Antipsychotic treatment

Istvan Bitter

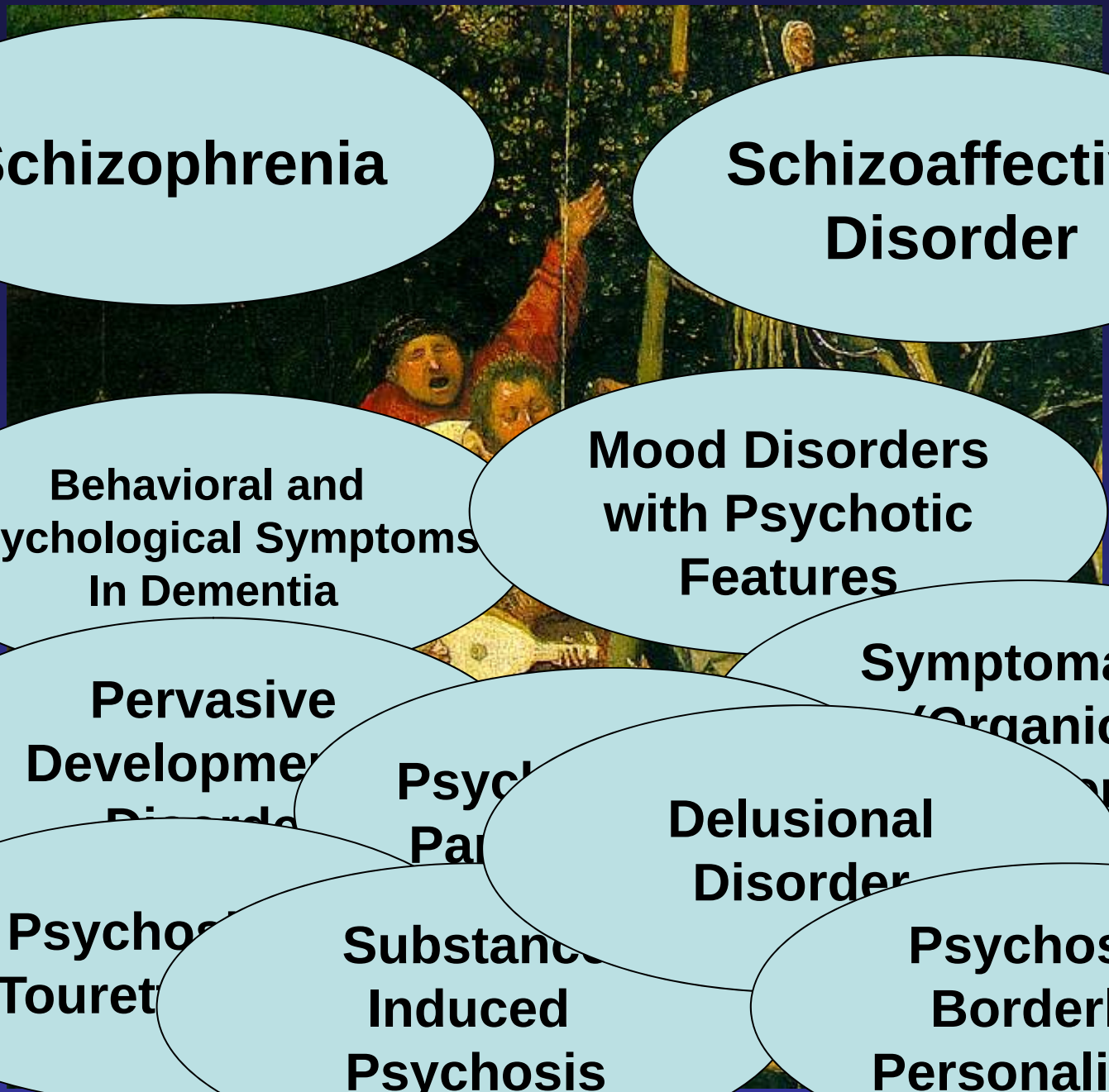
24 February 2010

Positive symptoms:
delusions, hallucinations, disorganized thinking, excitement, agitation, aggressivity, other behavioral disturbances

Negative symptoms:
blunted affect, emotional or social withdrawal, apathy, alogia, avolition

Affective symptoms:
anxiety, depression

Cognitive symptoms


Schizophrenia
Schizoaffective Disorder
Behavioral and Psychological Symptoms In Dementia
Mood Disorders with Psychotic Features
Pervasive Developme
Symptomatic (Organic)
Psyc
Pa
rs
Delusional Disorder
Psycho
Touret
Substanc
Induced Psychosis
Psychosis in Borderline Personality Dis.

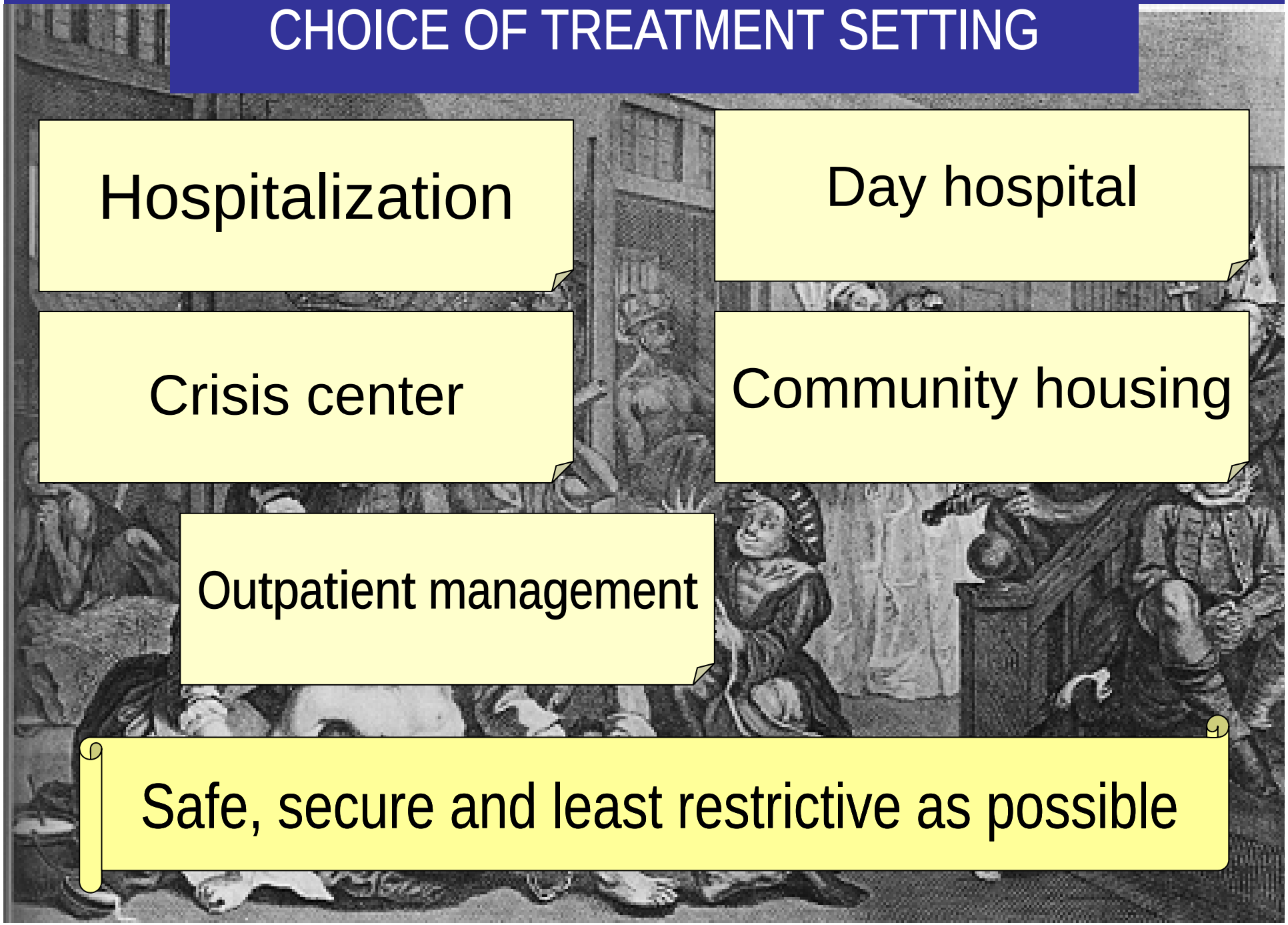
AIMS OF TREATMENT OF ACUTE PSYCHOSIS

- to prevent harm and worsening of the pt's state
- control disturbed behavior
- suppress symptoms
- rapid return to the best level of functioning
- develop an alliance with the patient and a close collaboration with the patient's family
- short- and long-term treatment plans
- connect the patient with appropriate maintenance and follow-up care in the community
- adjust aims of treatment within a context of the community in which it takes place

ASSESSMENT OF PATIENT

- Diagnosis
- Evaluate risk of potential suicidal and/or antisocial and agressive behavior
- Evaluate possible consequences of delaying treatment
  - Poor treatment response and overall outcome
  - Rejection; difficult acceptance or reintegration into the community

CHOICE OF TREATMENT SETTING



Hospitalization

Day hospital

Crisis center

Community housing

Outpatient management

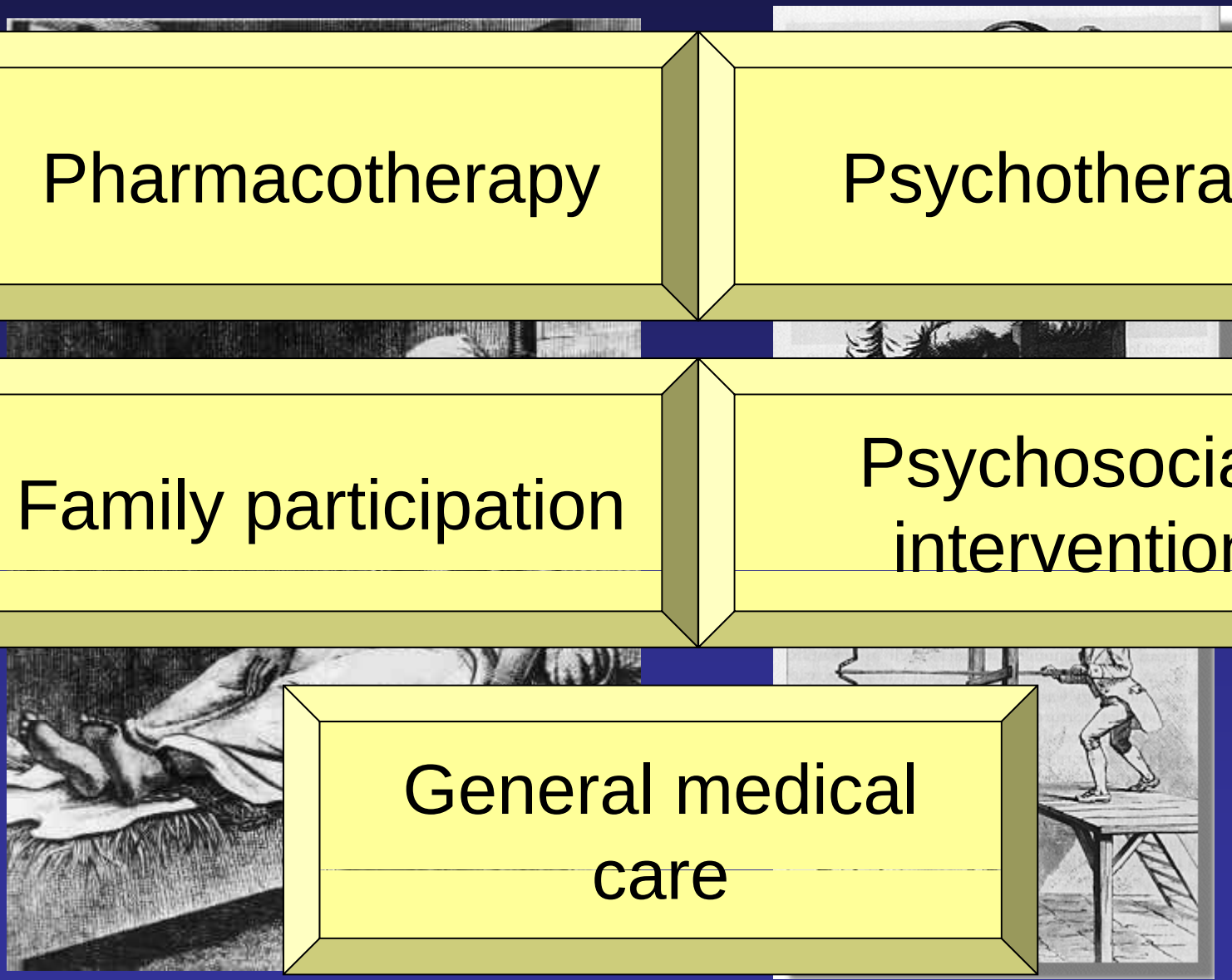
Safe, secure and least restrictive as possible

CHOICE OF TREATMENT SETTING

Depends on:

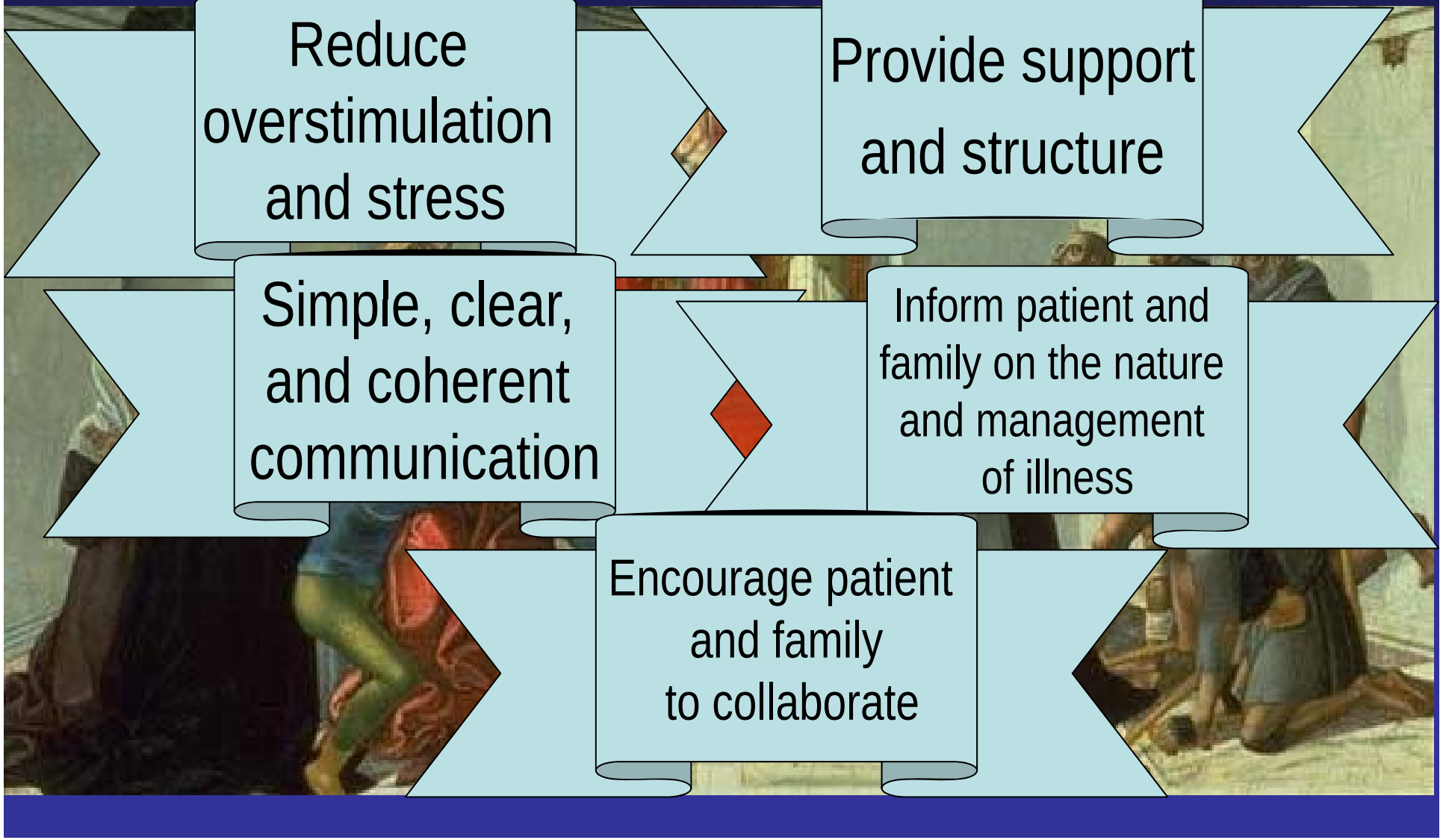
- severity of symptoms
- patient's social situation and support
- cooperation
- need for specific therapy
- availability of various treatment options
- specific health care systems
- patient's preferences

COMPLEX TREATMENT APPROACH



- Pharmacotherapy
- Psychotherapy
- Family participation
- Psychosocial intervention
- General medical care

PSYCHOTHERAPEUTIC INTERVENTIONS IN THE ACUTE PHASE



MANAGEMENT OF AGITATED OR VIOLENT PT.

Assure security of the staff and the patient

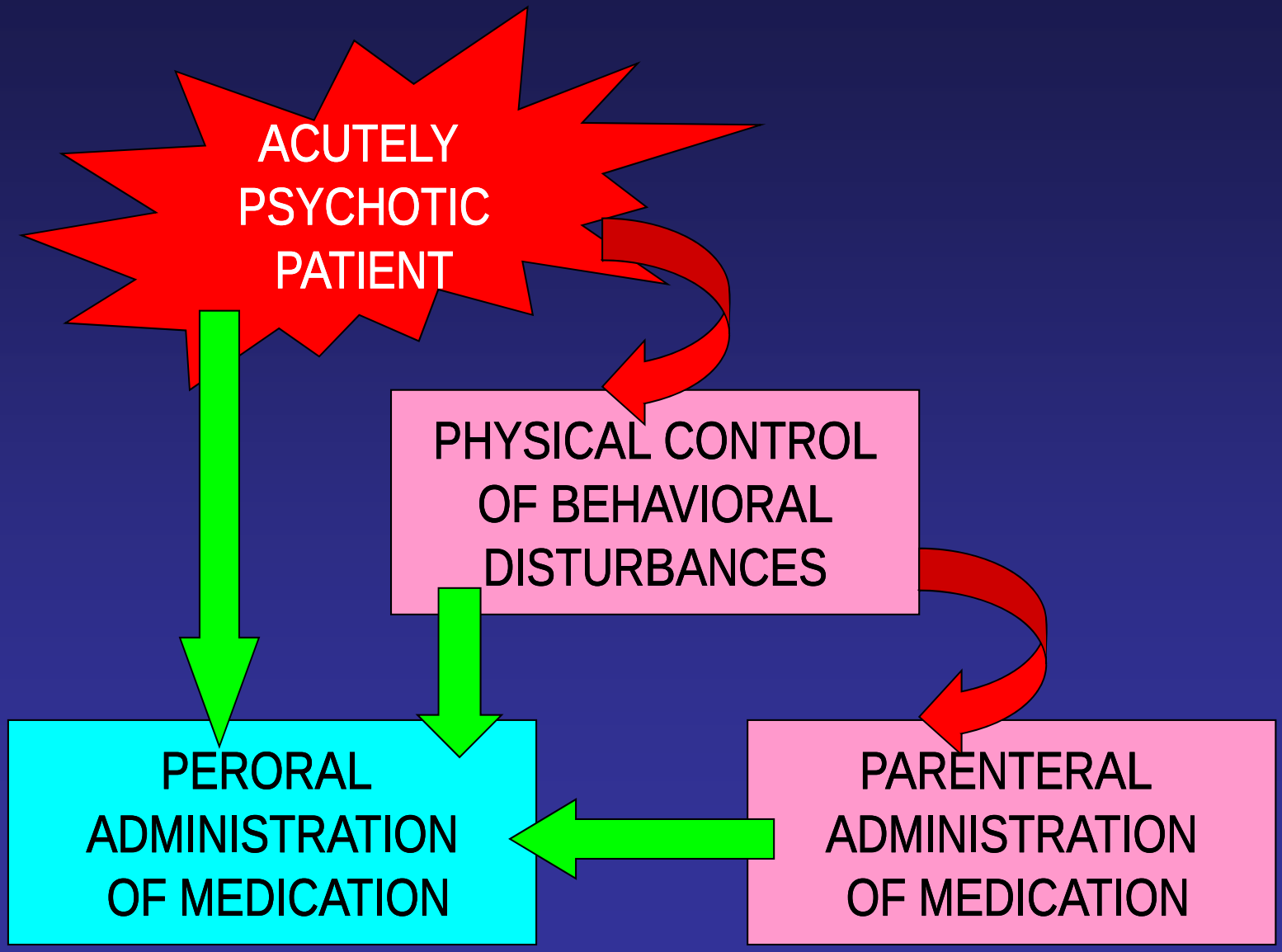
Sufficient help and overwhelming power

MANAGEMENT OF AGITATED OR VIOLENT PATIENT

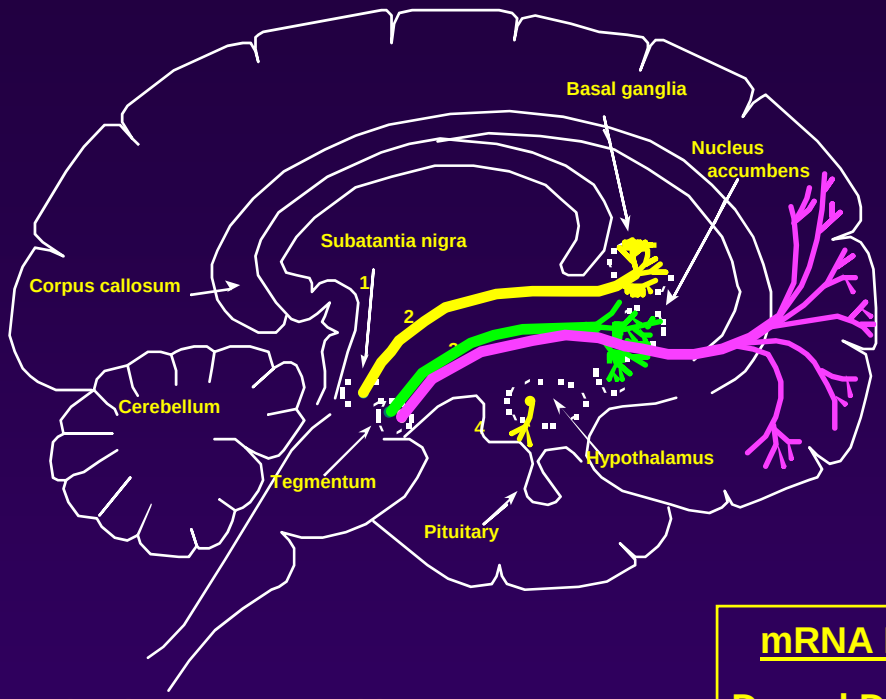
Placement in a secure setting: seclusion, restraints

Preferred intramuscular administration of medication ("rapid tranquilization")

MANAGEMENT OF ACUTELY PSYCHOTIC PT.



Dopaminergic pathways



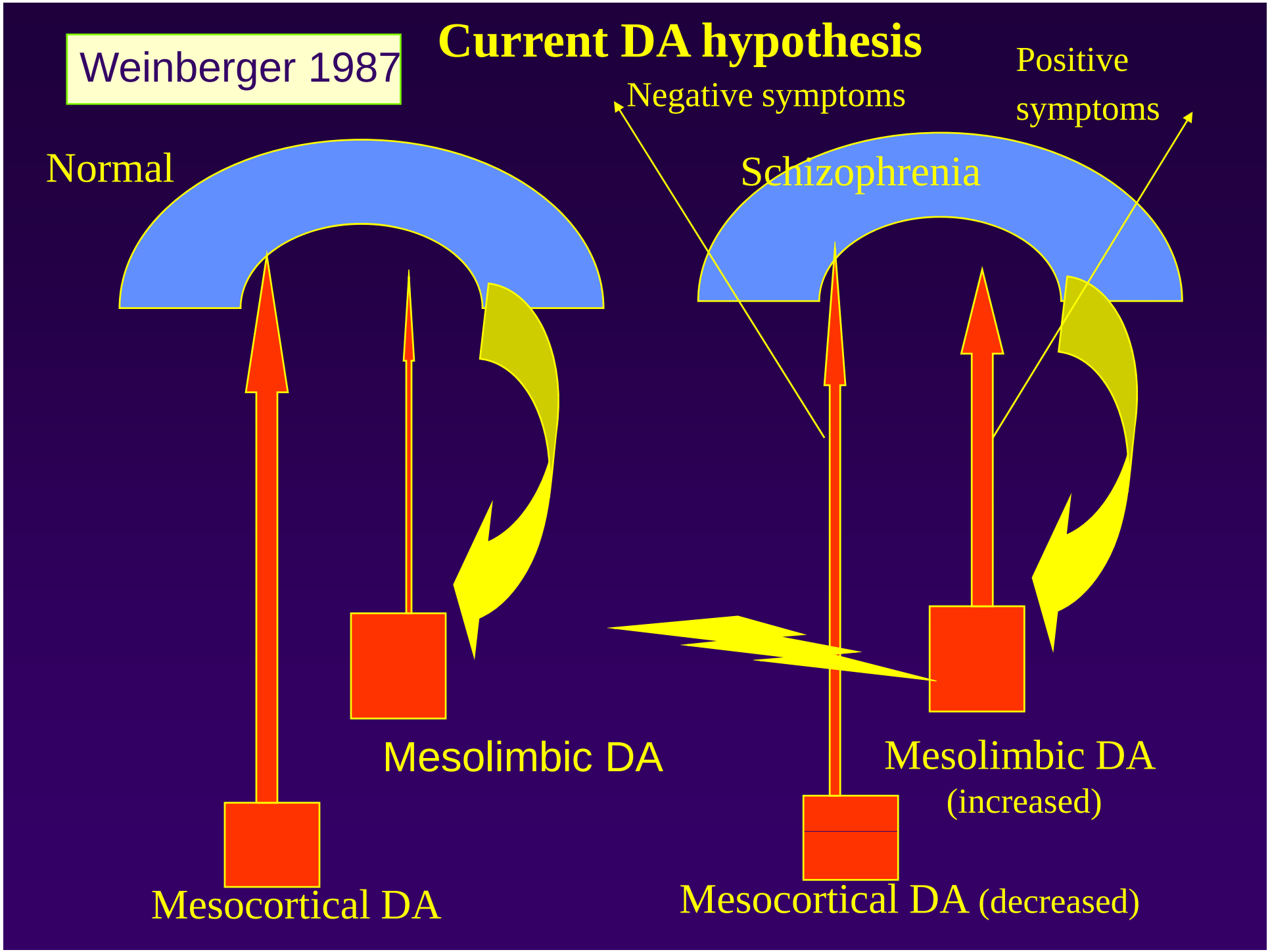
Hales RE, Yudofsky SC. *Textbook of Neuropsychiatry*.

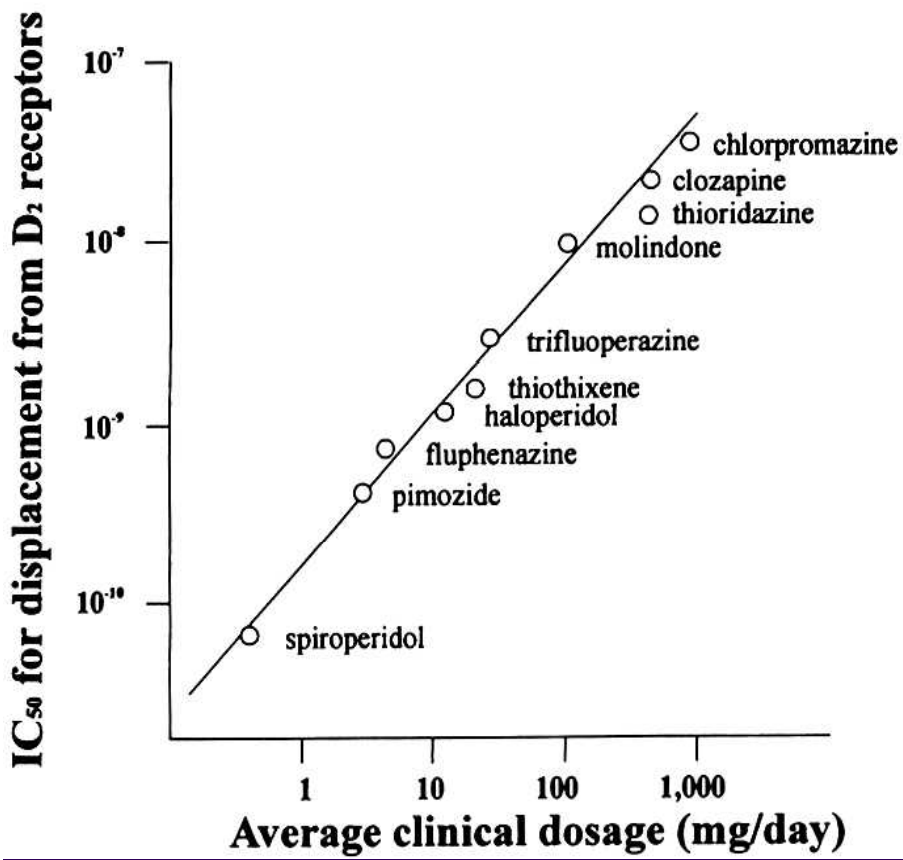
mRNA Localization

D_1 and D_2: caudate/putamen
D_3: n. accumbens
D_4: cortex/hippocampus

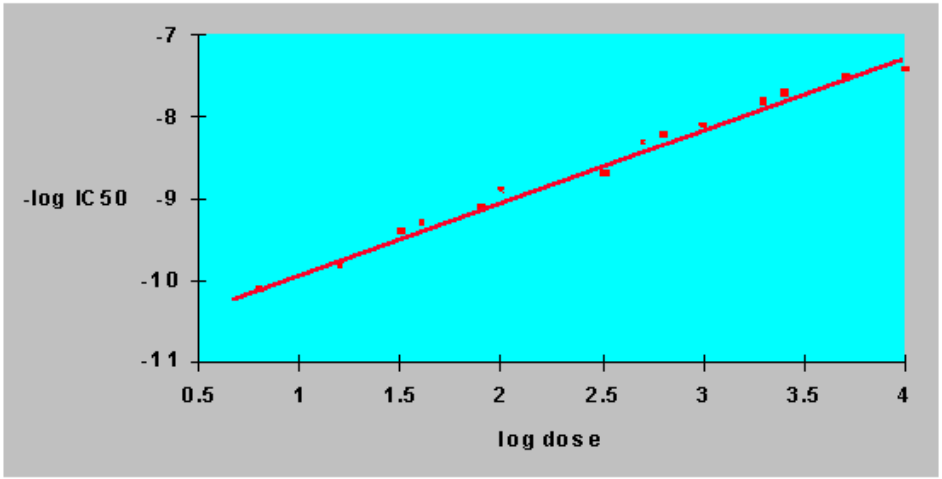
The four major dopamine tracts:

1) nigrostriatal
2) mesolimbic
3) mesocortical
4) tuberohypophyseal


Weinberger 1987
Current DA hypothesis
Negative symptoms
Positive symptoms
Normal
Schizophrenia
Mesolimbic DA
Mesolimbic DA (increased)
Mesocortical DA
Mesocortical DA (decreased)



D_2 receptor affinity and clinical dose of antipsychotics



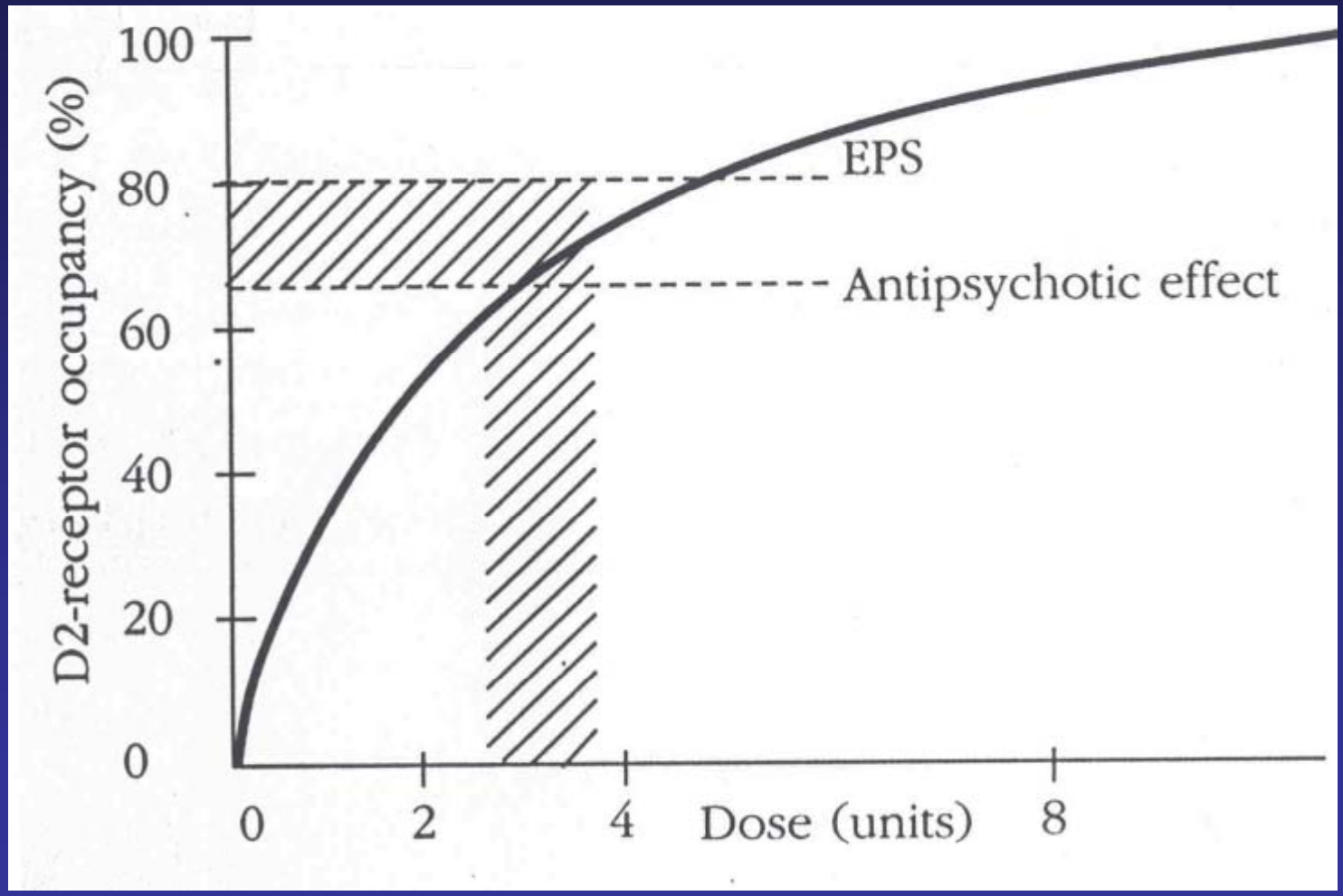
CONVENTIONAL ANTIPSYCHOTICS

- Most frequently used: haloperidol
- Effective in control of positive symptoms and agitation
- Shorten duration of psychotic episode
- Reduce number of relapses
- Available in various drug forms (liquid, inject.)

CONVENTIONAL ANTIPSYCHOTICS: SIDE EFFECTS I. - induced by DA blockade

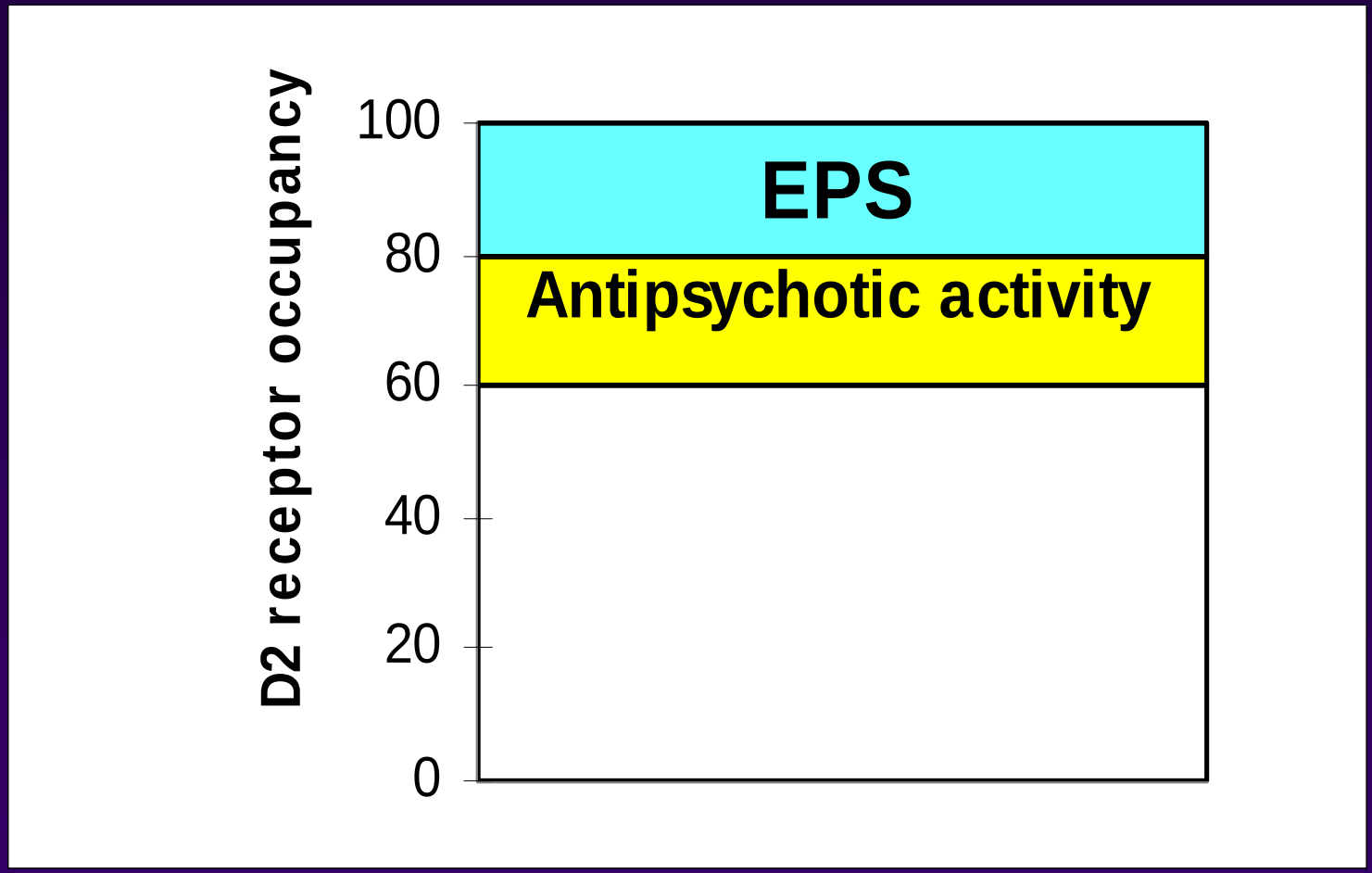
- Extrapyramidal side effects (EPS):
  - parkinsonism, dystonia, akathisia; tardive dyskinesia
- Increase of prolactin levels
  - galactorhea, impairment of menstrual cycle, sexual dysfunctions
- Neuroleptic malignant syndrome

RELATIONSHIP BETWEEN THE DOSE AND D_2 RECEPTOR OCCUPANCY



Farde et al., 1992

D2 recetor occupancy, antipsychotic activity and EPS



CONVENTIONAL ANTIPSYCHOTICS: SIDE EFFECTS II.

- Anticholinergic effects:
  - dry mouth, blurred vision, constipation, tachycardia, urinary retention, cognitive impairments, confusion, delirium
- Antihistaminic effects;
  - sedation, weight gain
- Antiadrenergic effects
  - orthostatic hypotension

CONVENTIONAL ANTIPSYCHOTICS: SIDE EFFECTS III.

- Allergy
- Photosensitivity
- Hepatic impairments (elevation of liver enzymes, jaundice)
- Pigmentary retinopathies; corneal opacities
- Leucopenia and agranulocytosis
- Pulmonary embolism
- QT prolongation
- Sudden death
- Seizures
- Neuroleptic-induced deficit syndrome?

CONVENTIONAL ANTIPSYCHOTICS: LIMITATIONS

- Less efficient in treatment of negative, affective (depressive), and cognitive symptoms
- Less effective in prophylaxis and control of relapses
- High number of non-responders and residual states
- High incidence of side effects
- High non-compliance rate

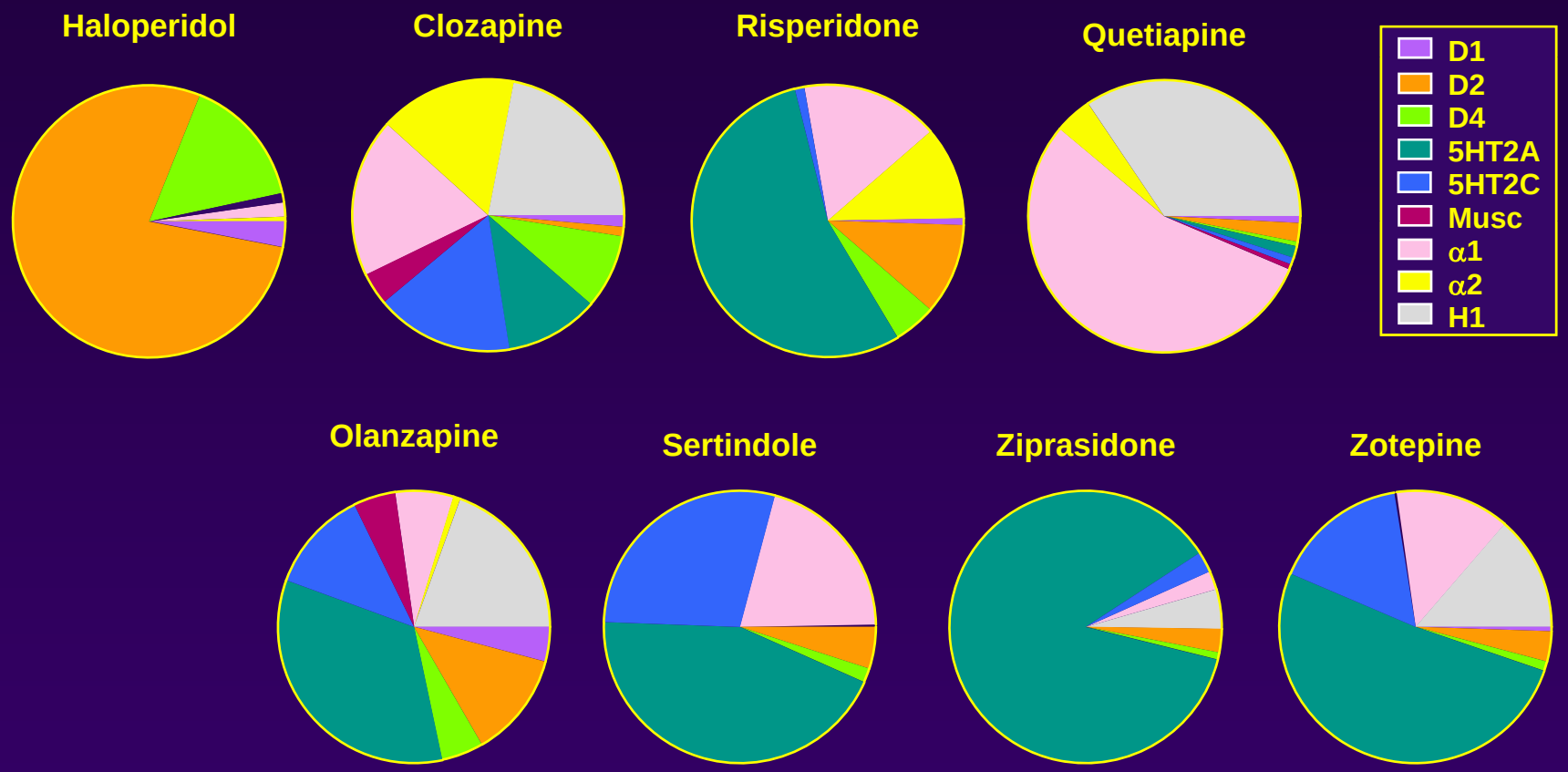
SECOND GENERATION ANTIPSYCHOTICS

"antipsychotics at least as (or more) efficacious and better tolerated regarding EPS than conventional antipsychotics"

Second generation antipsychotics

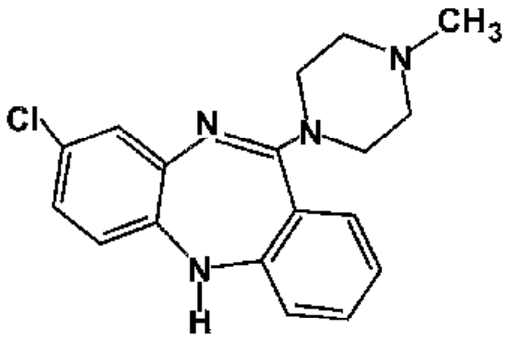
- Amisulpirid (Amitrex and generic)
- Aripiprazol (Abilify)
- Clozapine („gold standard”) (Leponex and generics)
- Olanzapine (Zyprexa and generics) – im formulation available
- Quetiapine (Seroquel and generics)
- Risperidone (Risperdal and generics)
- Sertindol (Serdolect)
- Ziprasidone (Zeldox) – im formulation available

Receptor selectivity vs multineurotransmitter activity

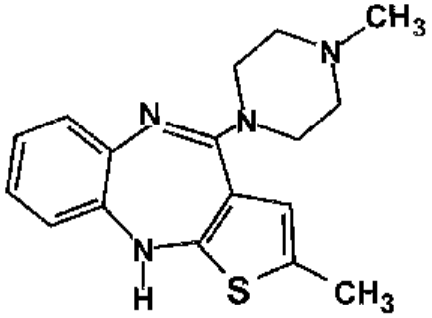


Data From Bymaster et al., 1996 & Schotte et al., 1996

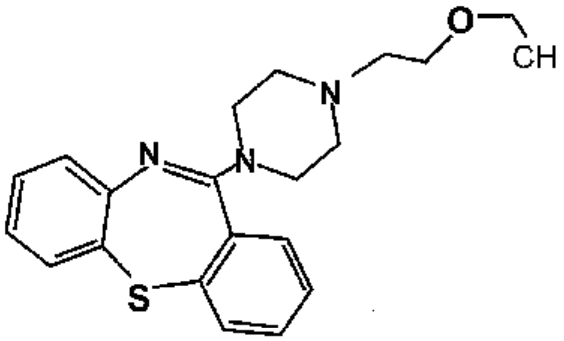
Second generation antipsychotics



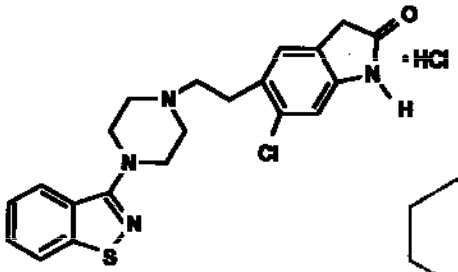
Clozapine



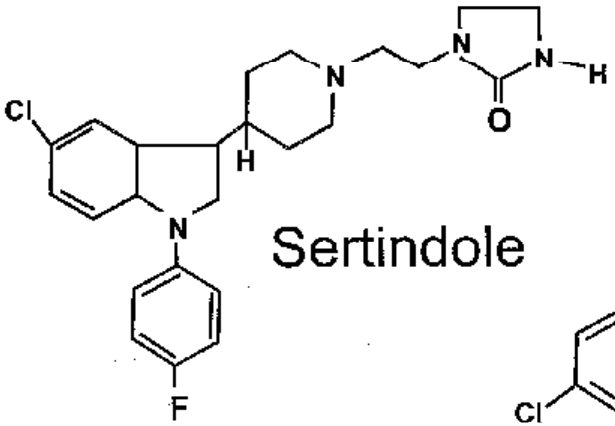
Olanzapine



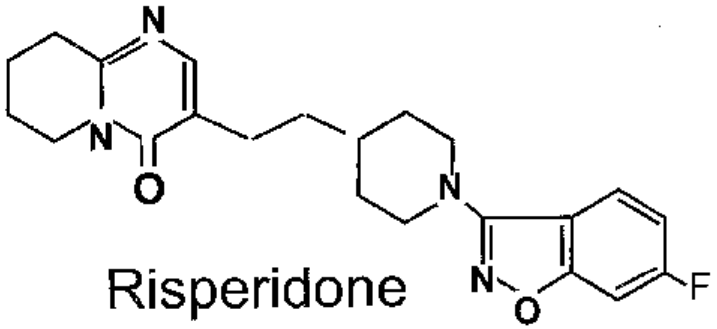
Quetiapine



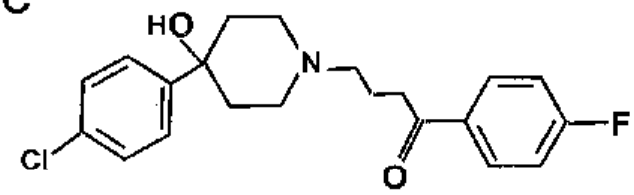
Ziprasidone



Sertindole



Risperidone



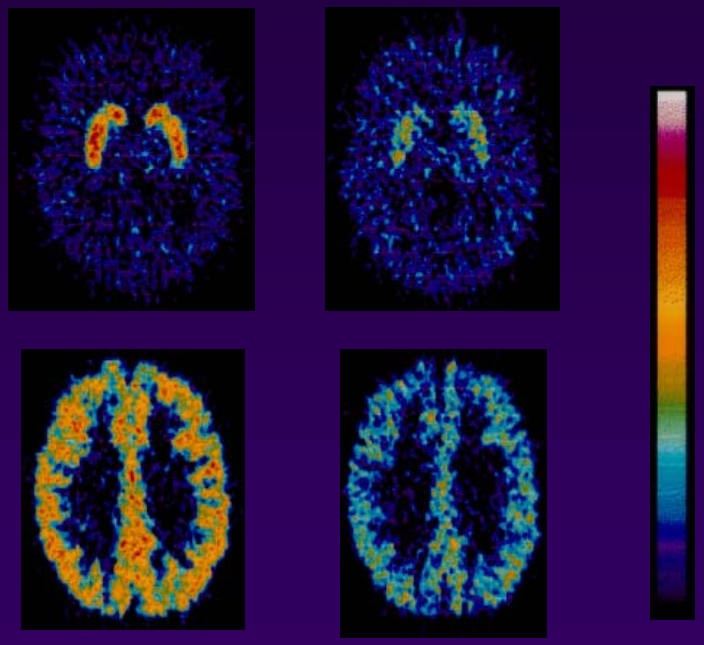
Haloperidol

Olanzapine: In Vivo Receptor Binding Affinity - 5-HT vs D_2

PET Study

D_2 Binding
[^{11}C]raclopride

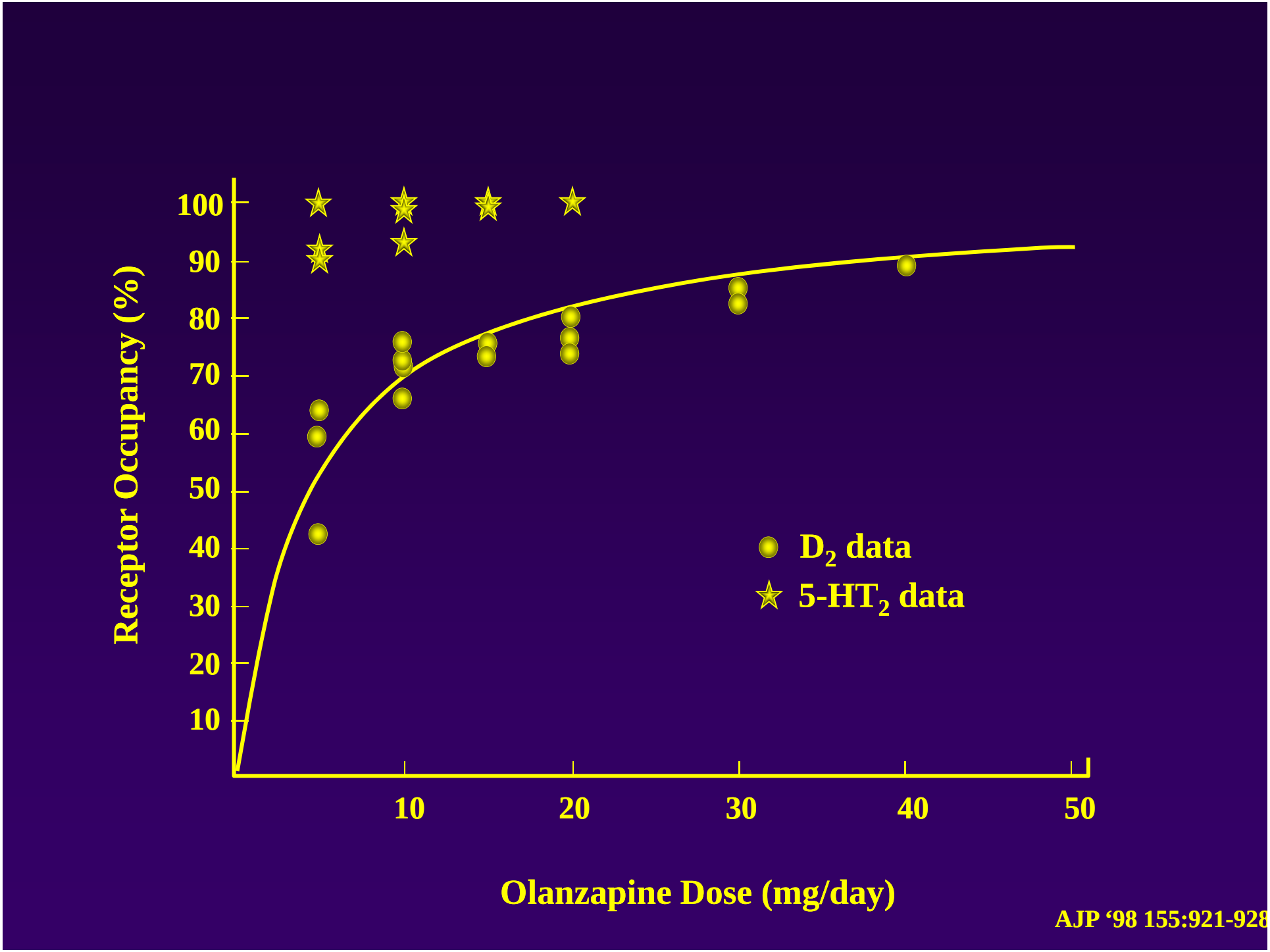
5HT Binding
[^{11}C]NMSP

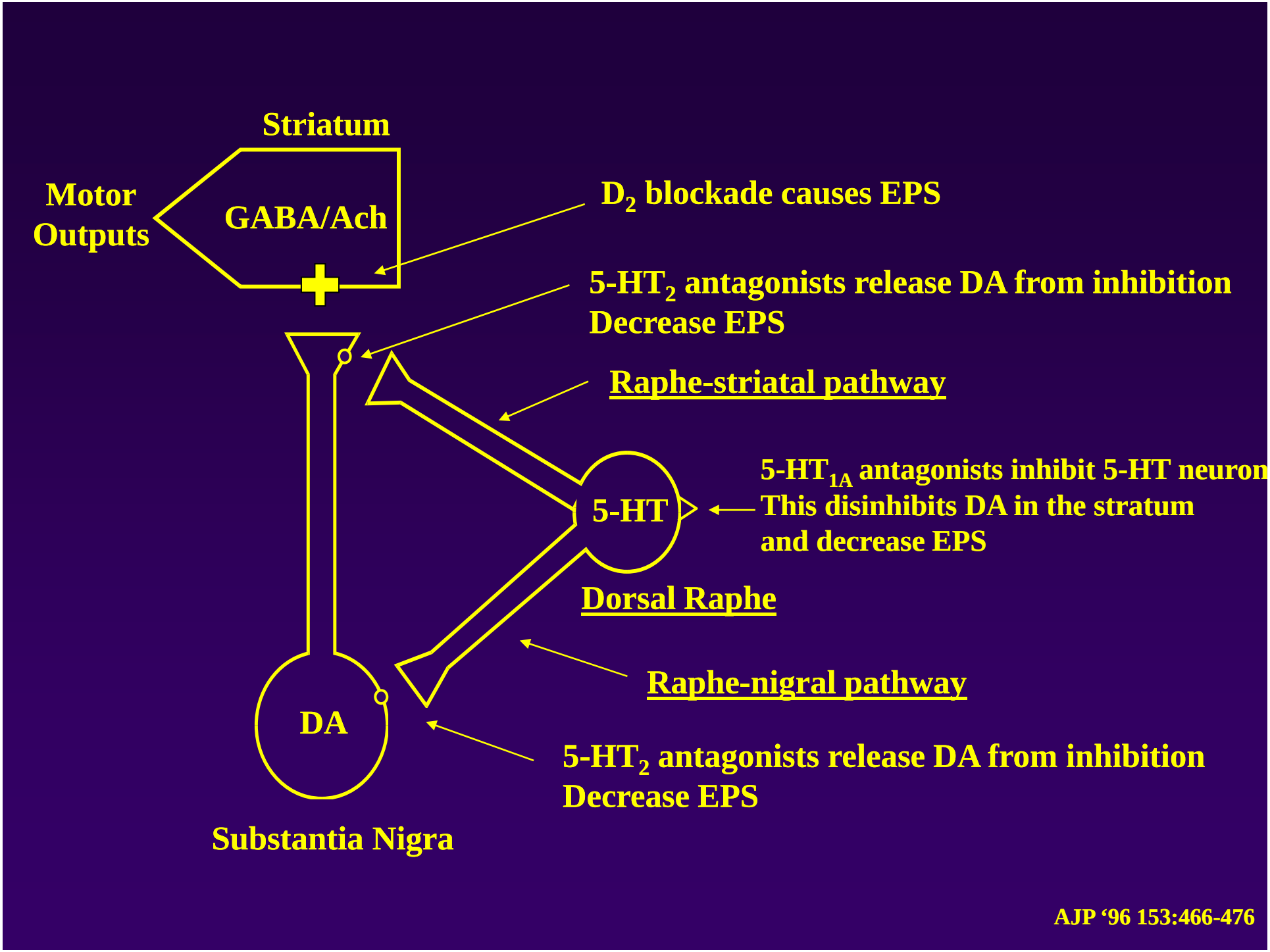


Baseline 10 mg olanzapine

- Single 10 mg Olanzapine dose given
- Greater 5HT (84%) than D_2 (61%) occupancy approximates clozapine and suggests a low EPSE profile in contrast to other antipsychotic drugs

Nyberg et al 1996


Receptor Occupancy (%)
100
90
80
70
60
50
40
30
20
10
10
20
30
40
50
Olanzapine Dose (mg/day)
D2 data
5-HT2 data
AJP '98 155:921-928


Striatum
Motor Outputs
GABA/Ach
D2 blockade causes EPS
5-HT2 antagonists release DA from inhibition
Decrease EPS
Raphe-striatal pathway
5-HT1A antagonists inhibit 5-HT neuron
This disinhibits DA in the stratum
and decrease EPS
5-HT
Dorsal Raphe
Raphe-nigral pathway
DA
5-HT2 antagonists release DA from inhibition
Decrease EPS
Substantia Nigra
AJP '96 153:466-476

PHARMACOLOGICAL PROPERTIES OF 2nd GENERATION ANTIPSYCHOTICS

- Extrastriatal blockade of D2 receptors
- Blockade of D2 < 5-HT2 receptors
- High dissociation constant of binding to D2 receptors
- Low cataleptogenic potential
- Wide range between antipsychotic effects and extrapyramidal symptoms inducing dosages

A POSSIBLE CLASSIFICATION OF THE 2nd GENERATION ANTIPSYCHOTICS ACCORDING TO THEIR MECHANISM OF ACTION

Pharmacodynamic Effects	Chemical Structure	Receptor Blockade				
		D2	5-HT2	Alpha 1	H-1	M
Selective dopamine (D2/D3) antagonists	Benzamides Amisulpride	++				
Serotonin/dopamine/alpha antagonists (SDA)	Benzisoxazoles Ziprasidone Risperidone Sertindole	++ ++ ++	+ + +	+ + +	 ± 	
Multi-acting receptor-targeted antipsychotics (MARTA)	Dibenzodiazepines Clozapine Olanzapine Quetiapine Zotepine	+ ++ + ++	+ + + +	+ + + +	+ + + +	+ + ±

Švestka, 2001

2nd GENERATION ANTIPSYCHOTICS: MOST FREQUENT SIDE EFFECTS

- Metabolic side effects including weight gain (H1)
- Sedation (H1, alpha1)
- Orthostatic hypotension (alpha2)
- EPS and hyperprolactinaemia

- Anticholinergic effects (M)
- ECG abnormalities - prolongation QTc
- Seizures
- Agranulocytosis (clozapine)
- Hypersalivation (clozapine)

AMISULPRIDE

Schizophrenia:

- effective for positive symptoms
- effective for negative and depressive symptoms

Other indications:

- Dysthymia
- Depression
- (Infantile autism)

CLOZAPINE

Schizophrenia:

well-documented antipsychotic efficacy

effective in treatment-resistant pt

improvement of negative, affective, cognitive Sx and suicidal behavior

Other indications:

psychosis in Parkinson's Disease

CLOZAPINE IN TREATMENT-RESISTANT SCHIZOPHRENIA

(Kane et al., 1988)

Design:

- patients who did not respond to 3 different antipsych.
- 6 weeks of open-label haloperidol treatment
- nonresponders (n=268) - 6 weeks of double-blind treatment with clozapine or chlorpromazine

Results:

Clozapine - 30% responders, improvement in positive and negative symptoms, BPRS, CGI, NOSIE

Chlotpromazine - 4% responders

OLANZAPINE

Schizophrenia:

antipsychotic efficacy

effective for negative and affective symptoms

Other indications:

Acute mania; depression

Cannabis-induced psychosis;

Tourette’s disorder

QUETIAPINE

Schizophrenia:

antipsychotic efficacy superior to placebo and similar to the first generation antipsychotics (studies with low dose!)

RISPERIDONE

Schizophrenia:

antipsychotic efficacy

effective for negative, affective, and cognitive (?) symptoms

Other indications:

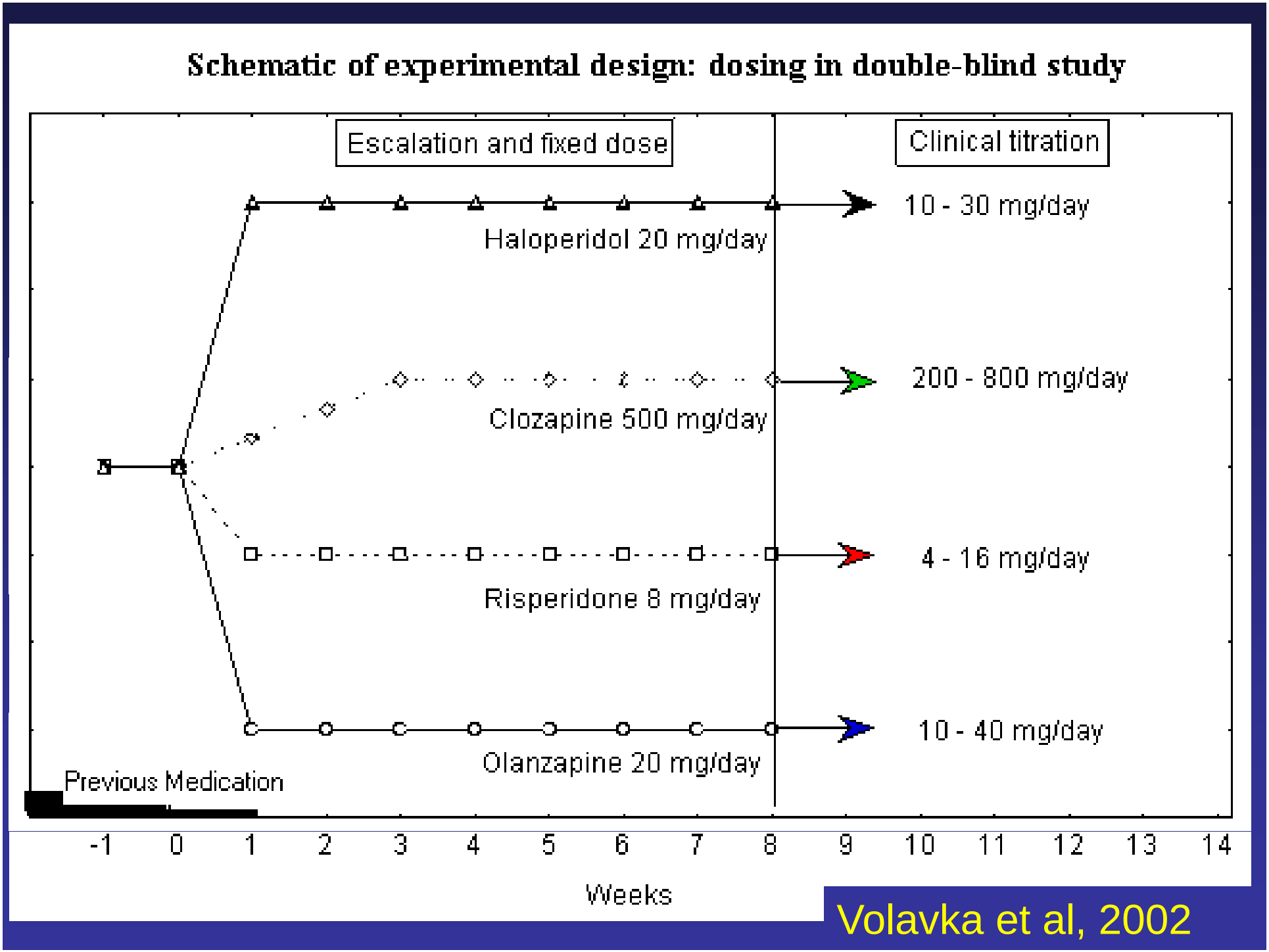
Mania; behavioral disturb. in children with mental retardation; pervasive developmental dis.; cocaine dependence; Tourette's disorder.

COMPARISON OF 2GA IN TREATMENT RESISTANT SCHIZOPHRENIA

(Volavka et al., 2002)

Design:

- 157 treatment resistant patients with schizophrenia or schizoaffective disorder
- 14 weeks of double-blind treatment: haloperidol, clozapine, olanzapine, risperidone


Schematic of experimental design: dosing in double-blind study
Escalation and fixed dose
Clinical titration
Haloperidol 20 mg/day
10 - 30 mg/day
Clozapine 500 mg/day
200 - 800 mg/day
Risperidone 8 mg/day
4 - 16 mg/day
Olanzapine 20 mg/day
10 - 40 mg/day
Previous Medication
-1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14
Weeks
Volavka et al, 2002

COMPARISON OF 2GA IN TREATMENT RESISTANT SCHIZOPHRENIA

(Volavka et al., 2002)

Results:

Total PANSS: CLO, OLZ, RIS - significant improvement

CLO, OLZ - superior over HAL

Positive Sx: CLO, OLZ - significant improvement

Negative Sx: CLO, OLZ - significant improvement

CLO, OLZ, RIS - superior over HAL

CLO - superior over RIS

ZIPRASIDONE

Schizophrenia:

antipsychotic efficacy similar to the first generation antipsychotics and superior to placebo

Other indications:

Children and adolescents with Tourette's disorder

ZOTEPINE

Schizophrenia:

antipsychotic efficacy similar to the first generation antipsychotics

ARIPIPRAZOL

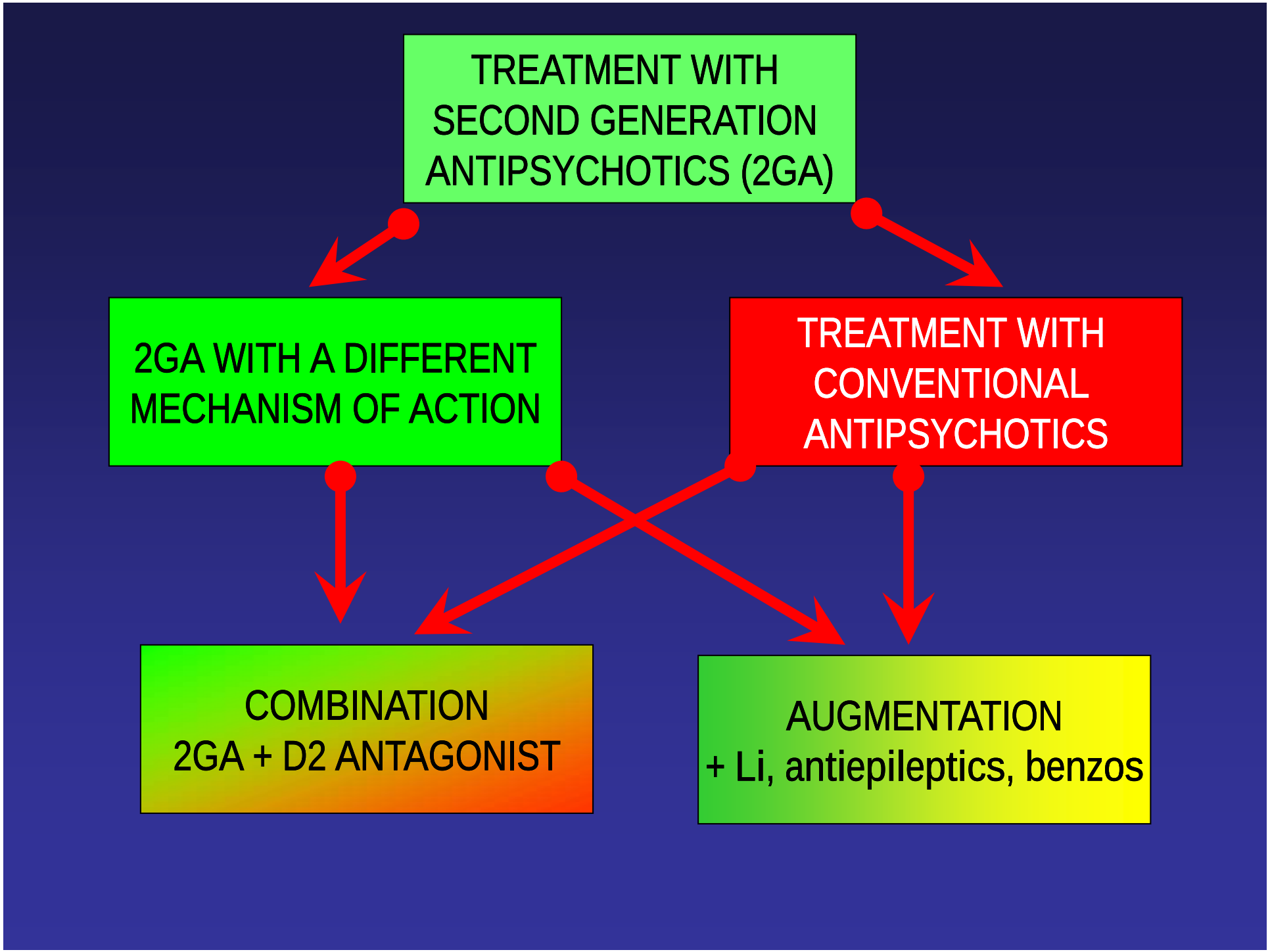
- dopamine antagonist and partial agonist

OTHER PSYCHOTROPIC DRUGS IN ACUTE PSYCHOSIS

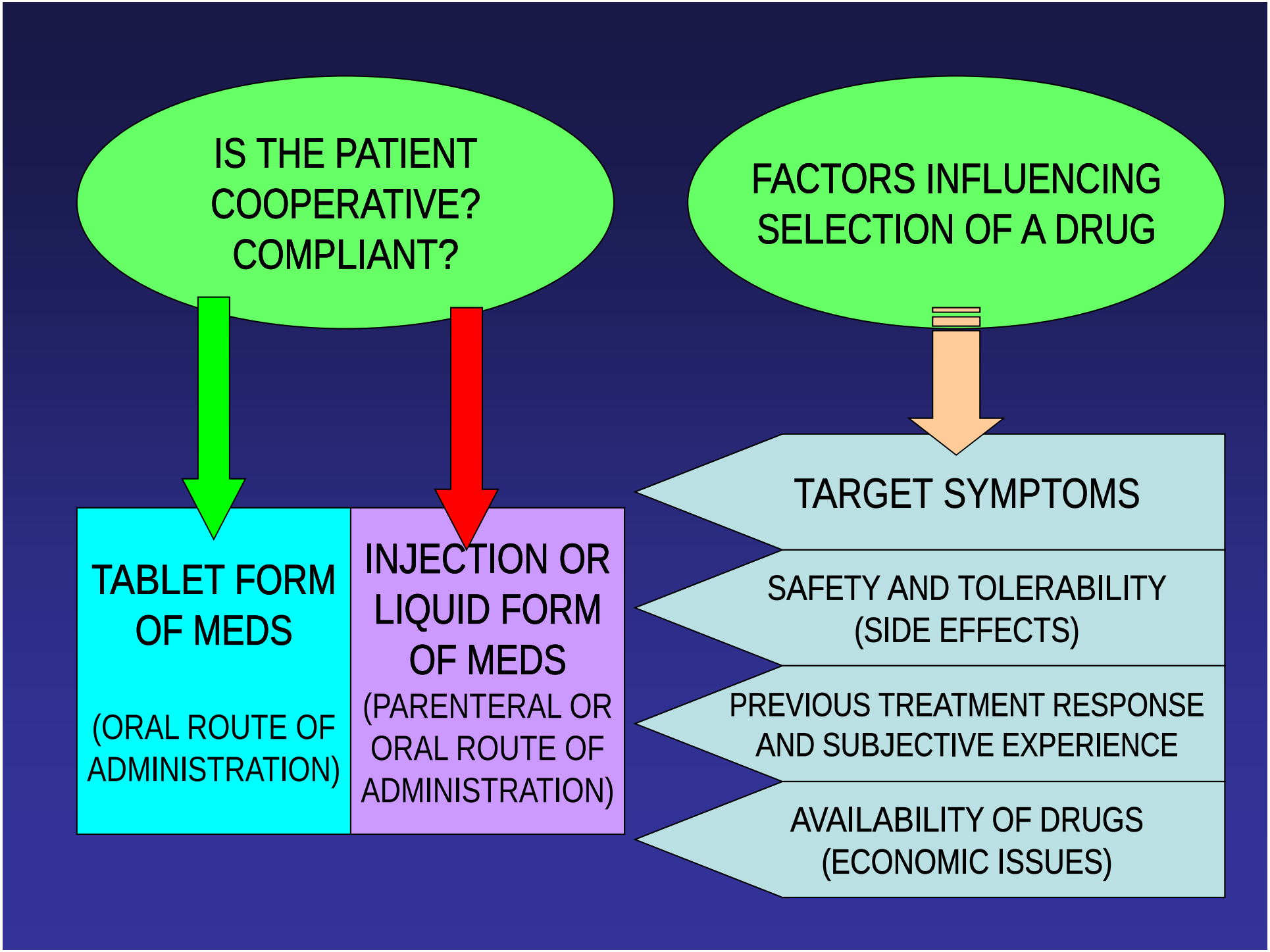
BENZODIAZEPINES – anxiety, agitation, insomnia, augmentation

ANTIDEPRESSANTS – depressive, negative Sx, anxiety

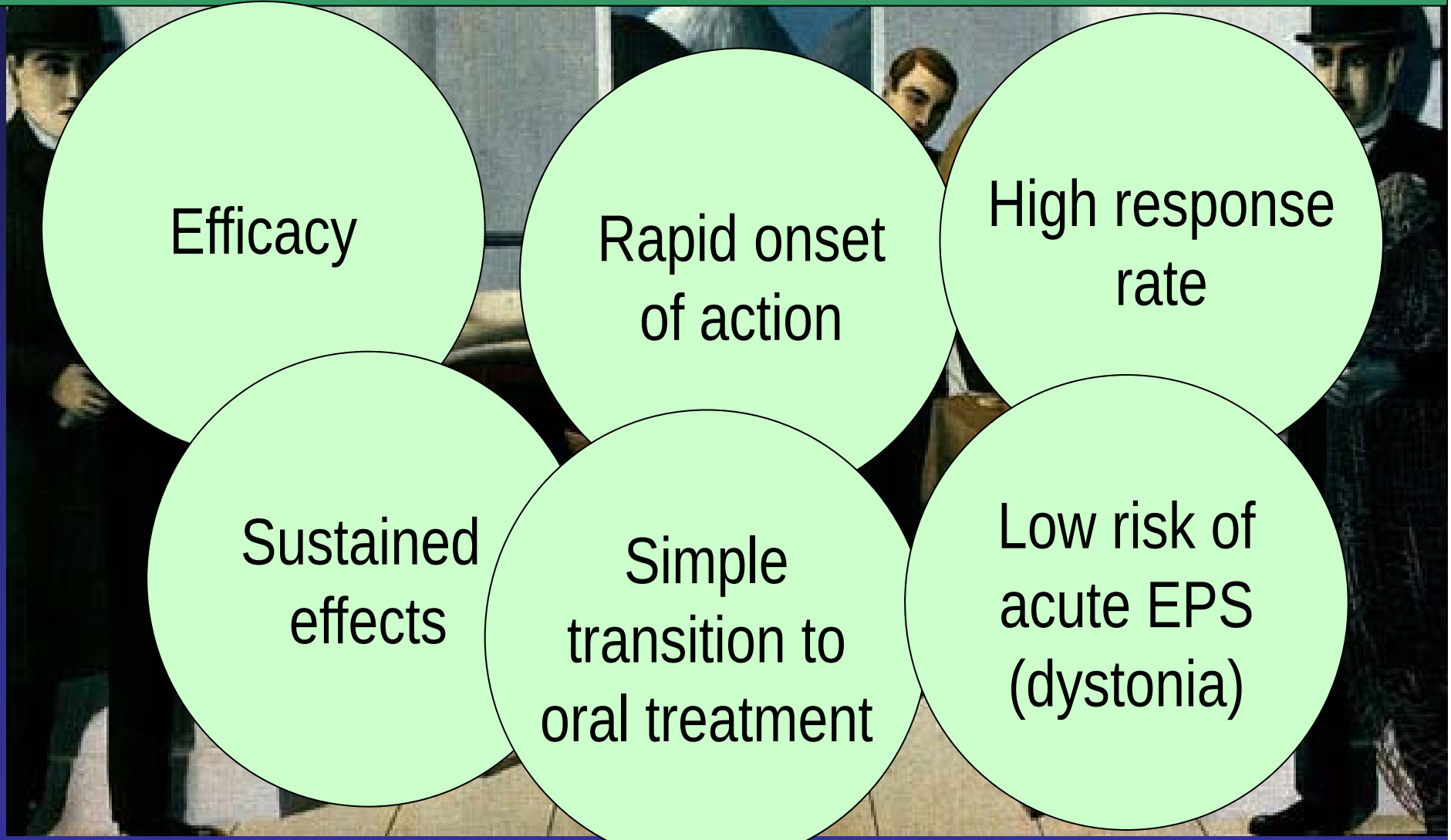
BETA-BLOCKERS – akathisia


TREATMENT WITH SECOND GENERATION ANTIPSYCHOTICS (2GA)
2GA WITH A DIFFERENT MECHANISM OF ACTION
TREATMENT WITH CONVENTIONAL ANTIPSYCHOTICS
COMBINATION 2GA + D2 ANTAGONIST
AUGMENTATION + Li, antiepileptics, benzos


THE CHOICE OF DRUG
To assure the best possible treatment
To bring a rapid relief
Not to stigmatize a patient
To be easily administered


IS THE PATIENT COOPERATIVE? COMPLIANT?
FACTORS INFLUENCING SELECTION OF A DRUG
TABLET FORM OF MEDS
(ORAL ROUTE OF ADMINISTRATION)
INJECTION OR LIQUID FORM OF MEDS
(PARENTERAL OR ORAL ROUTE OF ADMINISTRATION)
TARGET SYMPTOMS
SAFETY AND TOLERABILITY (SIDE EFFECTS)
PREVIOUS TREATMENT RESPONSE AND SUBJECTIVE EXPERIENCE
AVAILABILITY OF DRUGS (ECONOMIC ISSUES)

INJECTION FORMS OF THE 2nd GENERATION AP



INTRAMUSCULAR OLANZAPINE

Schizophrenia – acute agitation

(Wright et al., 2001)

- n=285
- 2 hrs; 24 hrs: OLZ=HAL>PL; (15; 30; 45 min: OLZ>HAL)
- EPS: 0.8% OLZ; 5.6% HAL;
- Dystonia: 7% HAL

Bipolar mania – acute agitation

(Meehan et al., 2001)

- n=201
- 2 hrs: OLZ > LOR; OLZ > PL
- 24 hrs: OLZ > PL; LOR = OLZ; LOR = PL

INTRAMUSCULAR ZIPRASIDONE

Acute psychosis

Brook et al., 2000
- n=132; 7 days
- ZIP > HAL

Lesem et al., 2001
- n=117; 24 hrs
- ZIP 10 mg > ZIP 2 mg

Daniel et al., 2001
- n=79; 24 hrs
- ZIP 20 mg > ZIP 2 mg

Lack of treatment adherence of doctors

I. Bitter[1]
J. C.-Y. Chou[2]
G. S. Ungvari[3]
W. K. Tang[3]
Z. Xiang[4]
A. Iwanami[5]
P. Gaszner[6]

Prescribing for Inpatients with Schizophrenia: An International Multi-Center Comparative Study

Original Paper

Background: This study compares prescription practices for acute inpatients with schizophrenia among six academic departments located in China, Japan, Hungary, and the U.S.

Methods: Prescription data for a sample of 429 inpatients from six academic departments were collected on a randomly chosen census day. All patients met criteria for schizophrenia according to DSM-IV and had a length of illness of at least two years.

Results: While patients at the different centers varied in their demographic and clinical characteristics, i.e., age, sex, and length of illness, a great variation in prescription patterns for antipsychotic and other psycho
within the same
and dose antipsy
psychotropic dru
with one or more other psychotropic drugs, including anticholinergics, anticonvulsants, benzodiazepines, and non-benzodiazepine hypnotics. Anticholinergic use was more common with typical antipsychotics. Rates of atypical antipsychotic drug use were lowest in the Japanese center. The Japanese center had by far the highest mean daily dose of antipsychotics.

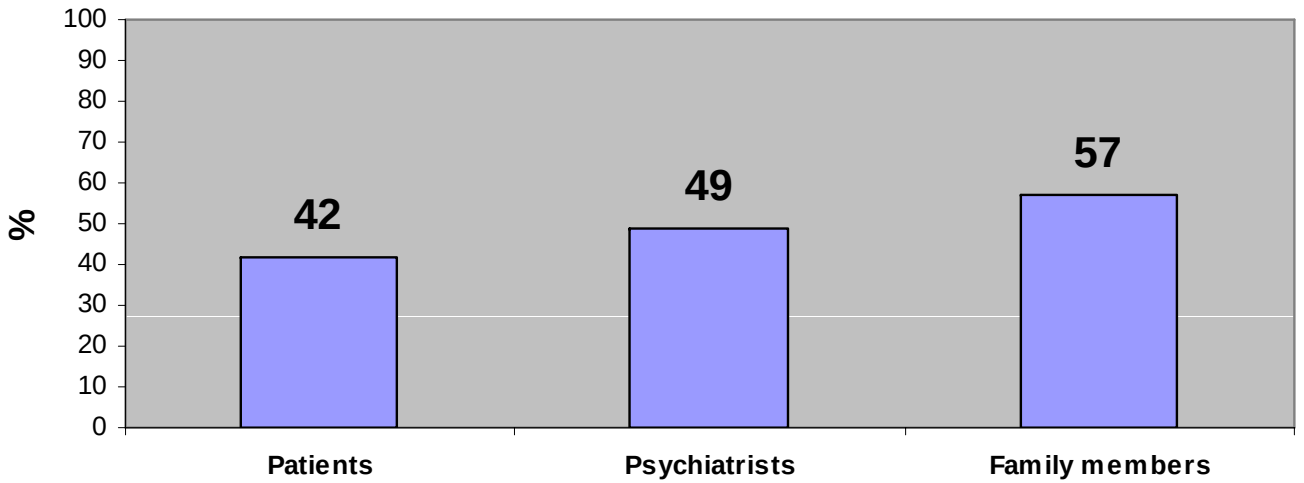
Conclusions: The results indicate that prescription patterns in different centers do not follow any specific guidelines for the treatment of schizophrenia. The results also confirm previous findings that prescribing practices for schizophrenia vary greatly among

Conclusions: The results indicate that prescription patterns in different centers do not follow any specific guidelines for the treatment of schizophrenia. The results also confirm previous findings

Bitter I et al. Prescribing for Inpatients... Pharmacopsychiatry 2003; 36: 143 – 149

Lack of treatment adherence of patients in schizophrenia

Estimated rates of noncompliance in schizophrenia by patients and their doctors and relatives



n=909 patients; 73 psychiatrists; 423 relatives

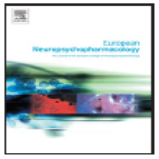
Meszaros,A., Bitter, I. The assessment of adherence using a questionnaire in patients suffering from schizophrenia. European Psychiatry, Vol 22, Suppl1, March 2007, S104

Regional differences in antipsychotic prescriptions and remaining on monotherapy (antipsychotic)

European Neuropsychopharmacology (2008) 18, 170–180

ELSEVIER

www.elsevier.com/locate/euroneuro



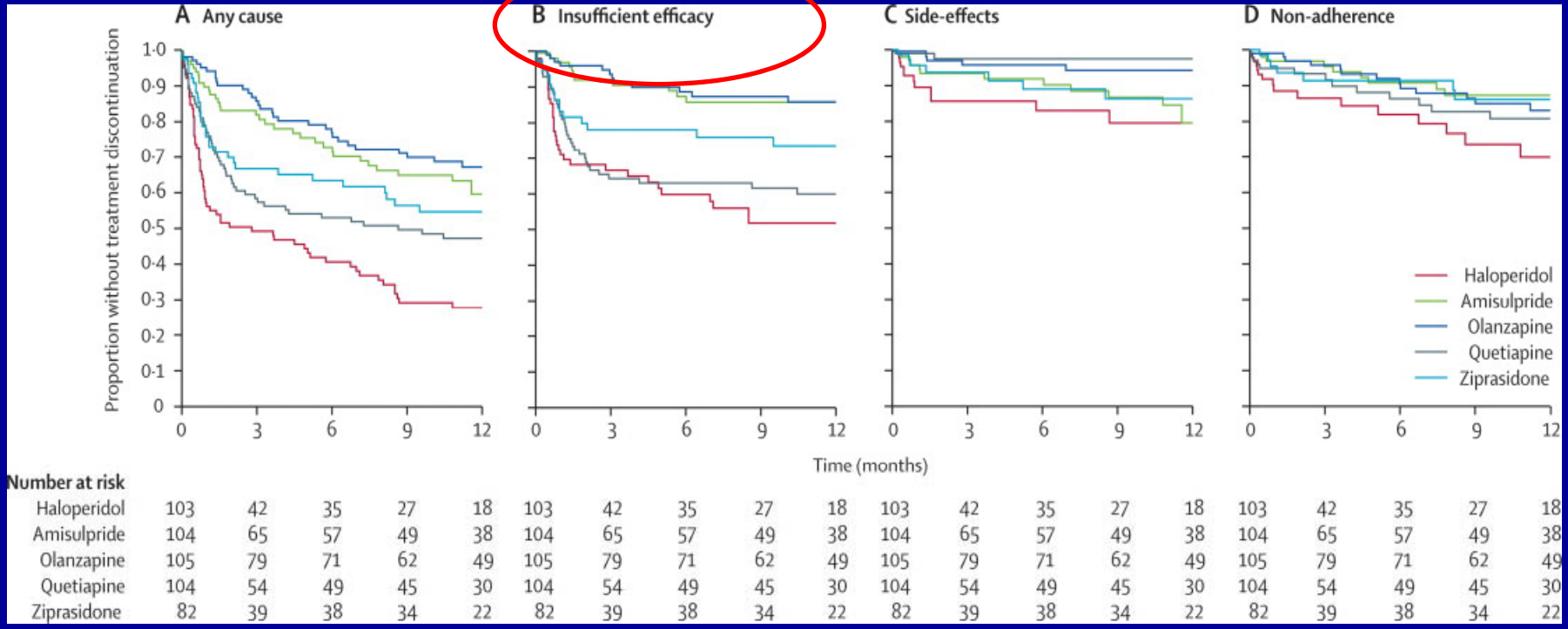
Antipsychotic prescription patterns in outpatient settings: 24-month results from the Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study

Istvan Bitter [a], Tamas Treuer [b,*], Yulia Dyachkova [b], Ferenc Martenyi [b], Margaret McBride [c], Gabor S. Ungvari [d]

Table 4 Predictive factors for remaining on monotherapy during the 24-month study period

Baseline characteristic	Reference category	Adjusted odds ratio	95% confidence interval	p value
Treatment				<0.001
Risperidone	(Olanzapine)	0.49	(0.41, 0.58)	
Quetiapine	(Olanzapine)	0.25	(0.17, 0.36)	
Clozapine	(Olanzapine)	0.55	(0.41, 0.77)	
Haloperidol	(Olanzapine)	0.20	(0.14, 0.27)	
CGI-S Overall score	(per unit difference in baseline score)	0.88	(0.82, 0.95)	<0.001
Extrapyramidal symptoms	(Presence)	0.67	(0.57, 0.79)	<0.001
Switched treatment	(Initiated treatment)	0.70	(0.56, 0.84)	<0.001
First-time antipsychotic use	(Previously untreated)	0.70	(0.52, 0.94)	0.019
Region				<0.001
Africa and Middle East	(Asia)	2.00	(1.53, 2.62)	
Central and Eastern Europe	(Asia)	1.75	(1.37, 2.23)	
Latin America	(Asia)	2.36	(1.85, 3.02)	

EUFEST – Reasons (time to) for treatment discontinuation



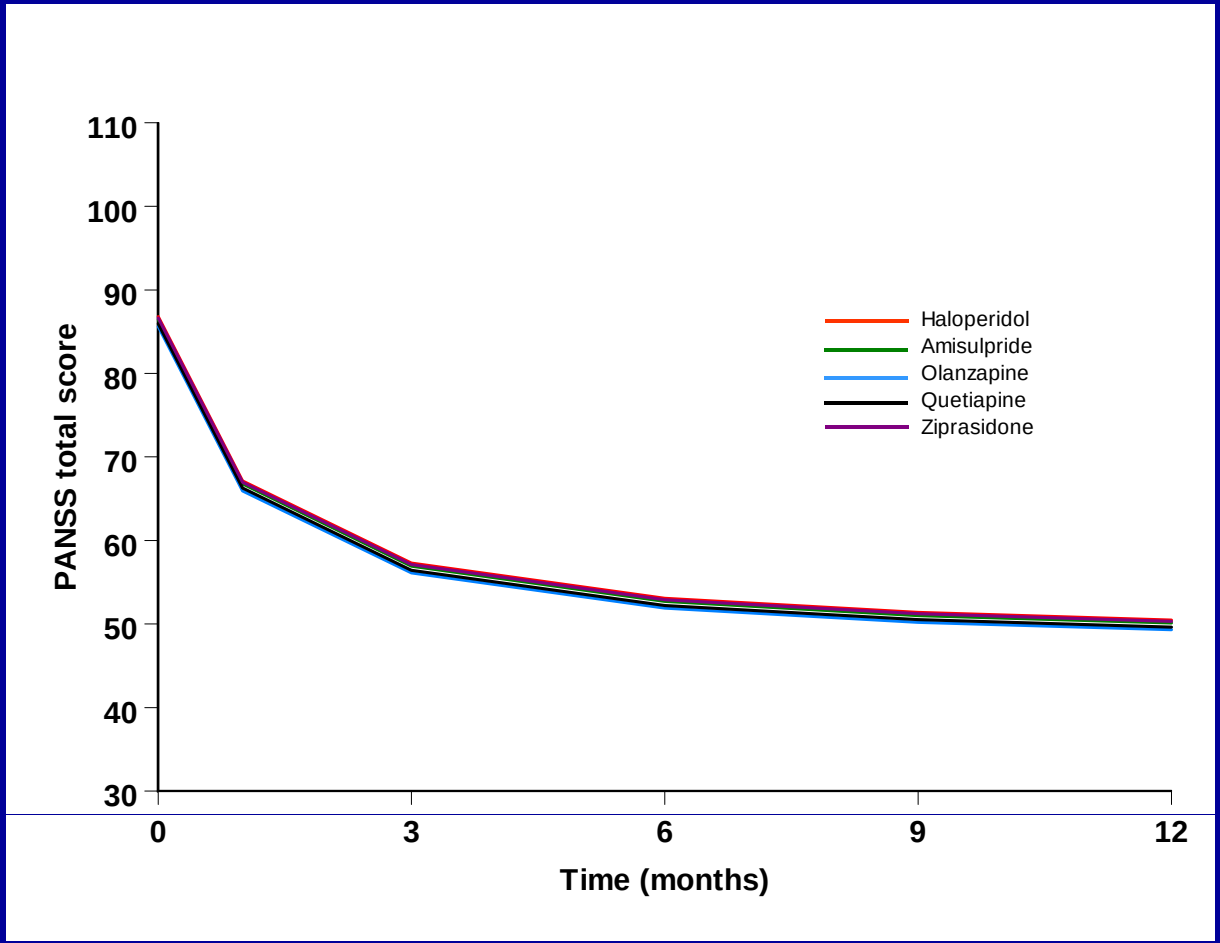
Number at risk																				
Haloperidol	103	42	35	27	18	103	42	35	27	18	103	42	35	27	18	103	42	35	27	18
Amisulpride	104	65	57	49	38	104	65	57	49	38	104	65	57	49	38	104	65	57	49	38
Olanzapine	105	79	71	62	49	105	79	71	62	49	105	79	71	62	49	105	79	71	62	49
Quetiapine	104	54	49	45	30	104	54	49	45	30	104	54	49	45	30	104	54	49	45	30
Ziprasidone	82	39	38	34	22	82	39	38	34	22	82	39	38	34	22	82	39	38	34	22

Time to treatment discontinuation because of any cause (A), insufficient efficacy (B), side-effects (C), and non-adherence (D)

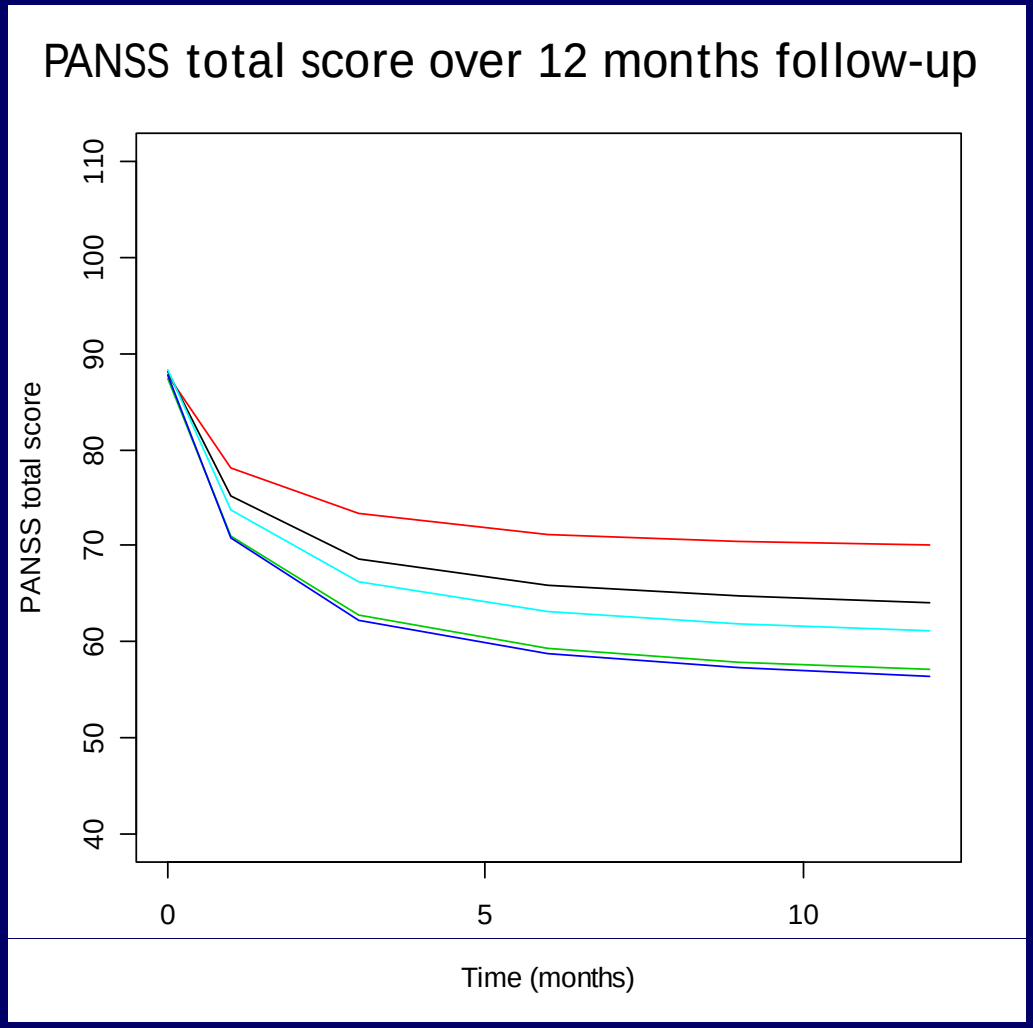
Kahn et al, Lancet, 2008

Improvement: Observed cases

PANSS total score over 12 months follow-up



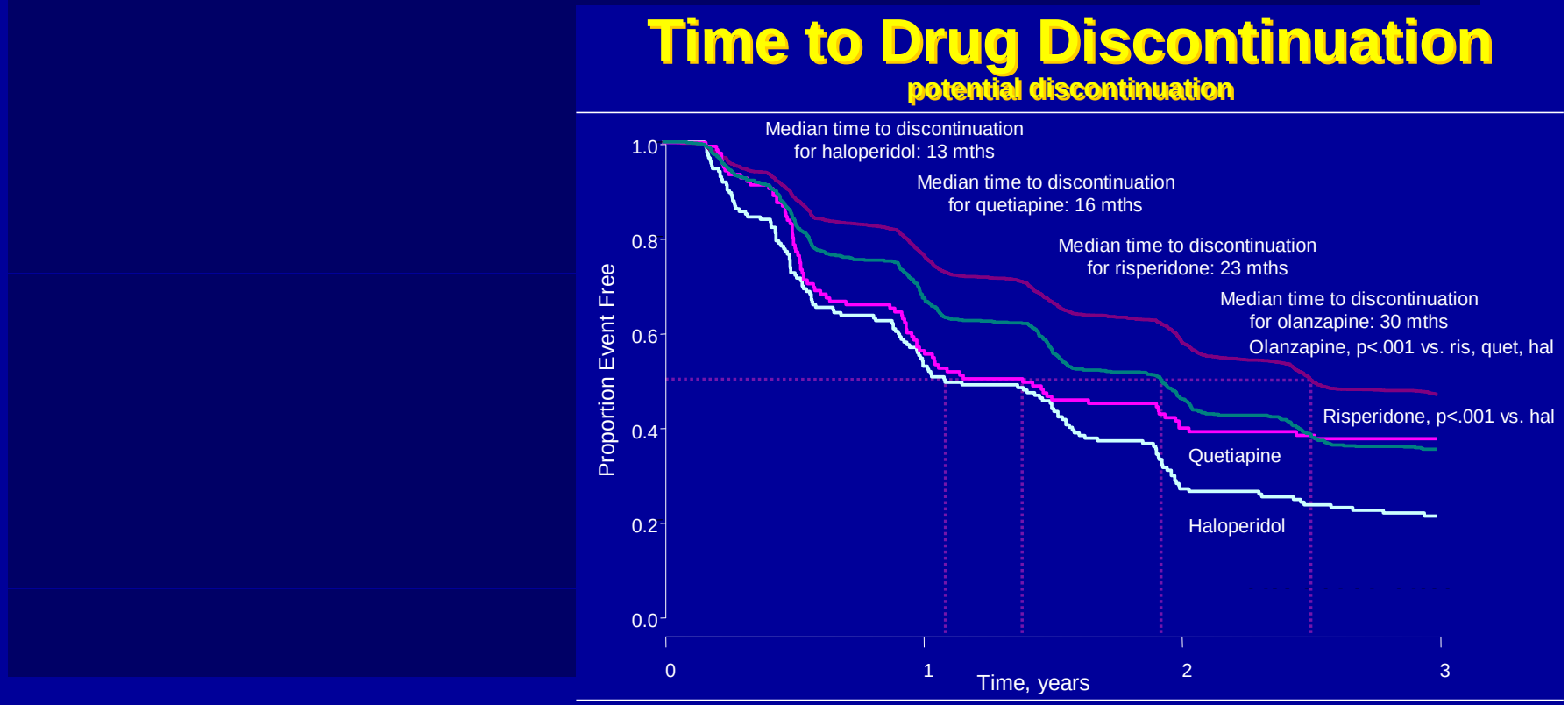
Improvement: LOCF



Drug Discontinuation: IC-SOHO 36 months data

(potential discontinuation)

	Olanzapine n=2641	Risperidone n=863	Quetiapine n=142	Haloperidol n=189
Number Discontinued	1476 (**56%**)	581 (**67%**)	91 (**64%**)	151 (**80%**)

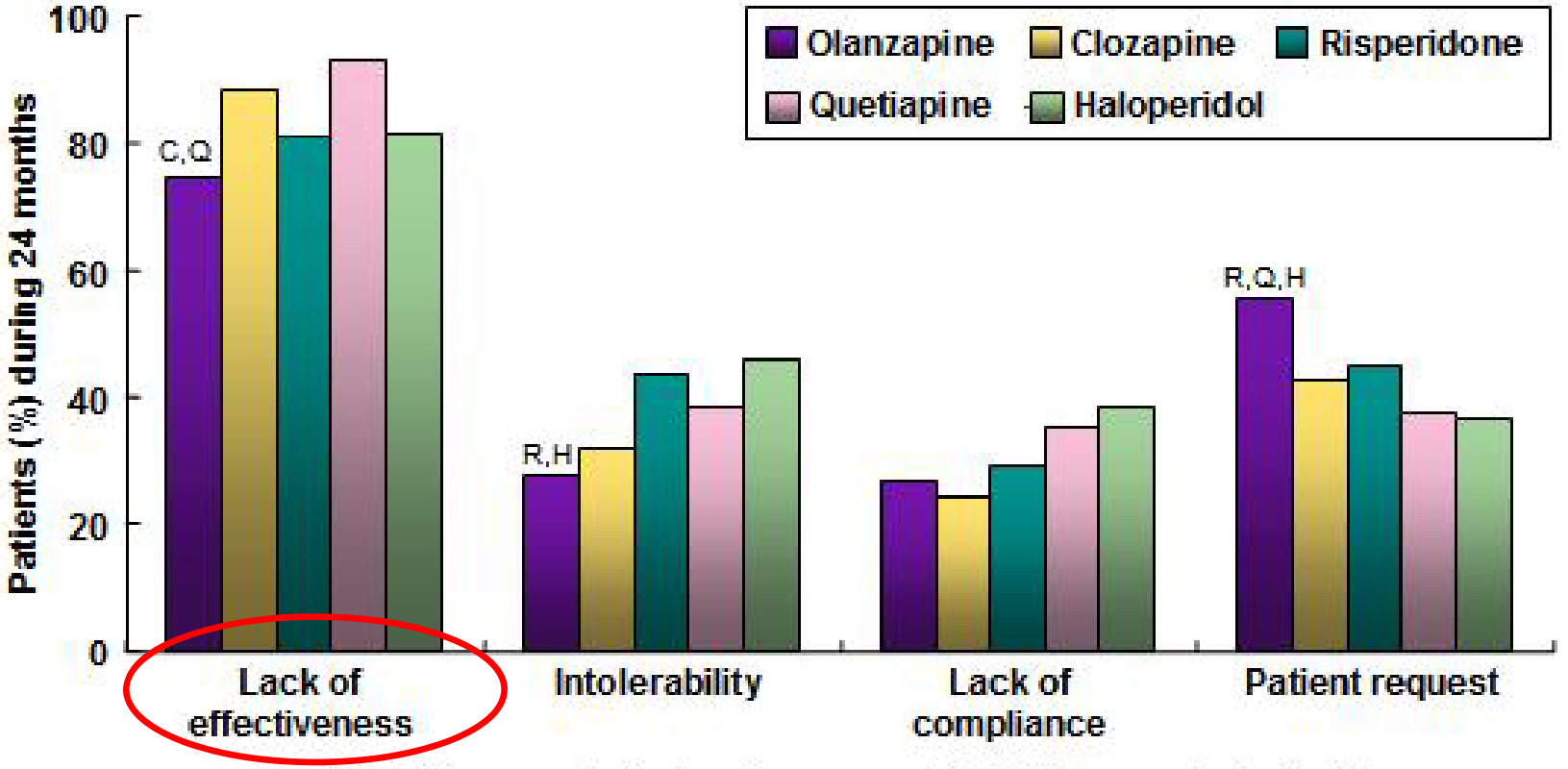


Dossenbach M et al, 3 yr IC-SOHO, presented at APA 2006

Dossenbach M et al, 3 yr IC-SOHO, presented at APA 2006

Reasons for Treatment Modifications IC SOHO 24-month

Reasons for treatment modification during 24-month study period



Bitter, I. et al., Eur. Neuropsychopharmacol. 2008, 18:170-180

Rehospitalization and mortality in schizophrenia related to „no antipsychotic treatment” (Finnish Cohort Study)

	No of relapses	Person years	Incidence	Crude relative risk (95% CI)	Adjusted relative risk (95% CI)	Fully adjusted relative risk (95% CI)
Perphenazine depot	53	187	0.28	0.41 (0.29 to 0.59)	0.45 (0.32 to 0.65)	0.32 (0.22 to 0.49)
Olanzapine	329	822	0.40	0.59 (0.45 to 0.75)	0.55 (0.43 to 0.72)	0.54 (0.41 to 0.71)
Clozapine	336	804	0.42	0.61 (0.47 to 0.79)	0.53 (0.41 to 0.69)	0.64 (0.48 to 0.85)
Chlorprothixene	79	146	0.54	0.79 (0.58 to 1.09)	0.83 (0.61 to 1.15)	0.64 (0.45 to 0.91)
Thioridazine	115	201	0.57	0.84 (0.63 to 1.12)	0.82 (0.61 to 1.10)	0.70 (0.51 to 0.96)
Perphenazine oral	155	327	0.47	0.69 (0.58 to 0.82)	0.78 (0.59 to 1.03)	0.85 (0.63 to 1.13)
Risperidone	343	651	0.53	0.77 (0.60 to 0.99)	0.80 (0.62 to 1.03)	0.89 (0.69 to 1.16)
Mixed or rare	775	1229	0.63	0.92 (0.73 to 1.17)	0.85 (0.67 to 1.08)	1.00 (0.78 to 1.28)
Haloperidol oral	73	107	0.68	1.00	1.00	1.00
Chlorpromazine	82	127	0.64	0.94 (0.69 to 1.29)	0.97 (0.71 to 1.33)	1.06 (0.76 to 1.47)
Levomepromazine	52	63	0.82	1.21 (0.84 to 1.73)	0.82 (0.58 to 1.18)	1.09 (0.76 to 1.57)
No antipsychotic drugs	2248	3362	0.67	0.98 (0.77 to 1.23)	1.01 (0.80 to 1.27)	1.16 (0.91 to 1.47)

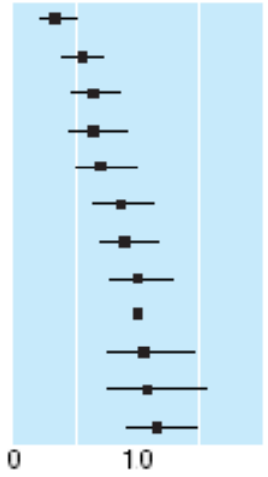


Fig 1 Relative risk of rehospitalisation by treatment. Adjusted for sex, calendar year, age at onset of follow-up, number of previous relapses, duration of first hospitalisation, and length of follow-up by a multivariate regression model alone (adjusted column) and by multivariate regression and the propensity score method (fully adjusted column)

Mortality was markedly elevated in patients not on any medication (adjusted RR 12.3, 95% CI 6.0–24.1), and the risk of suicide was even higher (RR 37.4, 5.1–276).

Tiihonen et al

BMJ, doi:10.1136/bmj.38881.382755.2F (published 6 July 2006)

11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study)

Jari Tiihonen, Jouko Lönnqvist, Kristian Wahlbeck, Timo Klaukka, Leo Niskanen, Antti Tanskanen, Jari Haukka

Lancet 2009; 374: 620–27

Published Online July 13, 2009 DOI:10.1016/S0140-6736(09)60742-X

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See Comment page 590

Department of Forensic Psychiatry, University of Kuopio and Niuvanniemi Hospital, Department of Clinical Physiology (Prof J Tiihonen M D), Department of Internal Medicine (Prof L Niskanen M D), Kuopio University Hospital, Kuopio, Finland; Department of Psychiatry, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland (Prof J Tiihonen,

Summary

Background The introduction of second-generation antipsychotic drugs during the 1990s is widely believed to have adversely affected mortality of patients with schizophrenia. Our aim was to establish the long-term contribution of antipsychotic drugs to mortality in such patients.

Methods Nationwide registers in Finland were used to compare the cause-specific mortality in 66 881 patients versus the total population (5·2 million) between 1996, and 2006, and to link these data with the use of antipsychotic drugs. We measured the all-cause mortality of patients with schizophrenia in outpatient care during current and cumulative exposure to any antipsychotic drug versus no use of these drugs, and exposure to the six most frequently used antipsychotic drugs compared with perphenazine use.

Findings Although the proportional use of second-generation antipsychotic drugs rose from 13% to 64% during follow-up, the gap in life expectancy between patients with schizophrenia and the general population did not widen between 1996 (25 years), and 2006 (22·5 years). Compared with current use of perphenazine, the highest risk for overall mortality was recorded for quetiapine (adjusted hazard ratio [HR] 1·41, 95% CI 1·09–1·82), and the lowest risk for clozapine (0·74, 0·60–0·91; p=0·0045 for the difference between clozapine *vs* perphenazine, and p<0·0001 for all other antipsychotic drugs). Long-term cumulative exposure (7–11 years) to any antipsychotic treatment was associated with lower mortality than was no drug use (0·81, 0·77–0·84). In patients with one or more filled prescription for an antipsychotic drug, an inverse relation between mortality and duration of cumulative use was noted (HR for trend per exposure year 0·991; 0·985–0·997).

with lower mortality than was no drug use (0·81, 0·77–0·84). In patients with one or more filled prescription for an antipsychotic drug, an inverse relation between mortality and duration of cumulative use was noted (HR for trend per exposure year 0·991; 0·985–0·997).

Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis

Stefan Leucht, Caroline Corves, Dieter Arbter, Rolf R Engel, Chunbo Li, John M Davis

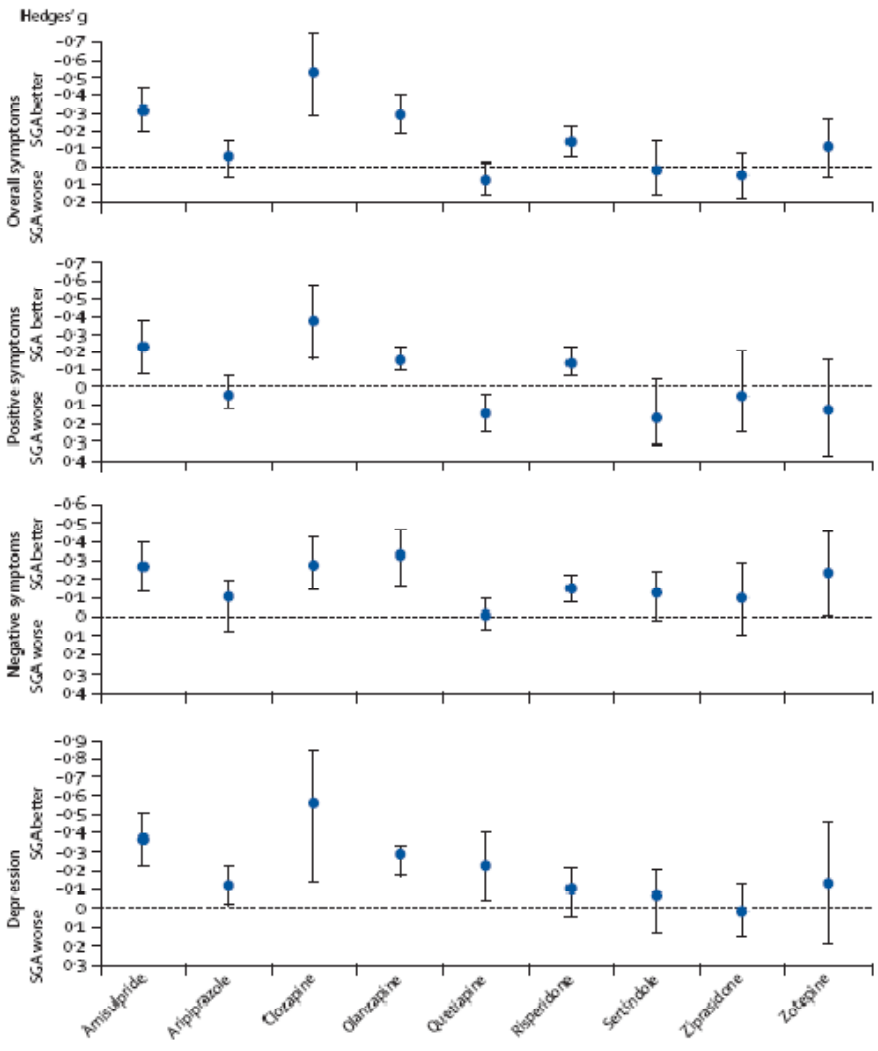

Figure 2: Second-generation versus first-generation antipsychotic drugs—efficacy in various domains
Data are Hedges' g (95% CI). Note that the results are significant at p< 0·05 if the 95% CIs do not overlap the x axis. SGA=second-generation antipsychotic drug.

Lancet 2009; 373: 31–41

Extrapyramidal side-effects

All second-generation antipsychotic drugs were associated with much fewer extra-pyramidal side-effects than haloperidol. NNT was between 2 for clozapine and 5 for zotepine

However, with the exception of *clozapine, olanzapine, and risperidone*, second-generation drugs have not been shown to be better than low-potency first- generation antipsychotic drugs,

Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis

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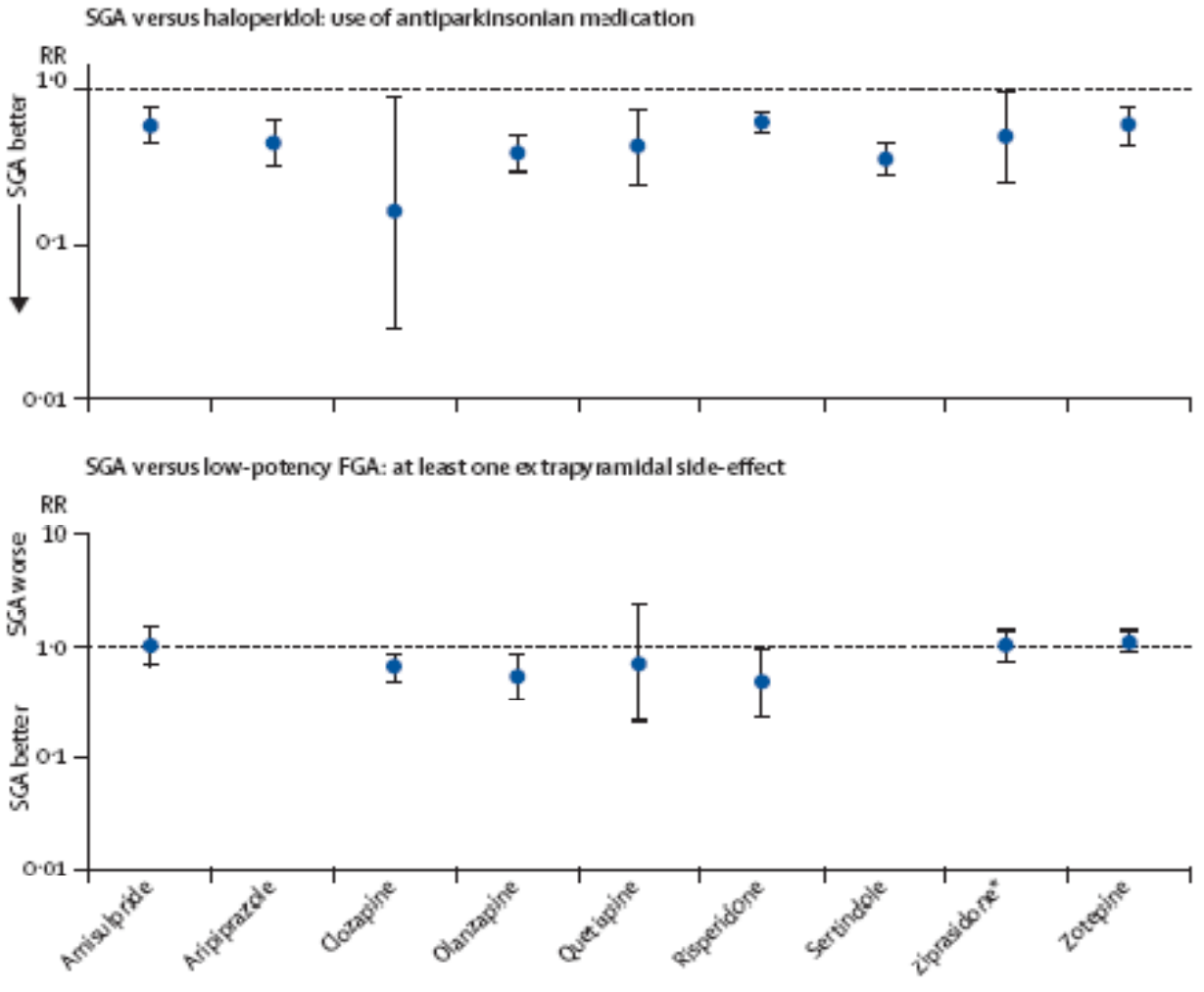

Figure 4: Extrapyramidal side-effects
Data are relative risk (RR; 95% CI). SGA=second-generation antipsychotic drug. FGA=first-generation antipsychotic drug. * Use of antiparkinsonian medication.

SUMMARY

- Second generation antipsychotics (SGA) improve positive and negative symptoms in acute psychosis; they may also affect affective symptoms and cognitive impairment
- SGA are better tolerated overall with less problematic side effects than firts generation/conventional antipsychotics
- SGA should be among the first-line options in treatment of acute psychotic disorders
- The choice of the specific antipsychotic drug for the specific patient must be individualized

SUMMARY II.