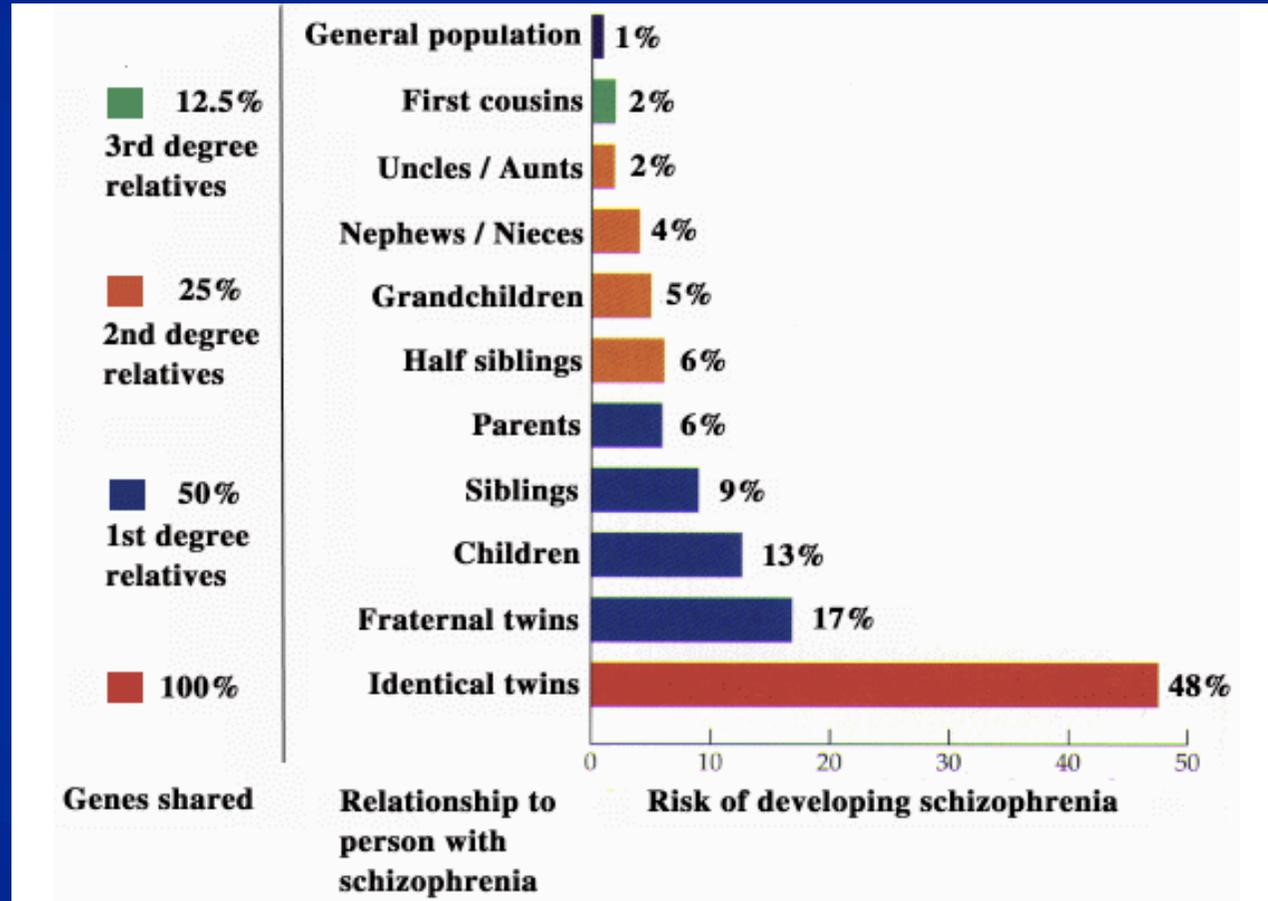


## Risks

- Genetic
- Pregnancy/birth
- Early childhood
- Early adolescence



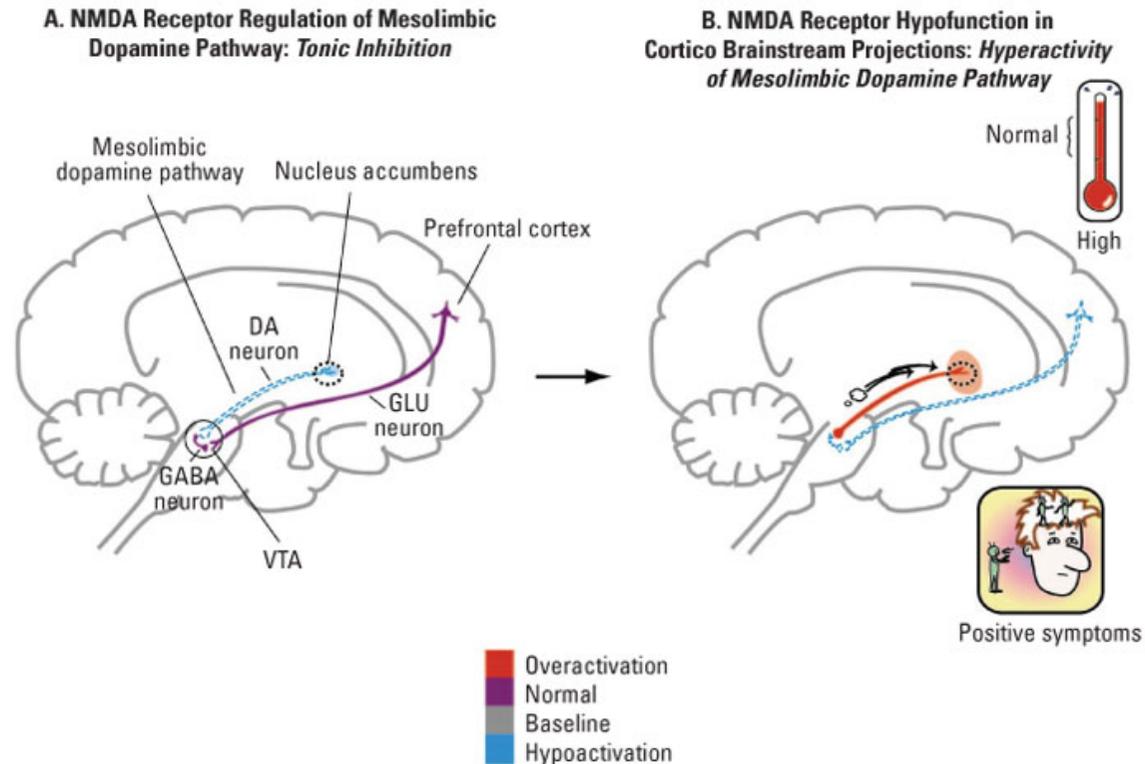
Heterogenous causes  
producing common phenotype



(Source: Gottesman, 1991)



**FIGURE 3.**  
**NMDA receptor hypofunction hypothesis and positive symptoms of schizophrenia<sup>2</sup>**



Stahl SM. *Essential Psychopharmacology*. 3rd ed. New York, NY: Cambridge University Press. In press. Reproduced with permission. Copyright Neuroscience Education Institute.

NMDA=*N*-methyl-D-aspartate; DA=dopamine; GLU=glutamate; GABA= $\gamma$ -aminobutyric acid; VTA=ventral tegmental area.

Stahl SM. *CNS Spectr*. Vol 12, No 4. 2007.



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## Treatment Considerations

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- Antipsychotic Treatment
- Other Medications (antidepressants, mood stabilizers)
- Psychotherapy
- Comprehensive Interventions



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## Targets for Treatment

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- Positive Symptoms: Hallucinations, delusions, disordered thinking and behavior
- Mood Symptoms: Depression, anxiety, mania
- Negative Symptoms: Lack of motivation, initiative, emotional expression
- Cognitive dysfunction
  - temporal lobe functions (memory, language)
  - frontal lobe functions (attention, mental flexibility)



## First-episode Treatment

- Highest chance of response/recovery
- Lack of effects of chronic illness
- Challenge of illness acceptance

Duration of untreated psychosis leads to increased

- Negative symptoms      ↘
- Cognitive dysfunction      →      associated with functional impairment



About 12 First-episode studies in the last 40 years

- 60-85% response rates based on positive symptoms
- Time to remission: mean=35 weeks, median 11 weeks
- No superiority of SGA
- Relapse rates 60-80%
- 80% associated with medication nonadherence (Robinson 1999)
- Duration untreated psychosis: worse outcome (Perkins 2005)
- Duration of persisting psychosis



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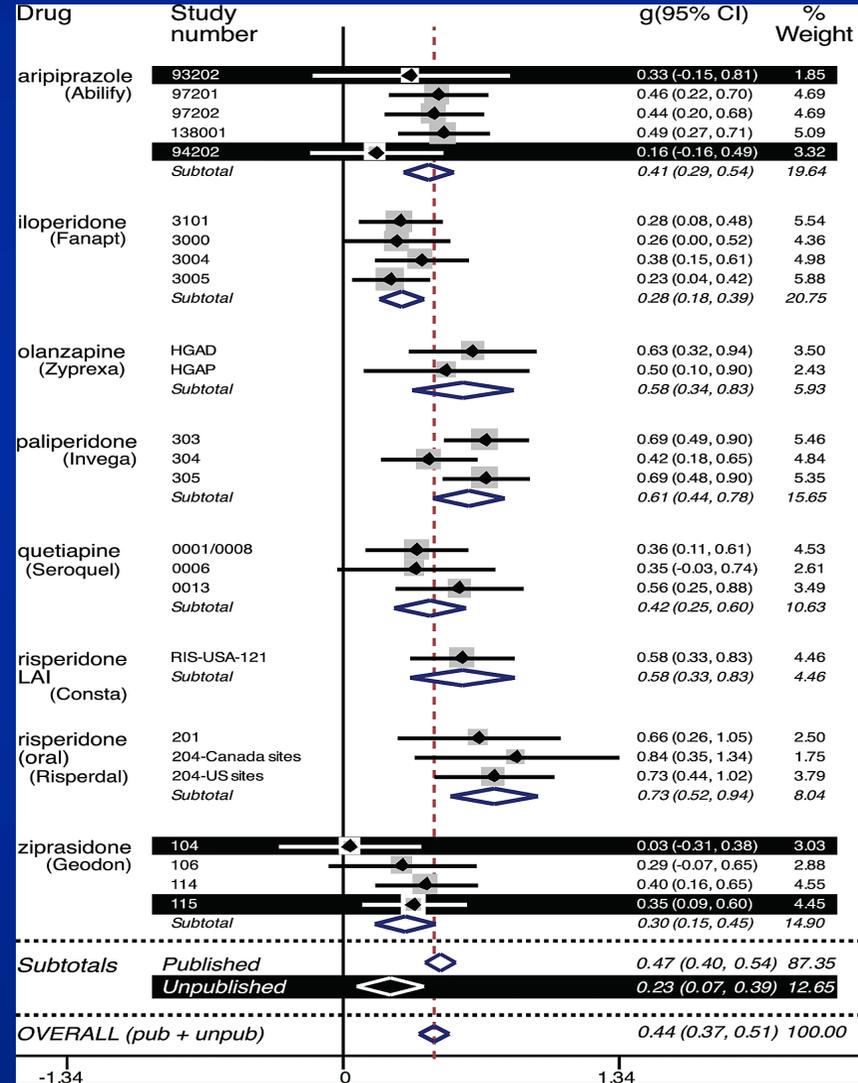
First-Generation Antipsychotics: e.g., haloperidol, perphenazine, chlorpromazine

Second-Generation Antipsychotics: e.g., clozapine, olanzapine risperidone,  
quetiapine, ziprasidone, aripiprazole

Effect: reduce positive symptoms within several days to months

Difference between First- and Second-Generation Antipsychotics

- effect on pathways
- improvement in depression, anxiety
- improvement in negative symptoms
- side effects s. a. acute dystonia, neuroleptic malignant syndrome (NMS), Parkinsonian symptoms, tardive dyskinesia





Treatment: dependent on patient's insight into symptom

- management of psychotic symptoms but not others
- relapse prevention: at least 1-2 years after first episode

Antipsychotic Medications: affect dopaminergic transmission in pathways projecting from the brainstem to the frontal and temporal brain areas

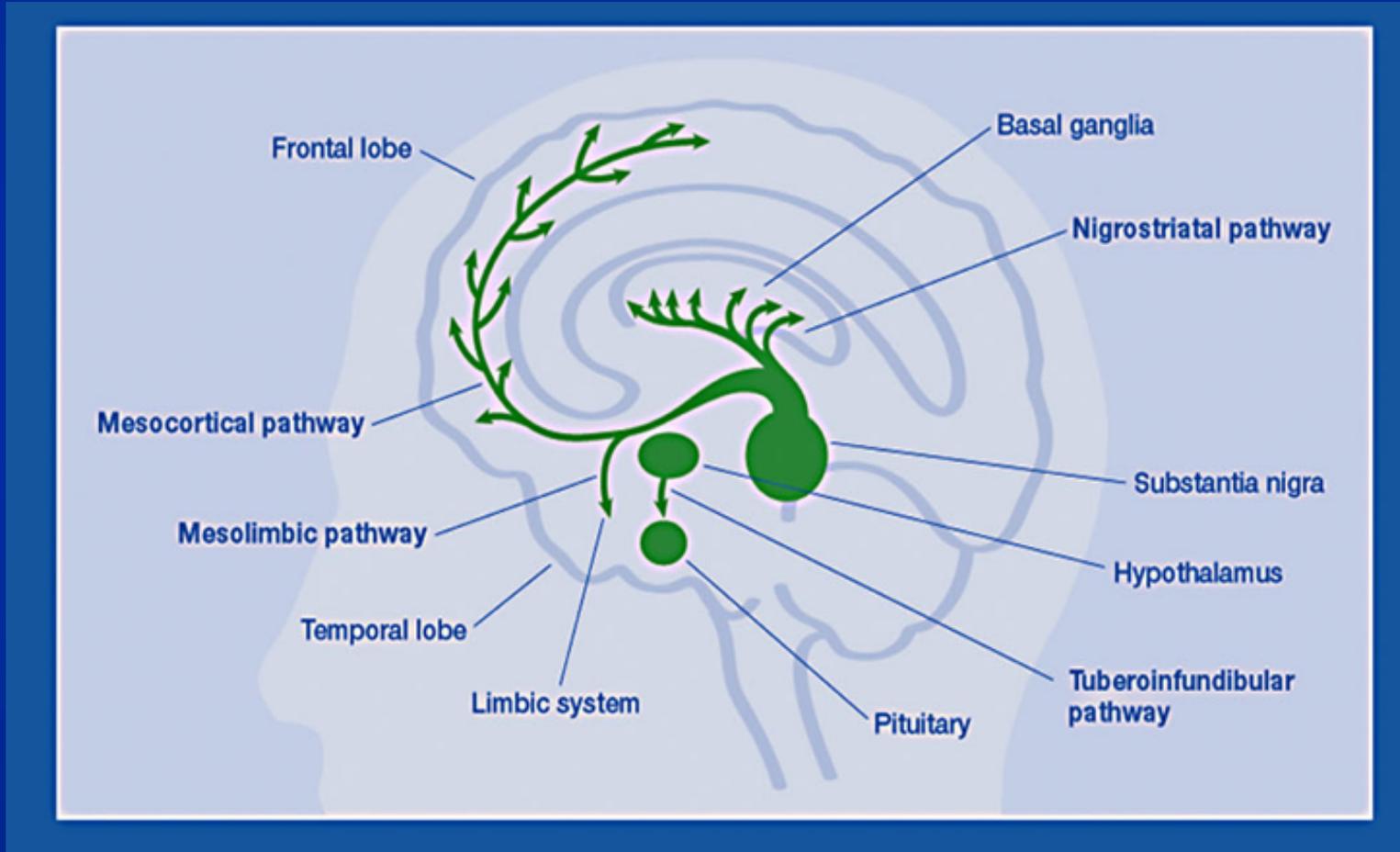
- 3 major pathways from brainstem to
- basal ganglia
  - temporal lobes
  - frontal lobes



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# Neurobiology and Genetics





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## Antipsychotics

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### How to decide on which antipsychotic medication?

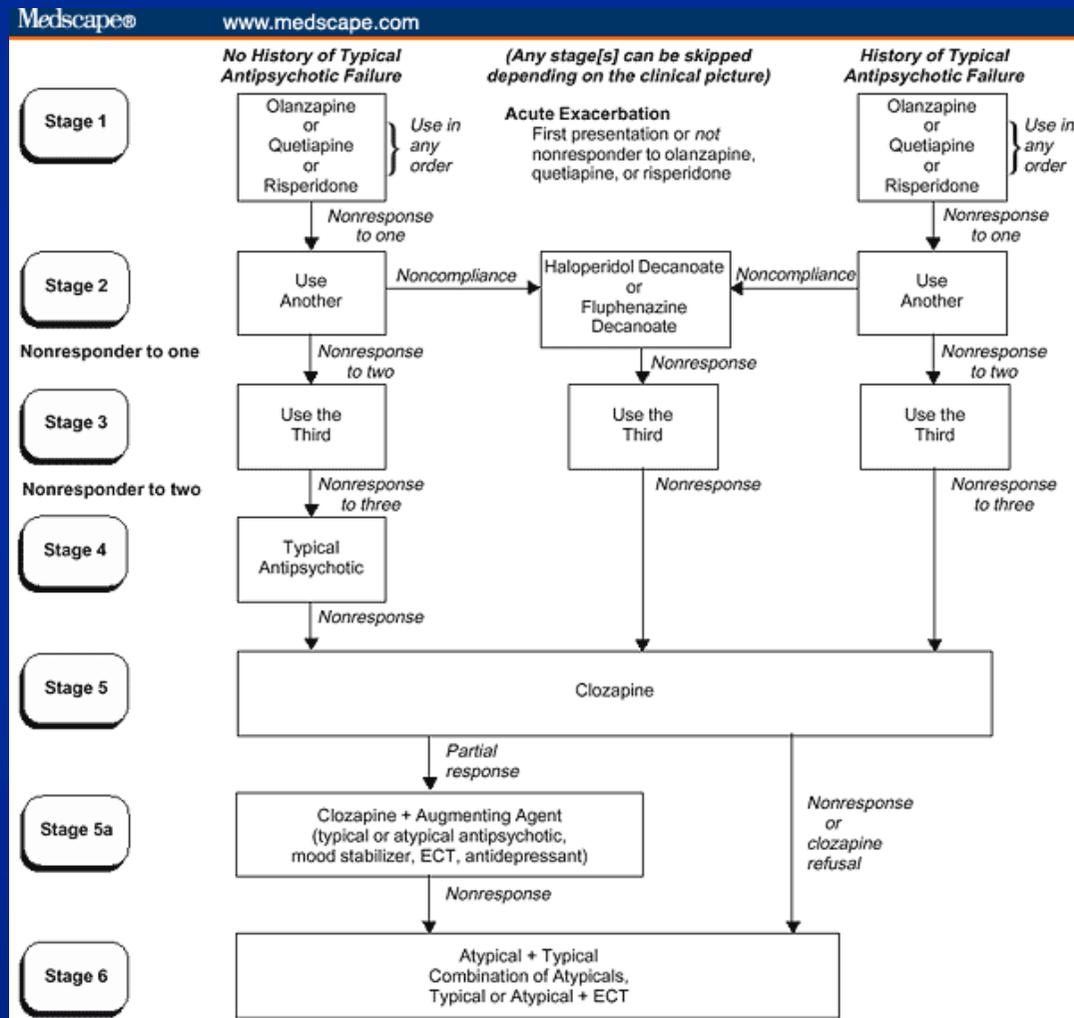
Effectiveness/Acuity of Illness: psychosis as primary target

Associated clinical symptoms, i.e., depression/anxiety, insomnia, restlessness/agitation.

Side effects: EPS, weight gain



## Texas Treatment Algorithm





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## Psychotherapy

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### Person

I cannot believe what anyone is saying or trust anyone.

The voices are too much!

I am scared, my feelings are gone.

I cannot think, I cannot sleep.

... why has my world changed?

### Provider

Take this medicine...



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# Psychotherapy

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But which one??

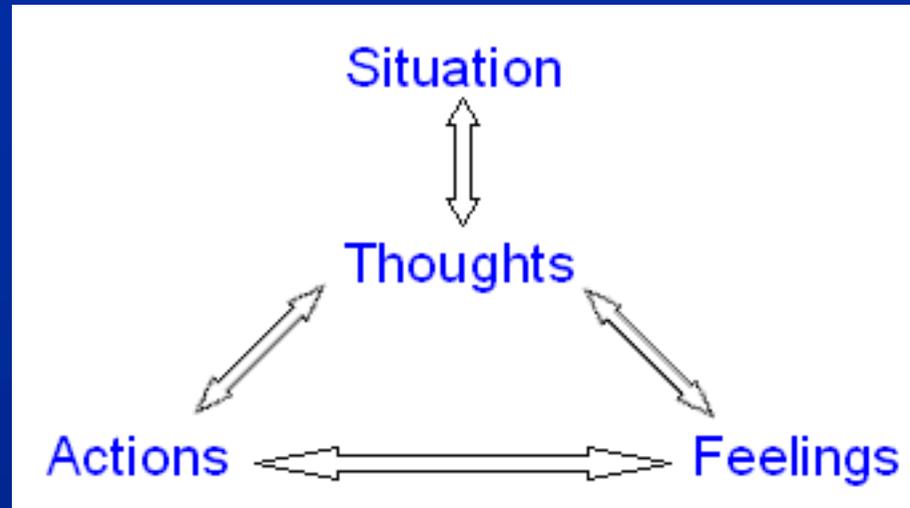
- CBT
- Behavior Therapy
- Supportive
- Family
- Motivational
- Dynamic
- Group
- Gestalt or Existential or Primal Scream???



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# Psychotherapy





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Applied to persons with

- acute and chronic schizophrenia
- targeting negative, depressive and positive symptoms

Cochrane Review (2013)

- Likely most effective on symptoms of depression
- No superiority regarding relapses, hospitalization rates, symptom changes compared to other psychotherapies, group therapy
- Superiority to med trials re drop-out rates



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## Most effective

- Symptom oriented
- Normalizing experience
- Supportive/ motivational
- Setting clear goals
- Involving family as care provider



b. Supportive Psychotherapy

focus on coping with symptoms  
social and occupational functioning

c. Cognitive Psychotherapy (recent application to schizophrenia)

identification of symptoms  
cognitive redirection

d. Cognitive Remediation: to improve difficulties with memory & attention

e. Family Education: supportive limit setting

referral to National Alliance for Mentally Ill (NAMI)

f. Combination Treatments: RAISE, PIER, schizophrenia PORT



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Initiatives over past 20 years in  
Australia, Scandinavia, UK, Germany

Recent US projects (RAISE, NAPLS, PIER/RWJ Foundation)

- ◆ No single, specific intervention
- ◆ Multidisciplinary

Community Mental Health Services Block Grant

2014-2015 SAMHSA 5% set aside funds



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Allowed us to offer comprehensive multicomponent treatment effort

◆ Clinical assessment

Diagnostic

Development/functional

Family assessment

◆ Personalized treatment plan

◆ Recovery oriented CBT with family involvement

◆ Medication management

◆ Family support and information group

◆ Cognitive remediation