Schizophrenia

Chronic disorder that occurs in 1% of the population.

It affects both men and women but the onset is different according to the gender

Figure by MIT OpenCourseWare.
Symptoms:
Illogical thinking
Inability to recognize reality
Hallucinations (voices insulting or commanding)
Absence of emotions, lack of feelings
Symptoms change over time

Functional Imaging studies revealed:
Decreased activity in the prefrontal area (hypofrontality)
Activation of cortical areas during hallucinations
Increased activity also in subcortical areas: i.e. limbic system
**Positive symptoms:**

Hallucinations  
Disorganized speech  
Treated with antagonist of D2 receptors, aggravated by increasing DA transmission

**Negative symptoms:**

Reduced speech  
Social withdrawal  
Intellectual impairment  
Loss of motivation/ emotions  

Treated with the “atypical antipsychotics”
Etiology of schizophrenia
Genetic components and environmental factors

Anatomical studies
There is an enlargement of the ventricles that is NOT caused by cell death. It is rather due to defects in development that precede the onset of the symptoms.

Also, there are changes in cellular structure not accompanied by gliosis. This suggests that the abnormalities occurred in the developmental process.
**Neurophysiological studies**

Hypofrontality

EEG show that in schizophrenics, the electrical activity evoked by a stimulus is not localized, as in normal subjects, but it is widespread in the brain.

**Genetic studies**

Linkage studies across affected individuals identified specific loci on chromosomes 13, 8, 22 and 6.

Microarray analysis revealed impairments of transcripts for the presynaptic function in the prefrontal area, but also defects in glutamatergic and GABAergic Transmission, energy metabolism and growth factors.

Schizophrenia is a neurodevelopmental disorder.
Amphetamine-induced stereotypy used in animal models for schizophrenia

High dosage of amphetamine induce DA release

Drugs that treat the symptoms of schizophrenia (neuroleptics) can cause motor impairment (catalepsy)

Gate hypothesis: schizophrenics fail to “gate” the stimulus they receive (as measured by PPI)

The second generation drugs reduce the negative symptoms, they have reduced side effects
Drugs that treat the symptoms of schizophrenia (neuroleptics) can cause motor impairment (catalepsy).

There are evidences of a reduced glutamatergic function (on DA neurons).

Some studies have found no differences in DA transmission in schizophrenics.

The second generation drugs reduce the negative symptoms, they have reduced side effects.
PPI is a measure of the “gate”
It is disrupted by systemic administration of DA agonists and reinstated by DA receptor-blocking antipsychotic drugs

PPI is also disrupted by systemic administration of serotonin agonists and Glutamate antagonists

<table>
<thead>
<tr>
<th>Generic name (trade name)</th>
<th>Sedation</th>
<th>Autonomic side effects (^a)</th>
<th>Hypotension (^b)</th>
<th>Motor disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Typical antipsychotics</strong></td>
<td></td>
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<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>Prochlorperazine (Compazine)</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Triflupromazine (Vesprin)</td>
<td>High</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Thioridazine (Mellaril)</td>
<td>Moderate-high</td>
<td>Moderate-high</td>
<td>Moderate-high</td>
<td>Low</td>
</tr>
<tr>
<td>Trifluoperazine (Stelazine)</td>
<td>Low-moderate</td>
<td>Low-moderate</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Fluphenazine (Prolixin)</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Perphenazine (Trilafon)</td>
<td>Low-moderate</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
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<tr>
<td>Mesoridazine (Serentil)</td>
<td>High</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Low</td>
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<tr>
<td>Thiothixene (Navane)</td>
<td>Low</td>
<td>Low-moderate</td>
<td>Low</td>
<td>Moderate-high</td>
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<tr>
<td>Haloperidol (Haldol)</td>
<td>Low</td>
<td>Very low</td>
<td>Low</td>
<td>High-very high</td>
</tr>
<tr>
<td>Loxapine (Loxitane)</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Molindone (Moban)</td>
<td>Moderate</td>
<td>Low</td>
<td>Very low</td>
<td>Low-moderate</td>
</tr>
</tbody>
</table>

\(^a\) Includes blurred vision, dry mouth, reduced gastric secretion and motility, urinary retention, and constipation.

\(^b\) Drop in blood pressure upon standing upright (orthostatic), dizziness, faintness, or blacking out.

Figure by MIT OpenCourseWare.
The mechanisms of action are not clear

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<tr>
<td><strong>Atypical antipsychotics</strong></td>
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</tr>
<tr>
<td>Clozapine (Clozaril)</td>
<td>Moderate-high</td>
<td>Moderate</td>
<td>Moderate-high</td>
<td>Low</td>
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<tr>
<td>Olanzapine (Zyprexa)</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Very low</td>
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<tr>
<td>Risperidone (Risperdal)</td>
<td>Low-moderate</td>
<td>Very low-low</td>
<td>Moderate</td>
<td>Low</td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Very low</td>
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<tr>
<td>Ziprasidone (Zeldox)</td>
<td>Low</td>
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