BIOLOGICAL TREATMENT IN PSYCHIATRY

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Pécs

Genes → Neurodevelopmental abnormality → Developmental insult

Deficient cortical control of subcortical DA activity

Stress → Increased subcortical DA release (stress related)

Endogenous sensitization

Sustained subcortical DA release (nonstress related)

Altered information flow in cortico-striatal-thalamocortical loops

(DA dependent)

Long-term plasticity

Psychotic episode (treatment responsive)

No treatment

(-)

Treatment

Altered information flow in cortico-striatal-thalamocortical loops

(DA dependent)

Chronic psychotic state (treatment unresponsive)

Schizophrenia, 2nd ed.

Dopamine Hypothesis of Schizophrenia

Mesocortical pathway
Hypoactivity; negative symptoms

Nigrostriatal pathway (part of EP system)

Tuberoinfundibular pathway
Hyperactivity; positive symptoms


Neurochemical Abnormalities in Schizophrenia

- Multiple neurotransmitters are likely to be involved
- Dopaminergic abnormalities
  - Increased DA activity in mesolimbic (so called "emotional") DA circuit and decreased DA activity in mesocortical (so called "thinking") DA circuit
- Abnormalities in other neurotransmitter systems are also likely
  - Serotonin, glutamate, norepinephrine, acetylcholine, GABA, others


TABLE 1. RELATIVE RECEPTOR AFFINITIES OF ATYPICAL ANTIPSYCHOTIC DRUGS

<table>
<thead>
<tr>
<th>Drug</th>
<th>D1</th>
<th>D2</th>
<th>D3</th>
<th>D4</th>
<th>a1</th>
<th>a2</th>
<th>H1</th>
<th>ACh</th>
<th>5-HT1</th>
<th>5-HT2</th>
<th>5-HT3</th>
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</thead>
<tbody>
<tr>
<td>Chlorpromazine</td>
<td>++</td>
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<tr>
<td>Ziprasidone</td>
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<tr>
<td>Quetiapine</td>
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<tr>
<td>Amoxapine</td>
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</tr>
</tbody>
</table>

TABLE 1: RELATIVE RECEPTOR AFFINITIES OF ATYPICAL ANTIPSYCHOTIC DRUGS

Drugs: Chlorpromazine, Imipramine, Reserpine, Haloperidol, Clozapine, and Quetiapine. Antipsychotics: Chlorpromazine, Imipramine, Reserpine, Haloperidol, Clozapine, Quetiapine. Glycyrrhetinic acid (glycyrrhizic acid), 17-α-hydroxyprogesterone (P450 2C19).
Anxiety therapy - neurobiological basis

- **GABA-A RECEPTOR COMPLEX (omega 1-6)**
  - Benzodiazepine-agonists decrease anxiety
- **SEROTONERGIC SYSTEM (dorsal raphe nucleus)**
  - 5-HT antagonists decrease anxiety
- **NORADRENERGIC SYSTEM (locus coruleus)**
  - Autoreceptor stimulators (clonidine) decrease anxiety, presynaptic alpha2 inhibitor yohimbine panic provoking, postsynaptic beta blockers effect
  - Dopaminergic system’s role is also likely

General principles of therapy

- Generally outpatient therapy
- Psychiatric hospitalisation needed:
  - Serious functional damage (comorbidity?)
  - Behavioural disturbance
  - Suicide ideation
- Pharmacological and psychotherapy
- Follow up - care
- Relapse prevention
- GP treatment - psychiatric consultation

The ideal anxiolytic medication?

- Effective in broad spectrum
- No sedation
- No effect on cognitive functions
- No tolerance - dependence
- No withdrawal symptoms and rebound anxiety
- Overdose is not life threatening

### TABLE 1. RECEPTOR PROFILES OF ATYPICAL ANTI-PsYCHOTICS

<table>
<thead>
<tr>
<th>Atypical Antipsychotic</th>
<th>Receptor Profile Characteristics</th>
<th>Chemical Structure</th>
<th>Pharmacological Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>D2, D3, 5-HT2, 5-HT1a, 5-HT1B</td>
<td>++</td>
<td>D2, 5-HT2</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>D2, D3, 5-HT2, 5-HT1a, 5-HT1B</td>
<td>++</td>
<td>D2, 5-HT2, 5-HT1a</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>D2, D3, 5-HT2, 5-HT1a, 5-HT1B</td>
<td>++</td>
<td>D2, 5-HT2, 5-HT1a</td>
</tr>
<tr>
<td>Szerotonin/dopamine</td>
<td>D2, D3, 5-HT2, 5-HT1a, 5-HT1B</td>
<td>++</td>
<td>D2, 5-HT2, 5-HT1a</td>
</tr>
<tr>
<td>Amisulpride</td>
<td>D2, D3, 5-HT2, 5-HT1a, 5-HT1B</td>
<td>++</td>
<td>D2, 5-HT2, 5-HT1a</td>
</tr>
</tbody>
</table>

### SGA effects

<table>
<thead>
<tr>
<th>Pharmacokinetic Effect</th>
<th>Chemical Structure</th>
<th>Receptor Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2, 5-HT2</td>
<td>++</td>
<td>D2, 5-HT2</td>
</tr>
<tr>
<td>Alpha</td>
<td>++</td>
<td>D2, 5-HT2</td>
</tr>
<tr>
<td>H1</td>
<td>++</td>
<td>D2, 5-HT2</td>
</tr>
<tr>
<td>M</td>
<td>++</td>
<td>D2, 5-HT2</td>
</tr>
</tbody>
</table>

**Selective DA (D2D3) antagonists**
- Benzamid(s)
- Amsulpride

**Serotonin/dopamine alpha antagonists (SDA)**
- Benzosartan(s)
- Ziprasidone
- Risperidone

**Multiple receptor antagonists (MARTA)**
- Dibenzamid(s)
- Clozarine
- Olanzapine
- Quetiapine
- Zotapine

**General principles of therapy**

- Generally outpatient therapy
- Psychiatric hospitalisation needed:
  - Serious functional damage (comorbidity?)
  - Behavioural disturbance
  - Suicide ideation
- Pharmacological and psychotherapy
- Follow up - care
- Relapse prevention
- GP treatment - psychiatric consultation

**The ideal anxiolytic medication?**

- Effective in broad spectrum
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**ANXIETY DISORDERS DRUG THERAPY**

- BENZODIAZEPINES
- SEROTONERGIC (5-HT1a) RECEPTOR PARTIAL AGONISTS
- ANTIDEPRESSANTS
- NORADRENERGIC DRUGS (beta-receptor blockers)
- SELEKTIVE HISTAMINERGIC (H1) RECEPTOR BLOCKERS
ANTIDEPRESSIVE DRUGS

- SSRI - citalopram, paroxetine, fluoxetine, sertraline, fluvoxamine,
- TCA, tetracyclic - amitriptylin, imipramin, maprotilin,
- SNRI - venlafaxin
- NaSSa - mirtazapin
- MAOI - moclobemid
- others - bupropion, tianeptin, stb

ANTIDEPRESSIVES - SSRI

- fluoxetine (Prozac, stb)
- fluvoxamine (Fevarin)
- paroxetine (Seroxat)
- citalopram (Seropram)
- sertraline (Zoloft)
serotomeric reuptake increase:
  - tianeptine (Coaxil)

OTHER ANTIDEPRESSIVES

„Dual action” „NaSSa” stb
SHT, NA selective venlafaxin (Efexcin), mirtazapin (Remeron)
SNRI - selektiv NA reuptake inhibition:
  - reboxetin (Edronax)
Selective NA és Da reuptake inhibition
  - bupropion (Wellbutrin)

TREATMENT OF BIPOLAR DISORDER, MANIC

1. Hospitalization (agitated behavior, protective environment, financial disaster)
2. Medication (mood stabil., antipsychotics, SGA)
   a/ Lithium carbonate (0.8-1.5 mEq/L)
   b/ Carbamazepine (600-1200 mg/day)
   c/ Valproic acid 600-1800 mg/day
Haloperidol
SGAs /Risperidon, olanzapine, quafiepin e.g.)
Treatment of depression

1. Hospitalization (suicide risk or impulsive behavior, psychotic form)
2. Out-patient treatment: frequent contact, support system of family
3. Medication
   a/ Tricyclic antidepressants
   b/ Tetracyclines
   c/ MAO Inhibitors
   d/ SSRI (paroxetin, sertalin, fluoxetin, citalopram)
   e/ SNRI (reboxetin)
   f/ dual action (venlafaxin)
   F/ NaSSa (mirtazapin)
4. Psychotherapy (cognitive psychotherapy, dynamic, and family)
5. ECT, Sleep deprivation, Light therapy
Reasonable Expectations of Successful Cholinesterase Inhibitor Therapy

- Improve, maintain, or slow decline in ADL and cognitive function
- Control troublesome behaviors
- Ease loss of independence
- Ease caregiver burden
- Delay placement in long-term care facility
Conclusions

- Alzheimer’s disease is primarily a diagnosis of inclusion, which can be made clinically.
- There are three key symptomatic domains in Alzheimer’s disease: Activities of daily living (ADL), Behavior, Cognition.
- Adverse events with cholinesterase inhibitors are generally dose-related and cholinergic in nature, and their frequency can be reduced with slower titration.

Addiction - therapy

- (1) detoxification, involving medications and supportive measures to minimize effects of the drug and of its withdrawal;
- (2) substitution therapy with related drugs, which may be temporary (as in withdrawal of sedatives);
- (3) deterrents to further ingestion of alcohol (e.g., disulfiram);
- (4) antianxiety or antidepressant medication;
- (5) group and individual psychotherapies intended to alter neurotic characteristics that promote psychological dependence.

Management of alcohol withdrawal syndromes

1. Thiamine; folic acid
2. Phenytoin or carbamazepine, in patients with a history of withdrawal seizures.
3. Haloperidol: 2-5 mg bid for patients with alcoholic hallucinosis.
4. For delirium tremens:
   - IV. IM. per os diazepam 10 mg (or lorazepam 2-4 mg), followed by 5-mg doses every 5 minutes until calm. Once the patient is stabilized, the dose may be tapered slowly over 4 or 5 days.
   - Seclusion and restraints as necessary.
   - Adequate hydration and nutrition.

Considerations for the therapy

- Antipsychotic medications can help reduce psychotic symptoms (e.g., hallucinations) or escalating anxiety or agitation.
- Benzodiazepines and alpha2-adrenergic agonists (e.g., clonidine) can help reduce excessive autonomic hyperactivity (e.g., elevated blood pressure, elevated pulse).
- Beta-blockers (e.g., propranolol) can help reduce excessive autonomic hyperactivity and somatic anxiety.
- For persons experiencing withdrawal seizures, an antiepileptic medication (e.g., phenytoin, carbamazepine) is often used prophylactically if seizure activity continues.

After detoxification, recommendations include one of the following:

- Continued treatment on an outpatient basis.
- Continued somatic and/or psychosocial treatment in a 21- to 28-day inpatient treatment program (helpful for patients who fail to stop drinking after repeated attempts at detoxification), possibly followed by a 6- to 24-month program in a long-term treatment facility.
Other somatic/biological but non-pharmacological therapies

- Sleep withdrawal (depression, ‘chronobiological model)
- Light therapy (seasonal, atypical depression)
- Psychosurgery (resistant OCD cases)
- ECT (th resistant depressive cases, catatonic schizophrenia)