MASSACHUSETTS GENERAL HOSPITAL
PSYCHIATRY ACADEMY

Drug Treatments in Schizophrenia
What Is on the Horizon?

"Indagandis sedibus et causis morborum"

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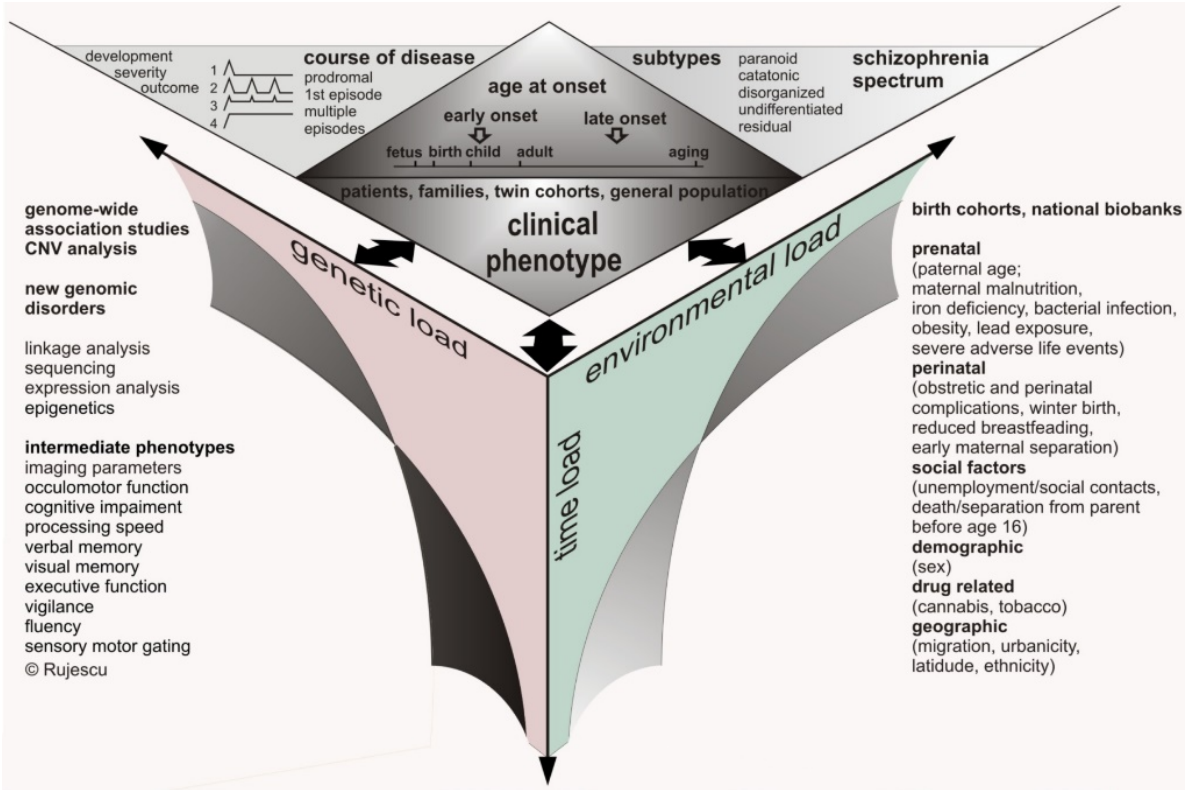
Potential Conflicts of Interest (January 2016 to Present)

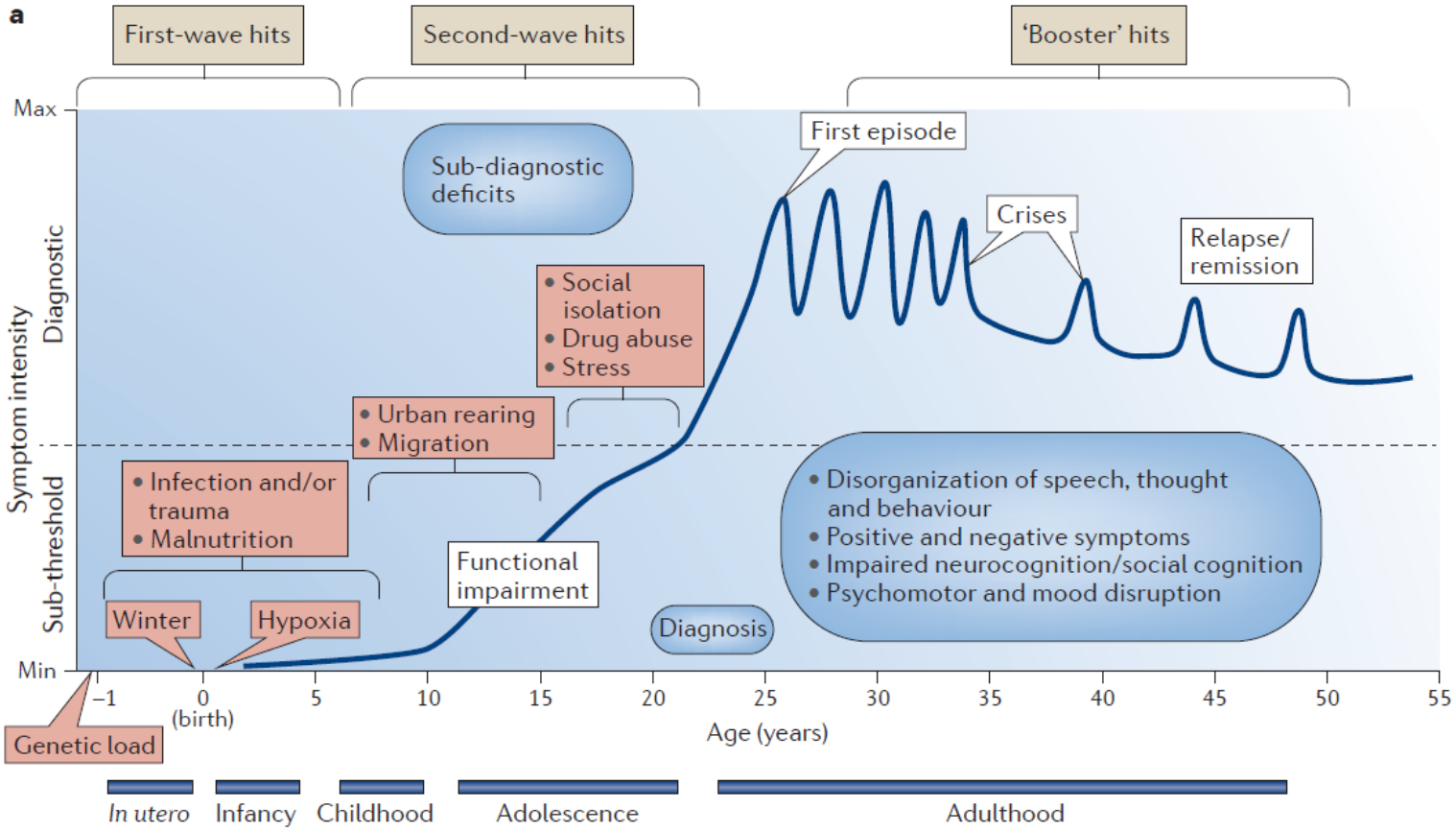
Dr. Kasper has received **grant/research support** from Lundbeck; he has served as a **consultant or on advisory boards** for Janssen, Lundbeck, and Schwabe; and he has served **on speakers bureaus** for Angelini, Krka Pharma, Lundbeck, Neuraxpharma, Schwabe, Servier and Sun Pharma.

Schizophrenias Are Multifactorial Diseases



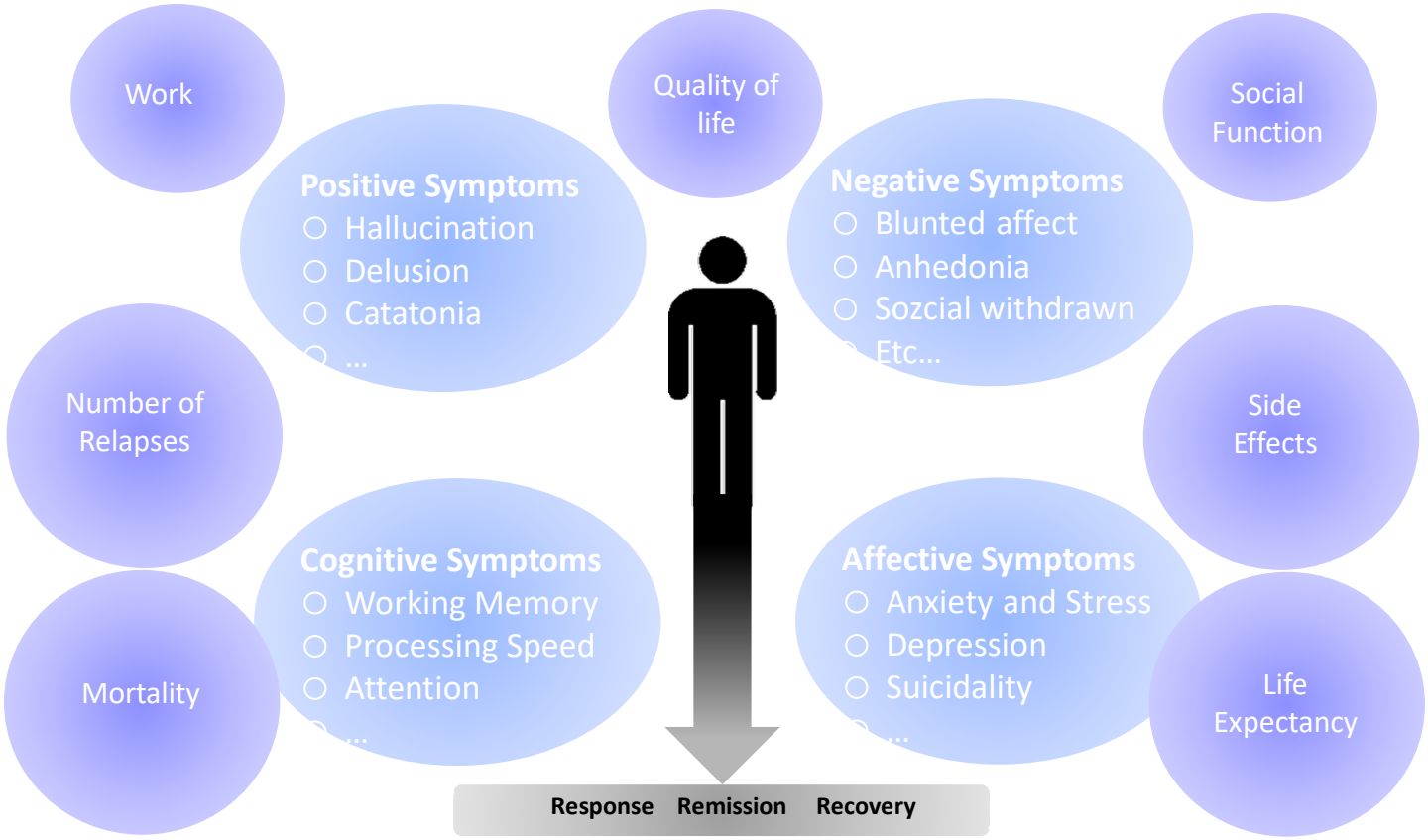
Rujescu, 2019

Schizophrenia: Course of illness



Millan et al., Nat Rev Drug Discov 2016

Schizophrenia: Impact of Symptomatology



Selecting Suitable Treatments for Schizophrenia Can Pose a Dilemma for Psychiatrists

In selecting treatments for schizophrenia, physicians consider variables related to the:[1,2]

An 'ideal' medication is one that can:[2]

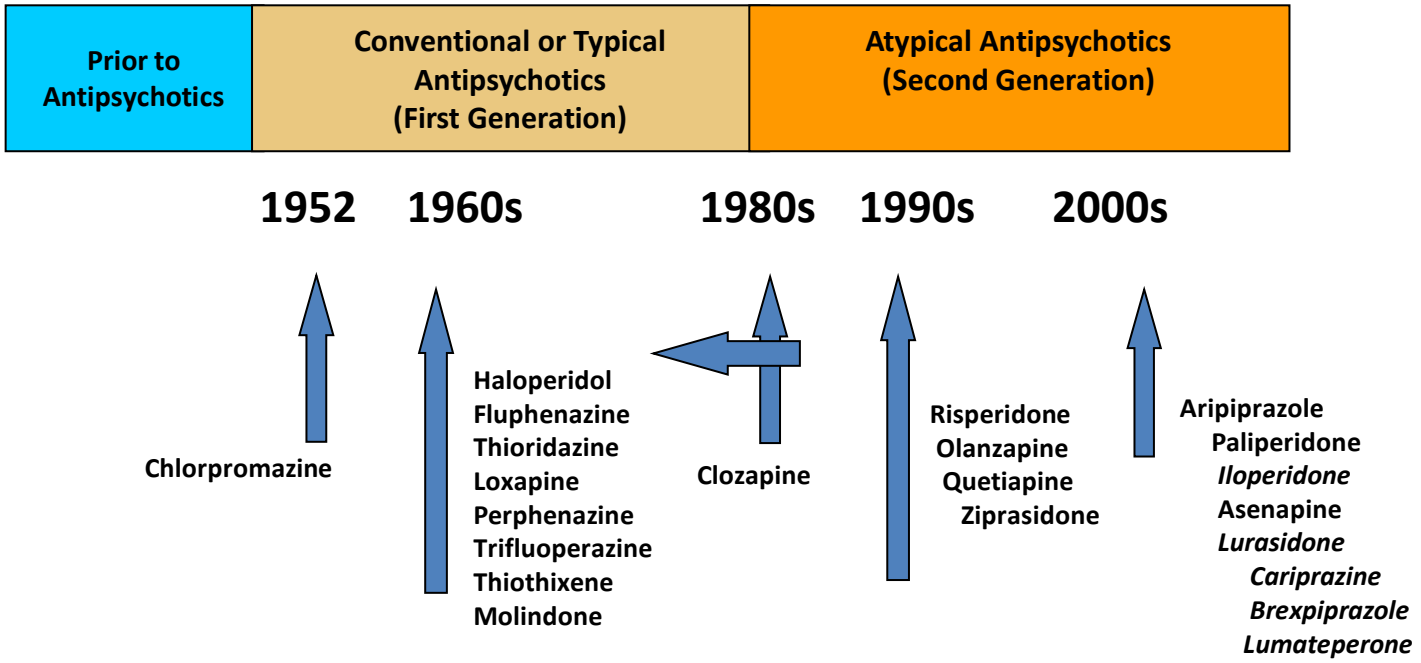
- Treat psychosis
- Lead to symptom resolution
- Lead to remission
- Overcome treatment resistance
- Prevent relapse
- Have a **benign side-effect profile**
- Alleviate anxiety and depression

The dilemma for physicians:
*providing **effective treatment** while **avoiding side effects***[3]

The need to assess how side effects interact with the patient's life[4-6]

1. Kane et al. Dialogues Clin Neurosci 2010;12(3):345–357
2. Correll. J Clin Psychiatry 2011;72(Suppl 1):9–13
3. Abidi & Bhaskara. Can J Psychiatry 2003;48(11):749–755
4. Leucht et al. Lancet 2013;382(9896):951–962
5. Uçok & Gaebel. World Psychiatry 2008;7(1):58–62
6. Barnes et al. J Psychopharmacol 2011;25(5):567–620

Options for Antipsychotic Therapies

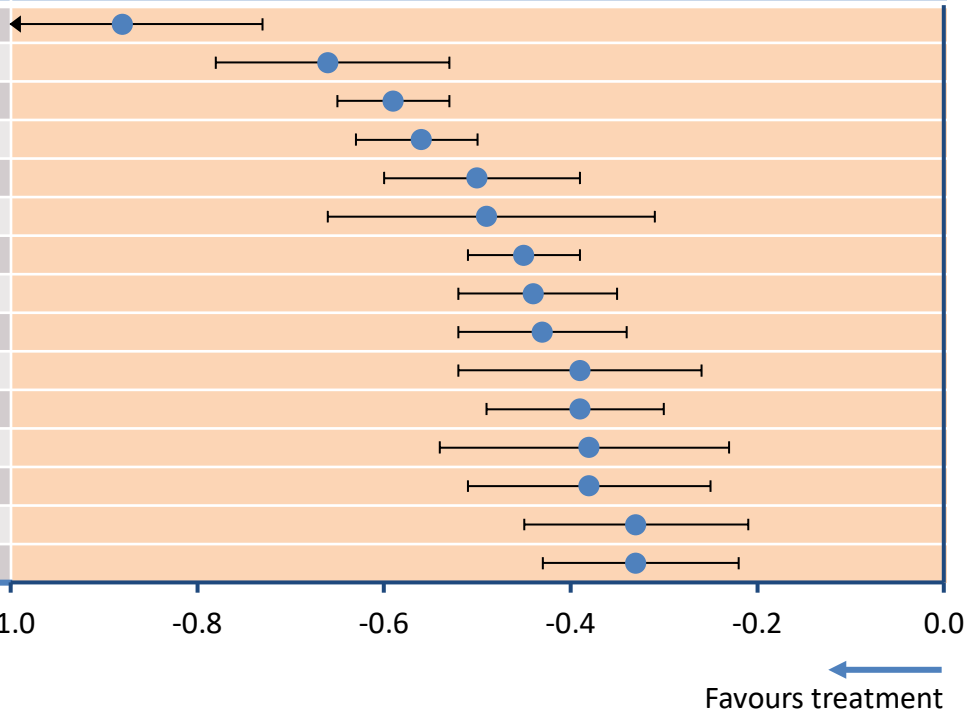


NbN: D2/5HT2 Blocker

Efficacy of Antipsychotics on Clinical Symptoms – Schizophrenia

Meta-analysis of antipsychotic efficacy (PANSS or BPRS) in schizophrenia

Antipsychotic	SMD (95% CrI)
Clozapine	-0.88 (-1.03, -0.73)
Amisulpride	-0.66 (-0.78, -0.53)
Olanzapine	-0.59 (-0.65, -0.53)
Risperidone	-0.56 (-0.63, -0.50)
Paliperidone	-0.50 (-0.60, -0.39)
Zotepine	-0.49 (-0.66, -0.31)
Haloperidol	-0.45 (-0.51, -0.39)
Quetiapine	-0.44 (-0.52, -0.35)
Aripiprazole	-0.43 (-0.52, -0.34)
Sertindole	-0.39 (-0.52, -0.26)
Ziprasidone	-0.39 (-0.49, -0.30)
Chlorpromazine	-0.38 (-0.54, -0.23)
Asenapine	-0.38 (-0.51, -0.25)
Lurasidone	-0.33 (-0.45, -0.21)
Iloperidone	-0.33 (-0.43, -0.22)



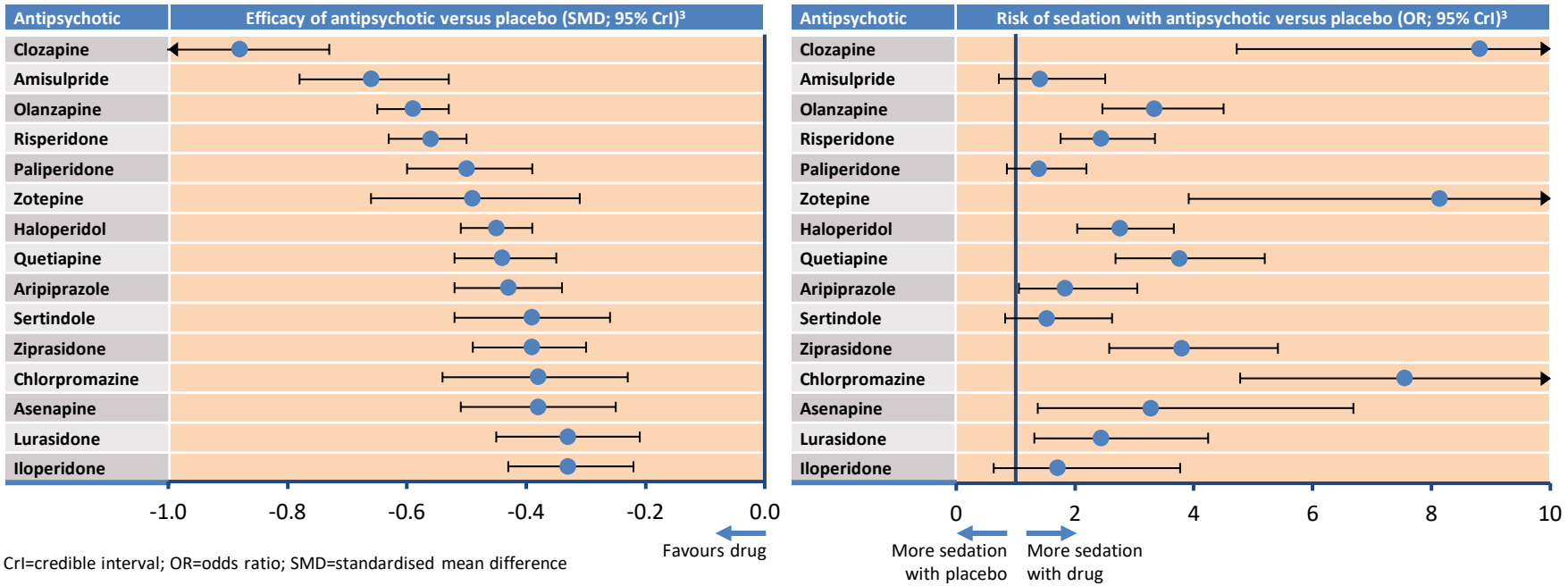
BPRS=Brief Psychiatric Rating Scale; CrI=credible interval; PANSS=Positive and Negative Syndrome Scale; SGA=second-generation antipsychotic; SMD=standardised mean difference

Leucht et al. Lancet 2013;382(9896):951–962

A Key Challenge for Physicians Is to Choose an Antipsychotic That Effectively Controls Symptoms of Schizophrenia, While Minimising Distressing or Harmful Side Effects[1]

Clinical benefits:[2,3] can be efficacious against positive, negative and cognitive symptoms, with decreased relapse risk and maintained stability

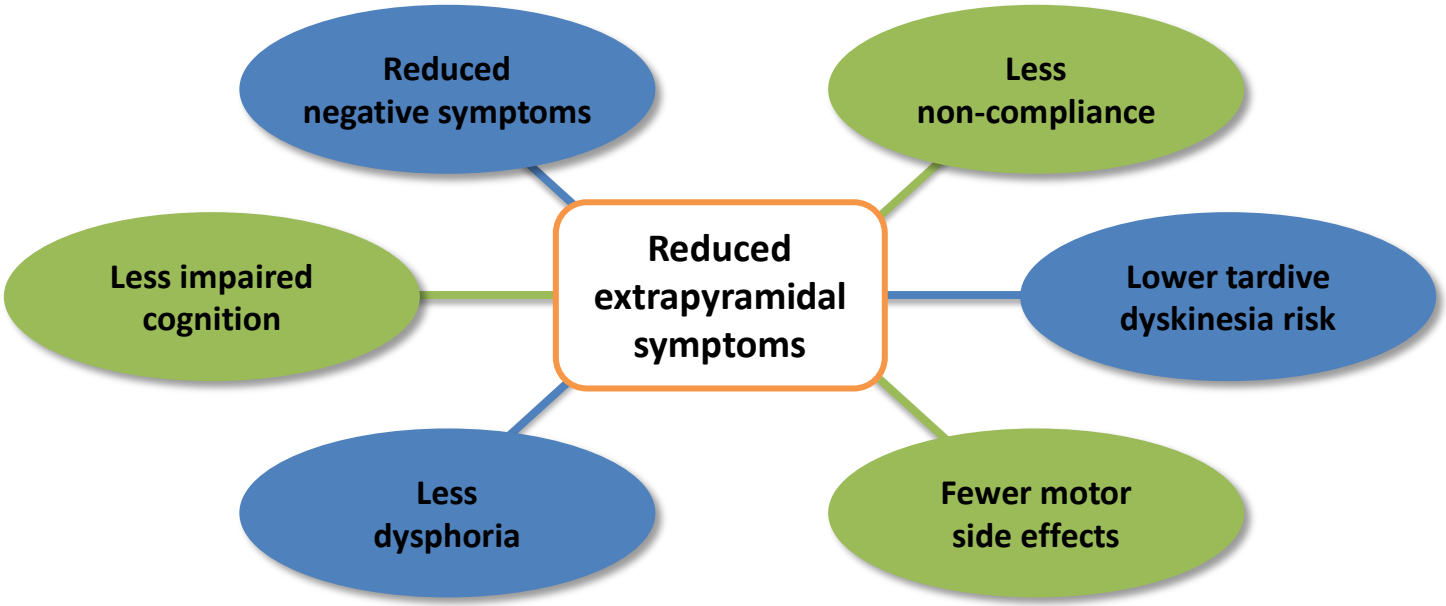
Side effects (examples):[2,3] sedation, akathisia, weight gain, metabolic effects, sleep disturbances, sexual dysfunction



CrI=credible interval; OR=odds ratio; SMD=standardised mean difference

1. Barnes et al. J Psychopharmacol 2011;25(5):567–620
2. Lehman et al. APA practice guideline 2010
3. Leucht et al. Lancet 2013;382(9896):951–962

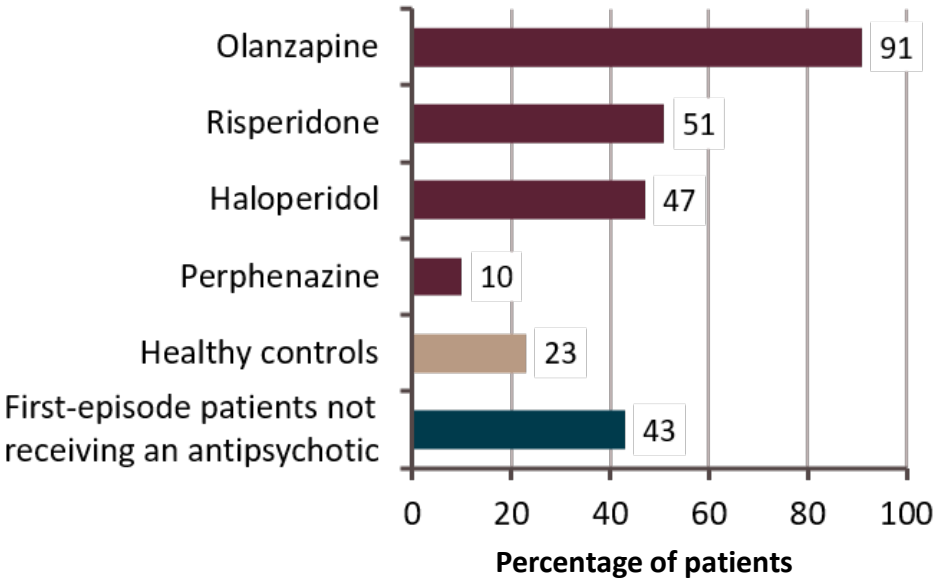
There May Be Multiple Clinical Benefits of Therapies with a Low Risk of Extrapyramidal Symptoms



Tandon & Jibson. Ann Clin Psychiatry 2002;14(2):123–129

Weight Gain Can Be a Major Issue Associated with Antipsychotic Drugs

Clinically significant weight gain in the first year of treatment in first-episode patients (%)[1]



A meta-analysis of 307 trials reported:[2]

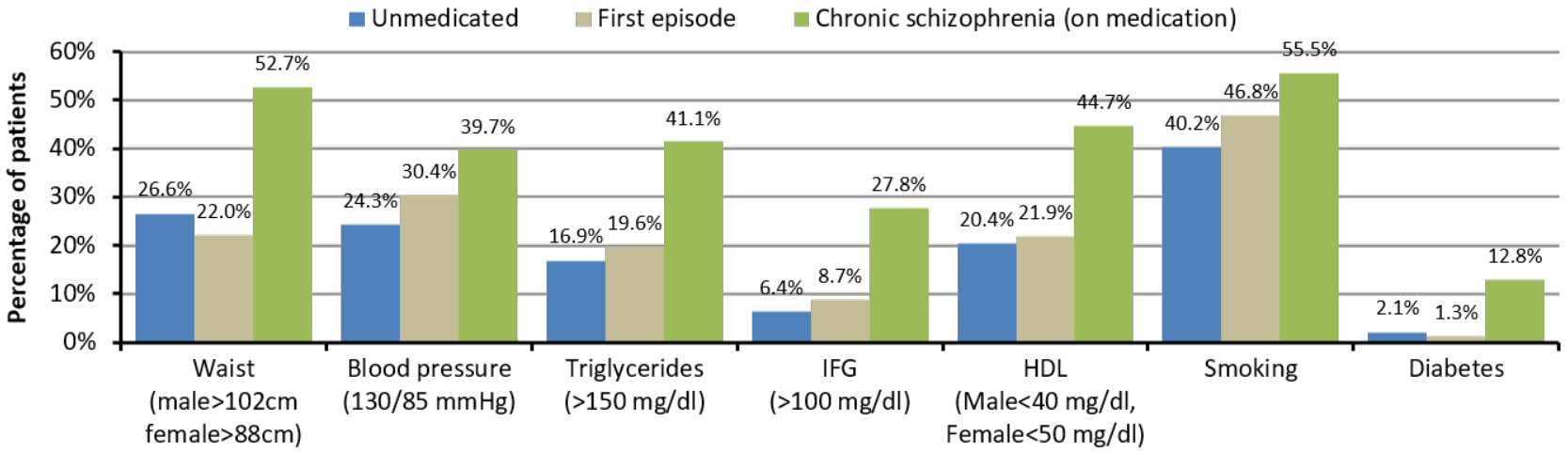
- Almost all antipsychotics showed a mean increase in **body weight**, **BMI**, and a degree of **clinically relevant weight gain** with increased duration of antipsychotic use
- Increases in weight gain and BMI were more pronounced in antipsychotic-naïve patients

Clinically significant/relevant weight gain is defined as a >7% increase in body weight from baseline; BMI=body mass index

1. Strassnig et al. Schizophr Res 2007;93(1–3):90–98
2. Bak et al. PLoS One 2014;9(4):e94112

Long-Term Antipsychotic Use Increases Metabolic Risk

Patients chronically treated with established antipsychotic medication are at higher metabolic risk than first-episode patients with schizophrenia



BP=blood pressure; HDL=high-density lipoprotein; IFG=impaired fasting glucose

Mitchell et al. Schizophr Bull 2013;39:295–305

Among patients with chronic medicated schizophrenia:

- 1 in 2 were overweight (waist size male >102 cm, female >88 cm)
- 2 in 5 had high blood pressure (>130/85 mmHg)
- 1 in 8 had diabetes

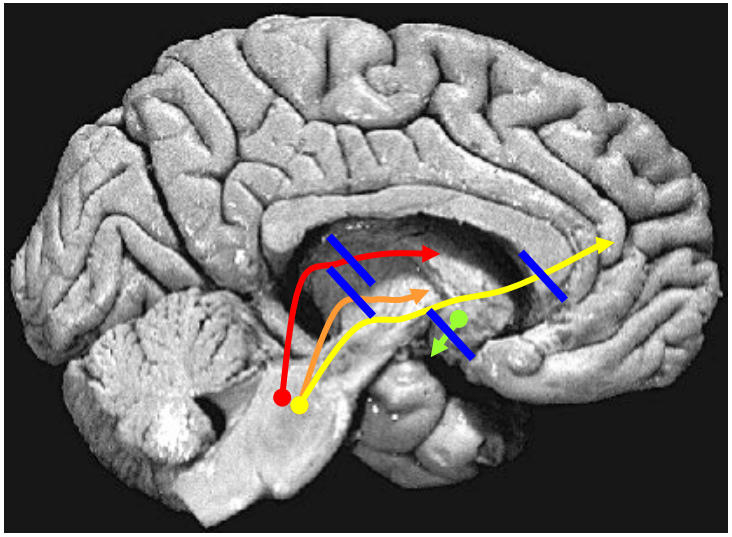
First-Generation Antipsychotics

- Characterised by antagonism at D_2 receptors
- D_2 receptor antagonism reduces hyperactivity in the mesolimbic dopamine pathway, reducing the positive symptoms of schizophrenia
- Despite demonstrated efficacy in treating the positive symptoms of schizophrenia, D_2 receptor antagonism can lead to treatment side effects
  - D_2 antagonism in the nigrostriatal pathways can result in **EPS**
  - D_2 antagonism in the tuberoinfundibular pathway can result in **prolactin elevation**
  - D_2 antagonism in the mesocortical pathway may cause or worsen negative and cognitive symptoms
  - Mesolimbic blockade may inadvertently block reward pathways (neurolepsis)

EPS=extrapyramidal symptoms

Stahl. Stahl's Essential Psychopharmacology. 4th edition, 2013, Cambridge University Press

Treatment with Pure D_2-Receptor Antagonists ("Therapeutic Dilemma" of Conventional Neuroleptics)



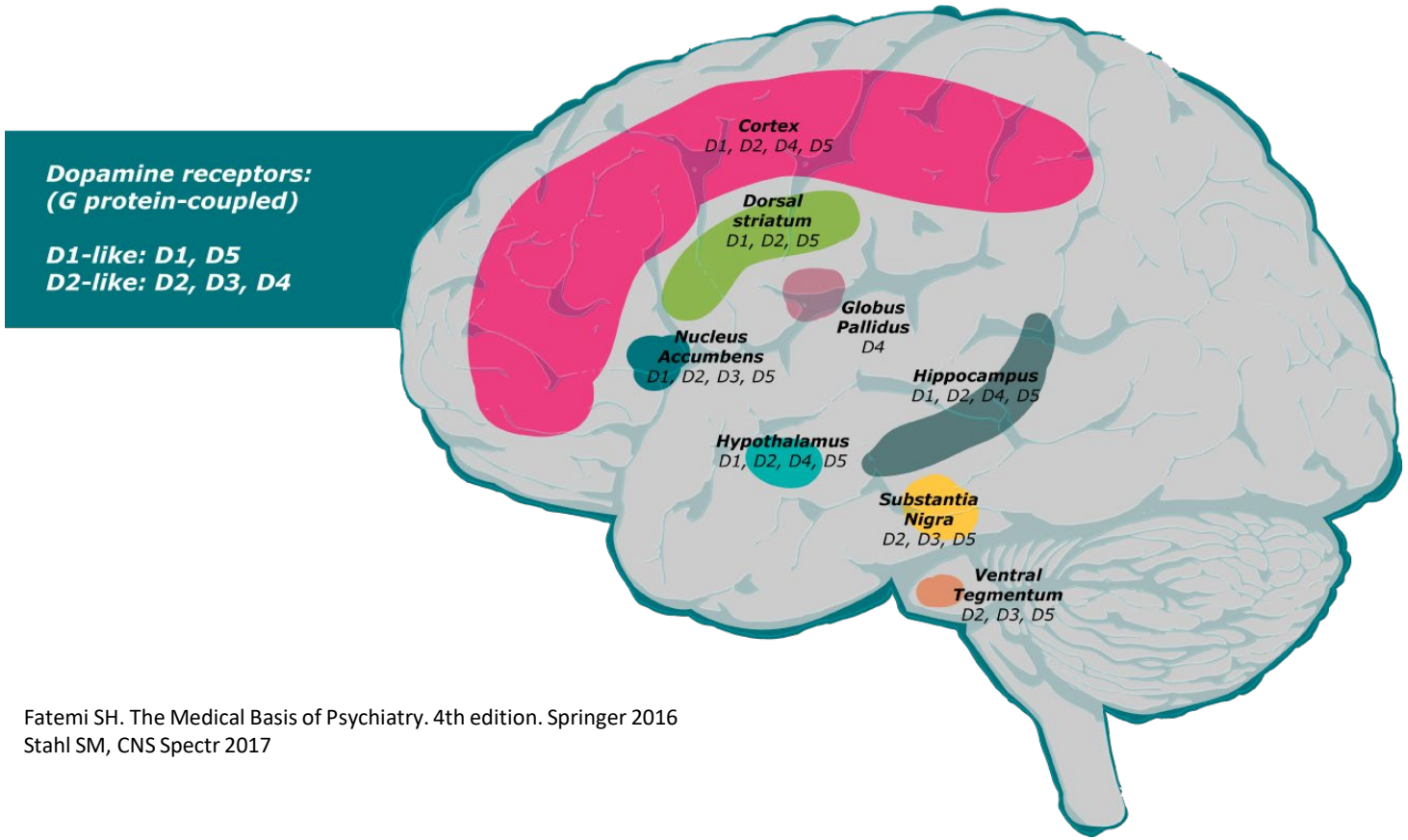
Improve positive symptoms by blocking dopamine hyperactivity in mesolimbic pathway

Worsen negative symptoms by blocking dopamine hypoactivity in mesocortical pathway

Induce extrapyramidal symptoms by blocking dopamine in nigrostriatal pathway

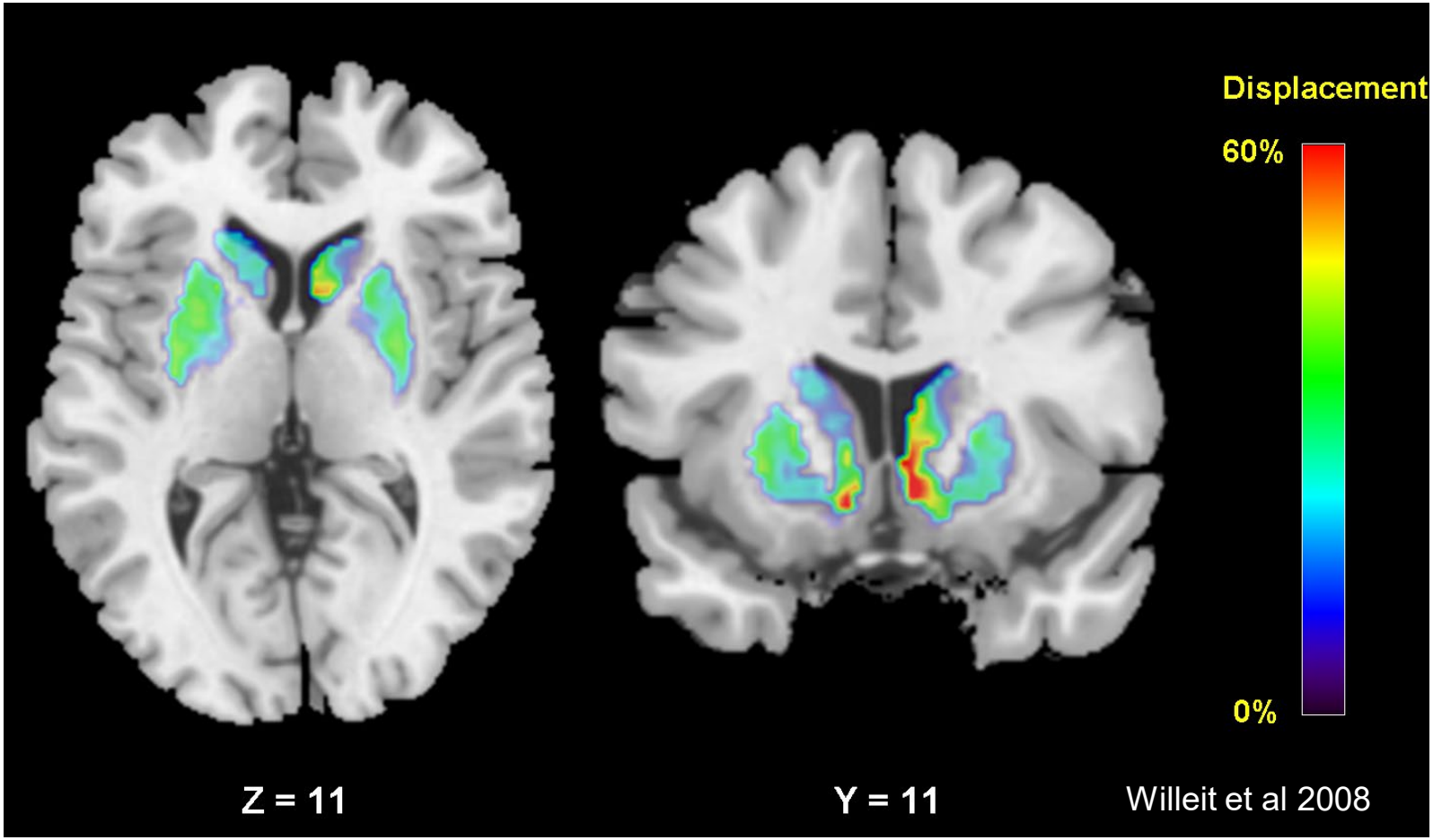
Disinhibit prolactin by blocking dopamine in tuberoinfundibular pathway

Dopamin-Rezeptor Subtypes and Distribution in CNS



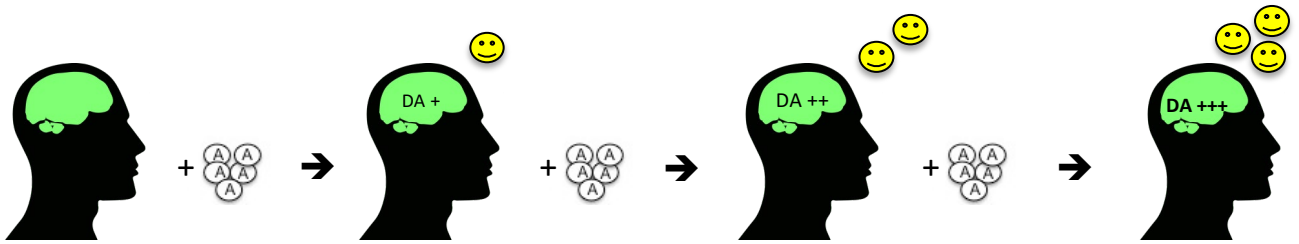
Fatemi SH. The Medical Basis of Psychiatry. 4th edition. Springer 2016
Stahl SM, CNS Spectr 2017

Relative Reduction of [^{11}C]-(+)-PHNO Binding After Amphetamine Ingestion

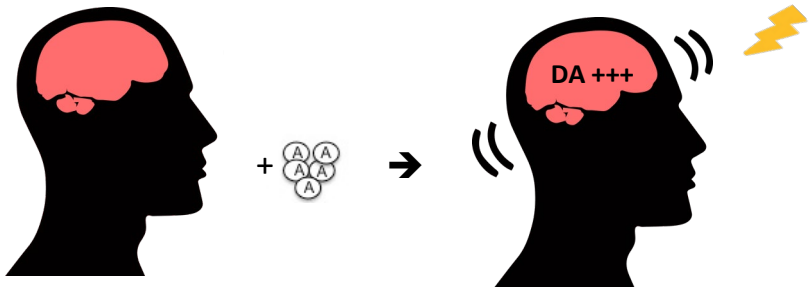


PHNO: a dopamine D 2/3 receptor agonistic radiotracer, is applied for investigating the dopaminergic system via positron emission tomography (PET)

Sensitization



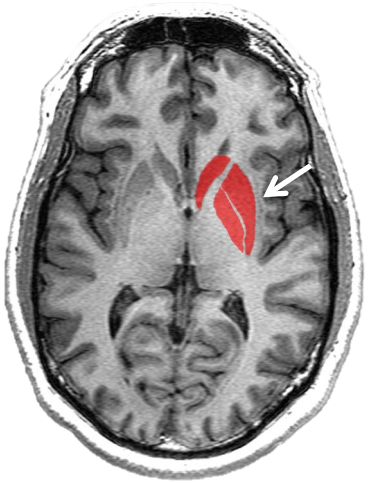
Schizophrenia

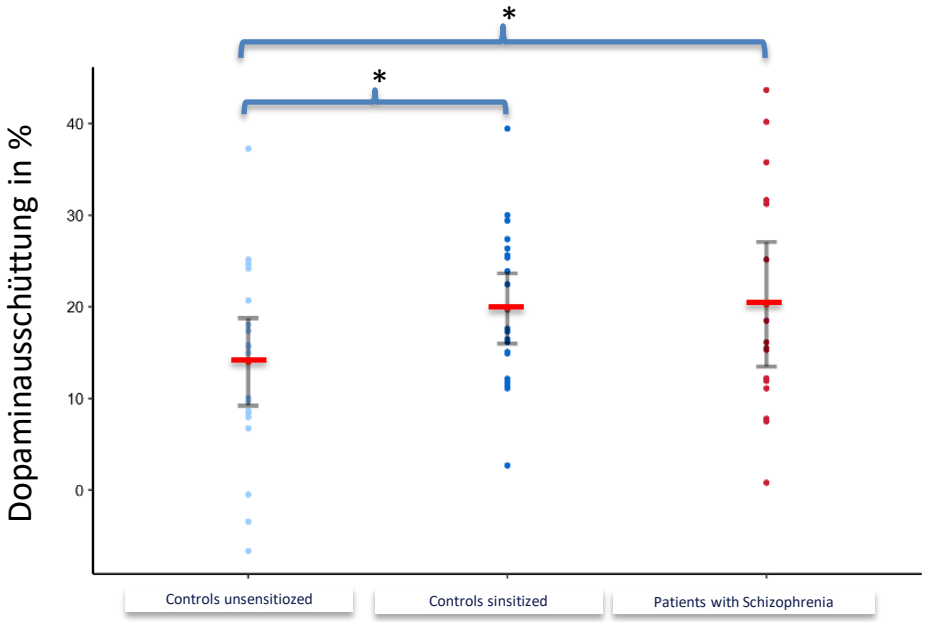


Laruelle et al 2000, 2013, Munro 2006, Boileau 2006, Weidenauer 2021

Patientens with Schizophrenia Transmit More Dopamine – Comparable to Healthy Controls After Sensitisation

Putamen

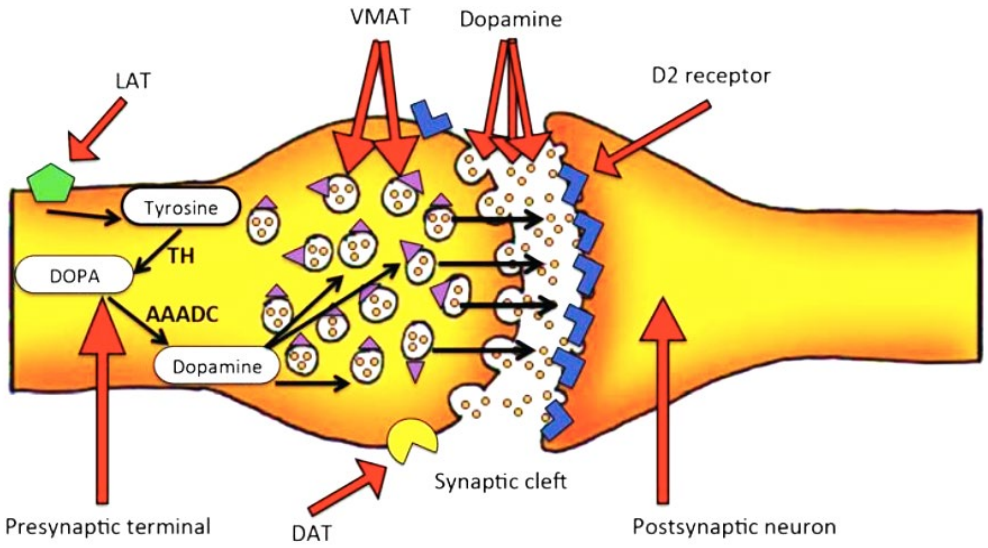




Weidenauer et al, Translational Psychiatry (in press)

Healthy controls n = 21
Patients with Schizophrenia n = 16
* *p<0.05 paired onesided t-test*

Pathology Is Pre-Synaptic
Treatment Is Post-Synaptic



Increased Dopamine Synthesis
Increased Dopamine Release

Antipsychotics work on $D_{2/3}$ Receptors

Fusar Poli et al 2011

Second-Generation Antipsychotics

- Compared with FGAs, SGAs have a broader pharmacological profile
- Most SGAs are **serotonin–dopamine antagonists (see also NbN)**
  - Antagonism at the serotonin 5-HT_{2A} receptor may reduce the risk of EPS by increasing dopamine release in the striatum, and may limit excessive prolactin release from pituitary cells by countering the disinhibition by dopamine
- However, EPS and prolactin elevation remain problematic side effects of SGAs, and the broad range other serotonergic, histaminergic, α-adrenergic, and muscarinic targets of SGAs may also contribute to other side effects

5-HT=5-hydroxytryptamine; FGA=first-generation antipsychotic; SGA=second-generation antipsychotic

Stahl. Stahl's Essential Psychopharmacology. 4th edition, 2013, Cambridge University Press

Antipsychotics Have a Rich Receptor Pharmacology, Which Contributes to Efficacy As Well As Side Effects

Receptor	Effects of blockade
D_2	Antipsychotic, anti-manic, anti-aggression
	EPS/akathisia, tardive dyskinesia, increased prolactin
α_1 adrenergic	Postural hypotension, dizziness, syncope
α_2-adrenergic	Antidepressant, increased alertness
	Increased blood pressure
H_1	Anxiolytic, sleep induction, anti-EPS/akathisia
	Sedation, weight gain
M_1	Anti-EPS/akathisia
	Memory, cognition, dry mouth
$M_{2\text{-}4}$	Blurred vision, constipation, urinary retention
5-HT_{1A} (partial agonism)	Anxiolytic, antidepressant, anti-EPS/akathisia
5-HT_{2A}	Anti-EPS/akathisia, antipsychotic (?)
5-HT_{2C}	Increased appetite/weight (?)

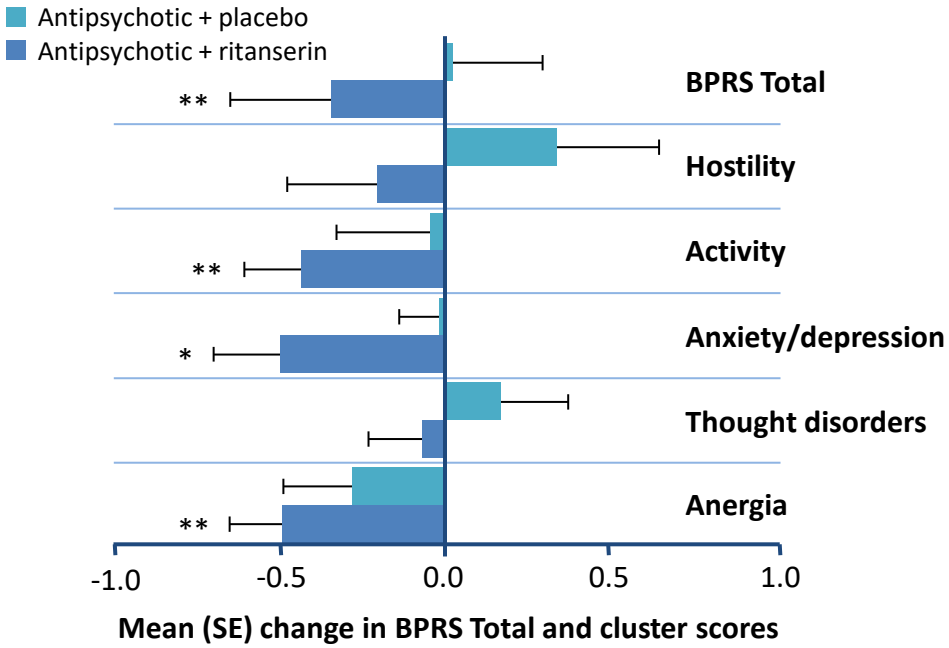
Efficacy

Side effects

Modified from: Correll. Eur Psychiatry 2010;25(Suppl. 2):S12–S21

Effect of Adding Ritanserin (5-HT_2 & 5-HT_7 Blockade) to Existing Conventional Antipsychotic Treatment

The effect of adjunctive ritanserin therapy on BPRS scores and extrapyramidal symptoms



- BPRS Total score significantly improved with adjunctive ritanserin therapy, compared with adjunctive placebo
- Additionally, EPS (measured using the Simpson–Angus Scale) significantly improved with adjunctive ritanserin therapy, but remained unchanged with adjunctive placebo

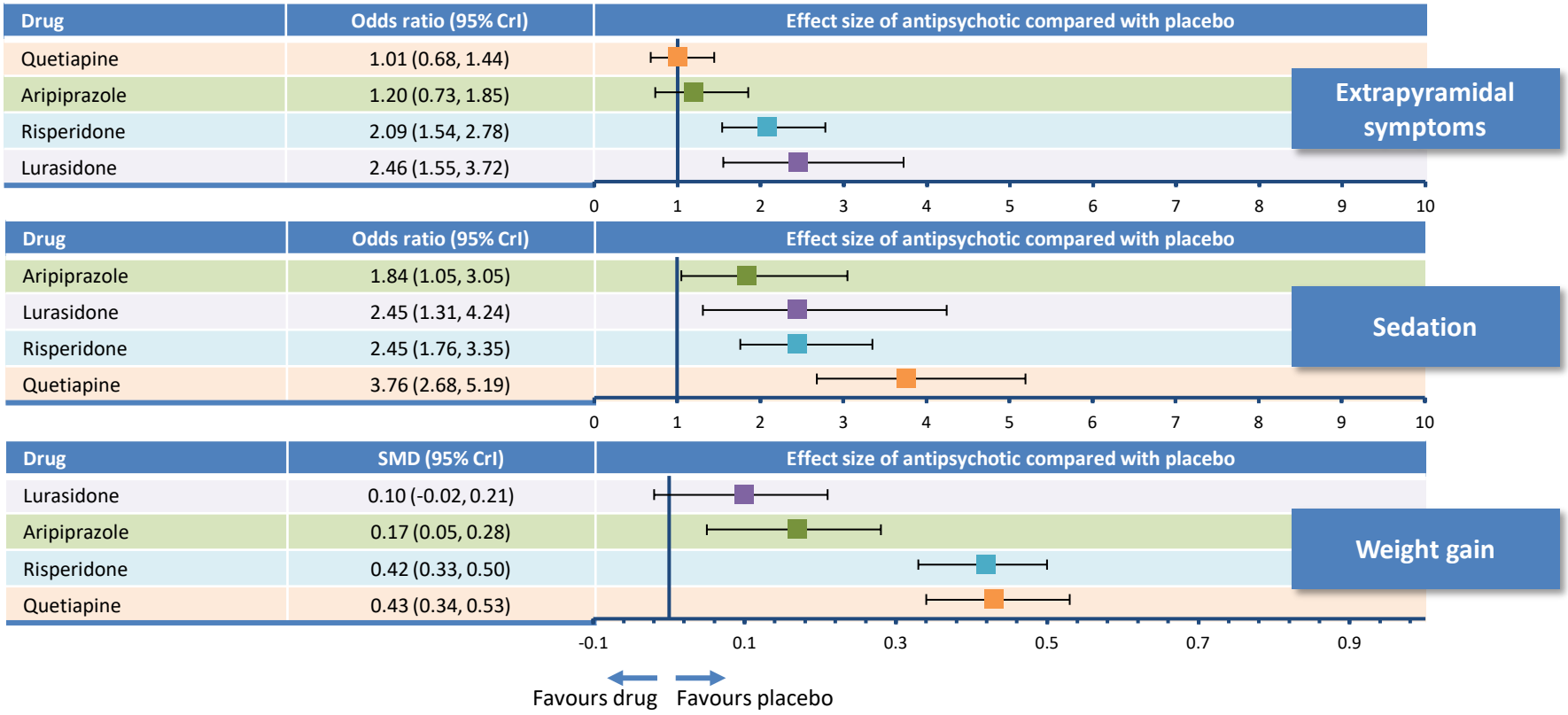
*p<0.05, **p<0.01 versus placebo; double-blind study of patients with chronic schizophrenia

O.Vinař, et al 1989: Ritanserin in schizophrenic patients.Activ.Nerv.Super. 31:107-109

Gelders. Br J Psychiatry 1989;155(Suppl 5):33–36;

Glennon et al. In: Neuropsychopharmacology – 5th Generation of Progress. Davis et al (Eds) Lippincott, Williams, & Wilkins, Philadelphia, Pennsylvania, 2002

Each Antipsychotic Binds to a Distinct Range of Receptor Targets, Which May Explain Differences in Side-Effect Profiles



EPS were assessed through the use of antiparkinson medication; CrI=credible interval; SMD=standardised mean difference

Leucht et al. Lancet 2013;382(9896):951–962

The Advent of D_2 Receptor Partial Agonists

- Despite antagonism at the 5-HT_{2A} receptor, the clinical advantages of SGAs remain limited by accompanying side effects
- D_2 receptor partial agonists may overcome this barrier
  - At the D_2 receptor, a minimal amount of intrinsic activity is sufficient to reduce D_2-related side effects; thus, partial agonism may reduce side effects, whilst maintaining antipsychotic efficacy
- Antipsychotics such as **aripiprazole, brexpiprazole, and cariprazine**, act as partial agonists at the D_2 receptor

Stahl. Stahl's Essential Psychopharmacology. 4th edition, 2013, Cambridge University Press; Lieberman. CNS Drugs 2004;18(4):251–267

Cariprazine

- Partial agonist at D_2 and D_3 receptors[1]
  - Whereas aripiprazole preferentially binds to D_2 receptors, **cariprazine demonstrates greatest affinity for D_3 receptors[1,2]**
  - Cariprazine has approximately **10-fold higher affinity for human D_3 compared with human D_{2L} and human D_{2S} receptors** (K_i 0.085, 0.490, and 0.692, respectively)[1]
- Partial agonist at 5-HT_{1A} receptors[1]

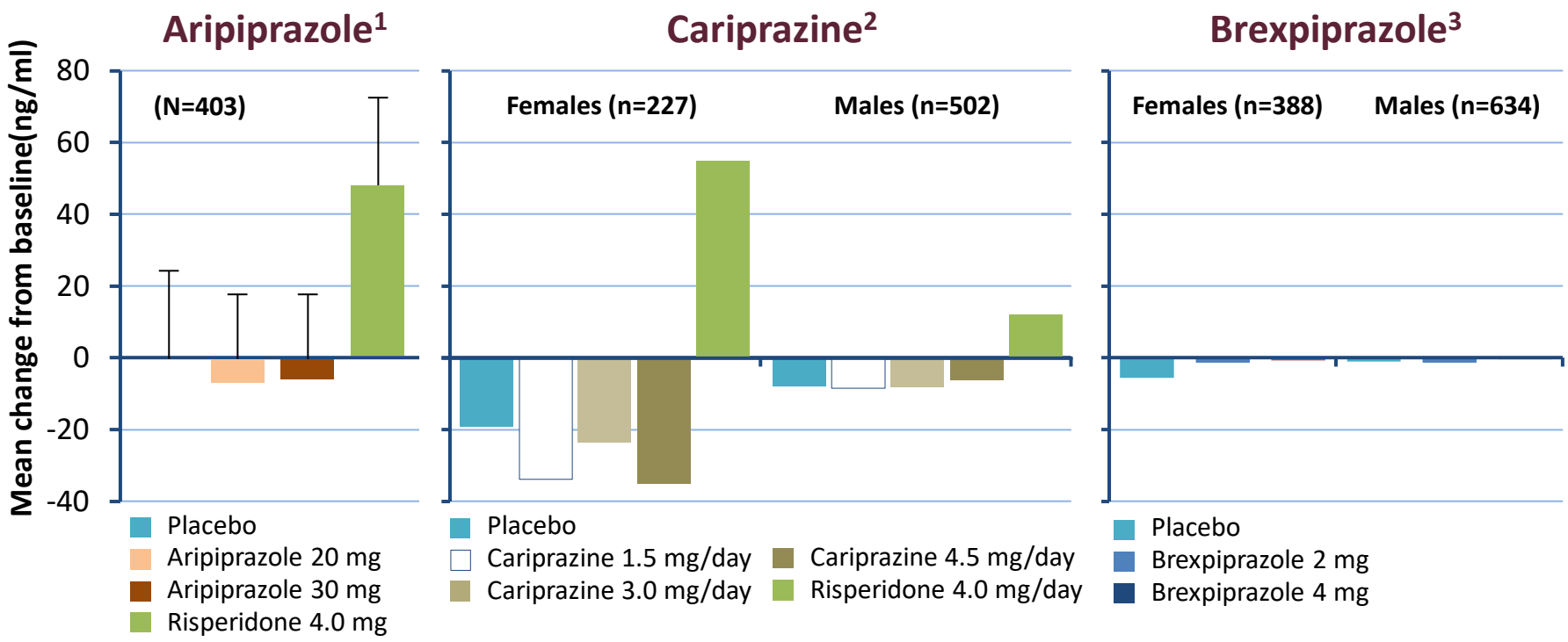
1. Kiss et al. J Pharmacol Exp Ther 2010;333(1):328–340
2. Shapiro et al. Neuropsychopharmacology 2003;28(8):1400–1411

Brexpiprazole

- Brexpiprazole is a serotonin–dopamine activity modulator that is a partial agonist at 5-HT_{1A} and dopamine D_2 receptors, and an antagonist at 5-HT_{2A} and noradrenaline alpha$_{1B/2C}$ receptors, all at similar potency
  - **Lower intrinsic activity at the D_2 receptor** compared with aripiprazole
  - **Greater potency compared with aripiprazole at the 5-HT_{2A}** (ED_{50} approximately 26 times higher for brexpiprazole compared with aripiprazole)

Maeda et al. J Pharmacol Exp Ther 2014;350:589–604

Profiles for Effect on Prolactin



Error bars are standard deviation; brexpiprazole data pooled from Beacon and Vector studies

1. Potkin et al. Arch Gen Psychiatry 2003;60(7):681–690
2. Durgham et al. Schizophr Res 2014;152(2–3):450–457
3. Correll et al. Schizophr Res 2016;174(1–3):82–92

Comparing Weight, Somnolence, & Akathisia by Number Needed to Harm (NNH)?

- When NNH vs. placebo is <10, AE is common

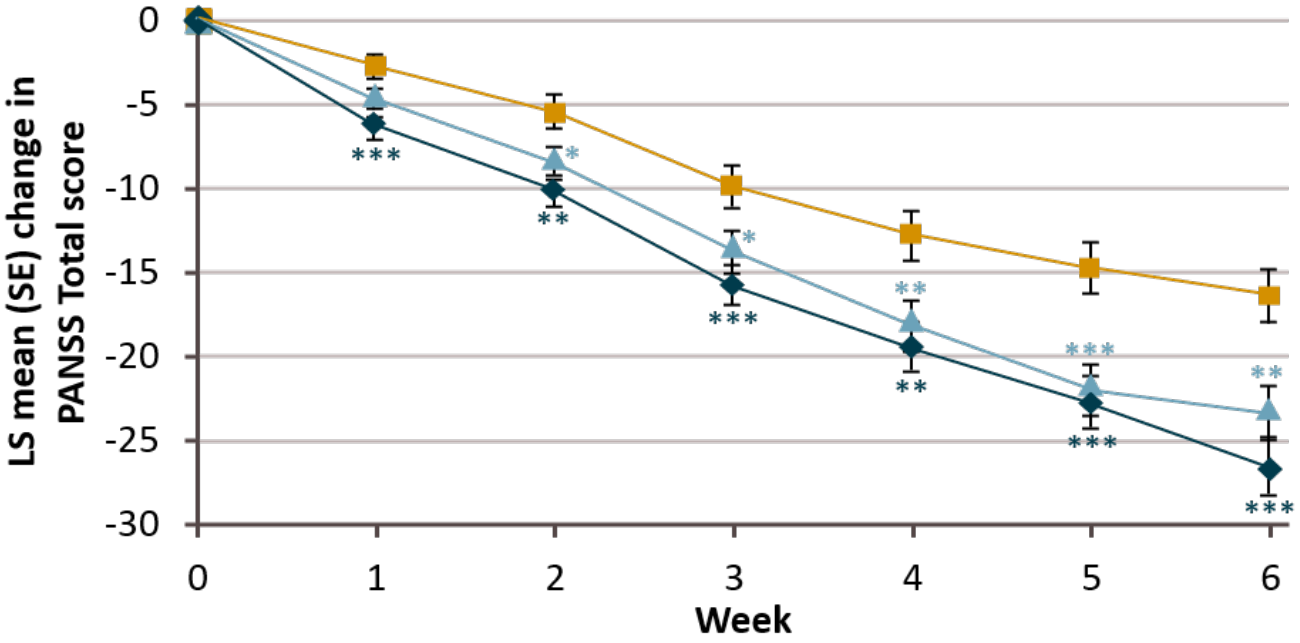
Medication	Weight gain ≥7%	Somnolence AEs	Akathisia AEs
Aripiprazole	21	20[a]	25
Brexpiprazole	17	50	112
Cariprazine (to 6 mg/day)	34	100	15
Lurasidone	67	11	10
Olanzapine	6[a]	7[a]	25
Paliperidone	35	42	39
Quetiapine IR	6	10[a]	ND
Risperidone (to 8 mg/day)	18[a]	13	15
Ziprasidone	16	15	100

[a]For schizophrenia and bipolar mania; AE=adverse event; IR=immediate release; ND=not determined

Citrome. Int J Clin Pract 2015;69:1211–1220

Cariprazine Efficacy on Schizophrenia Symptoms

Change from baseline in PANSS score (MMRM, ITT population)



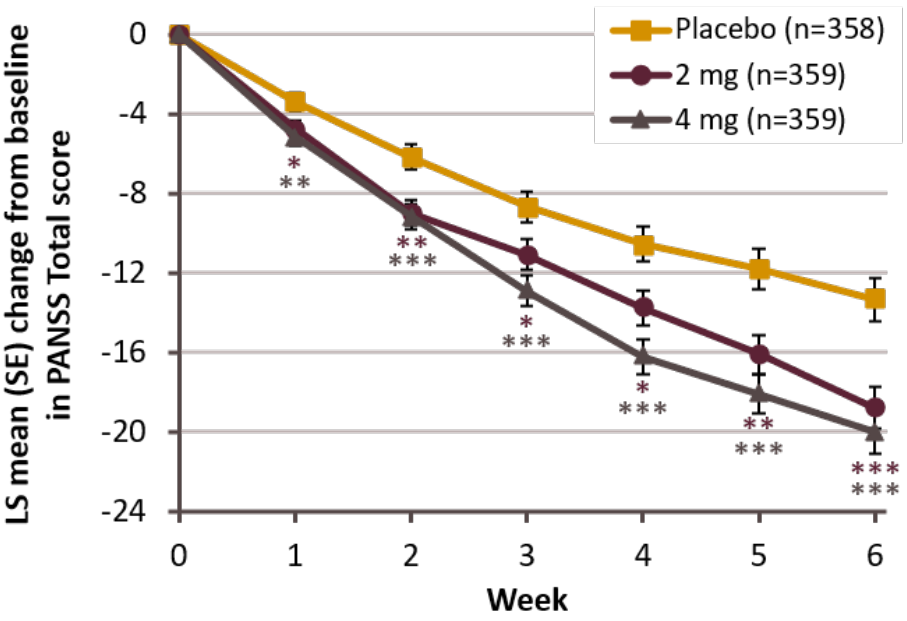
LS mean difference from placebo at Week 6:
Cariprazine 3–6 mg/day:
-6.8, p=0.003
Cariprazine 6–9 mg/day:
-9.9, p<0.001

*p<0.05, **p<0.01; ***p<0.001 vs placebo
ITT=intent-to-treat; MMRM=mixed-effects model with repeated measures

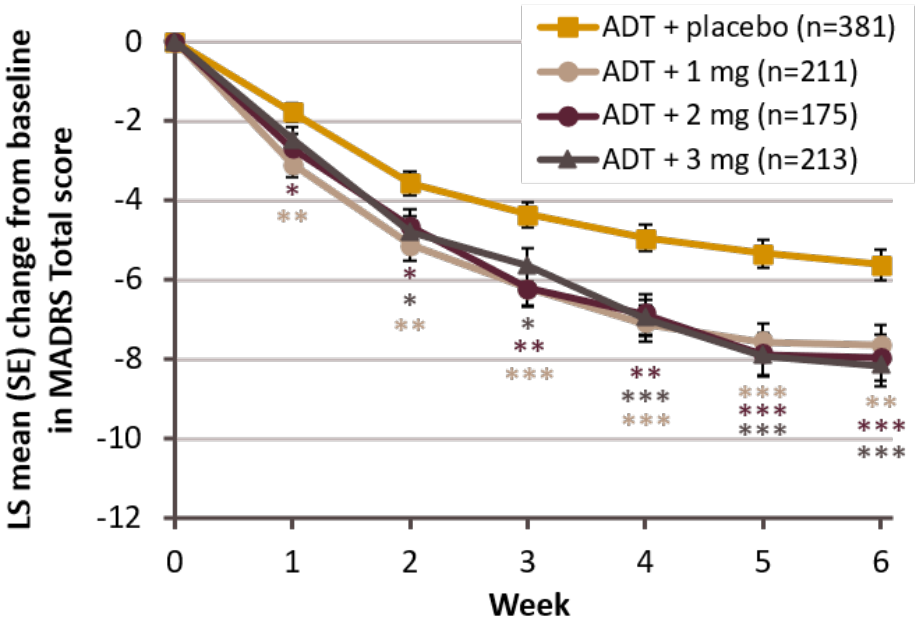
Kane et al. J Clin Psychopharmacol 2015;35(4):367–373

Newer SGA Improved Tolerability Without Loss of Efficacy

Brexpiprazole in schizophrenia[1]



Adjunctive brexpiprazole in MDD[2]



*p<0.05, **p<0.01, ***p<0.001 versus placebo; pooled data from Beacon and Vector (schizophrenia), and Pyxis and Polaris (MDD)
ADT=antidepressant therapy; LS=least squares

1. Correll et al. Schizophr Res 2016;174(1–3):82–92
2. Thase et al. Curr Psychiatry Rev [submitted]

Roluperidone (MIN-101)

Efficacy and Safety of MIN-101: A 12-Week Randomized, Double-Blind, Placebo-Controlled Trial of a New Drug in Development for the Treatment of Negative Symptoms in Schizophrenia

Michael Davidson, M.D., Jay Saoud, Ph.D., Corinne Staner, M.D., Nadine Noel, Ph.D., Elisabeth Luthringer, R.N., Sandra Werner, Ph.D., Joseph Reilly, M.S., Jean-Yves Schaffhauser, Pharm.D., Jonathan Rabinowitz, Ph.D., Mark Weiser, M.D., Remy Luthringer, Ph.D.

Objective: The authors assessed the efficacy, safety, and tolerability of MIN-101, a compound with affinities for sigma-2 and 5-HT_{2A} receptors and no direct dopamine affinities, in comparison with placebo in treating negative symptoms in stabilized patients with schizophrenia.

Method: The trial enrolled 244 patients who had been symptomatically stable for at least 3 months and had scores of at least 20 on the negative subscale of the Positive and Negative Syndrome Scale (PANSS). After at least 5 days' withdrawal from all antipsychotic medication, patients were randomly assigned to receive placebo or 32 mg/day or 64 mg/day of MIN-101 for 12 weeks. The primary outcome measure was the PANSS negative factor score (pentagonal structure model). Secondary outcome measures were PANSS total score and scores on the Clinical Global Impressions Scale (CGI), the Brief Negative Symptom Scale, the Brief Assessment of Cognition in Schizophrenia, and the Calgary Depression Scale for Schizophrenia.

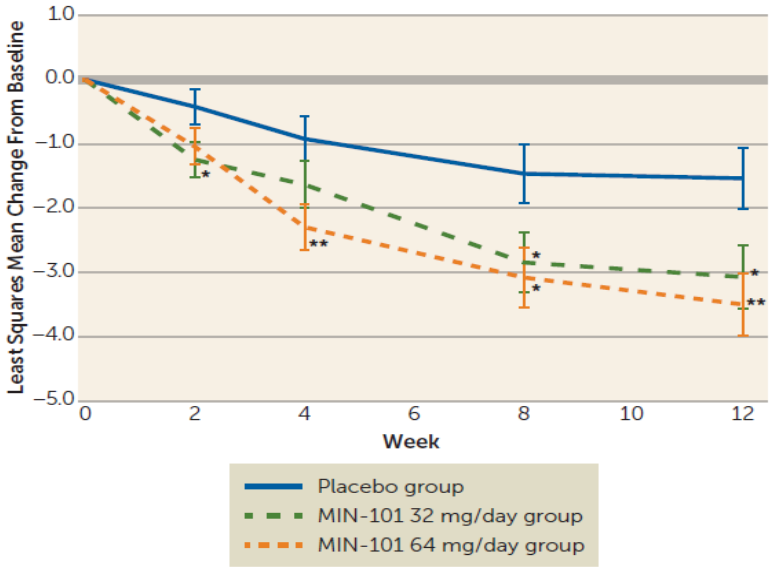
Results: A statistically significant difference in PANSS negative factor score was observed, with lower scores for the MIN-101 32 mg/day and 64 mg/day groups compared with the placebo group (effect sizes, d=0.45 and d=0.57, respectively). Supporting these findings were similar effects on several of the secondary outcome measures, such as the PANSS negative symptom, total, and activation factor scores, the CGI severity item, and the Brief Negative Symptom Scale. There were no statistically significant differences in PANSS positive scale score between the MIN-101 and placebo groups. No clinically significant changes were observed in vital signs, routine laboratory values, weight, metabolic indices, and Abnormal Involuntary Movement Scale score.

Conclusions: MIN-101 demonstrated statistically significant efficacy in reducing negative symptoms and good tolerability in stable schizophrenia patients.

Am J Psychiatry 2017; 00:1–8; doi: 10.1176/appi.ajp.201717010122

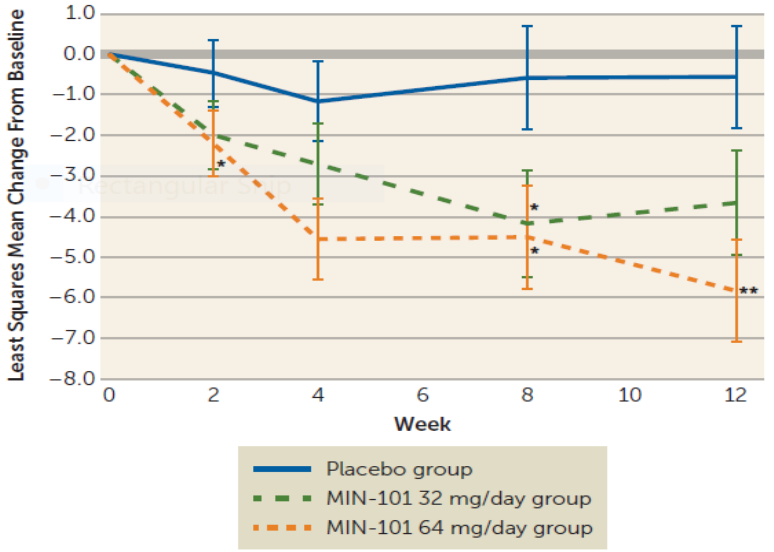
Roluperidone: Results

FIGURE 1. Change From Baseline in the Five-Factor PANSS Negative Subscale Scores in Patients With Schizophrenia Treated With MIN-101 or Placebo[a]



[a] PANSS=Positive and Negative Syndrome Scale. Ns for weeks 0, 2, 4, 8, and 12, respectively, are as follows: for the placebo group, 79, 79, 75, 62, and 54; for the MIN-101 32 mg/day group, 76, 75, 68, 56, and 51; and for the MIN-101 64 mg/day group, 79, 78, 66, 59, and 54. Error bars indicate standard error of the mean. Reported p values indicate comparison with the placebo group.
*p≤0.05. **p≤0.01.

FIGURE 2. Change From Baseline in PANSS Total Scores in Patients With Schizophrenia Treated With MIN-101 or Placebo[a]



[a] PANSS=Positive and Negative Syndrome Scale. Ns for weeks 0, 2, 4, 8, and 12, respectively, are as follows: for the placebo group, 79, 79, 75, 62, and 54; for the MIN-101 32 mg/day group, 76, 75, 68, 56, and 51; and for the MIN-101 64 mg/day group, 79, 78, 66, 59, and 54. Error bars indicate standard error of the mean. Reported p values indicate comparison with the placebo group.
*p≤0.05. **p≤0.01.

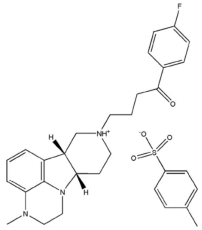
*** Significant effect on depression, and a significant effect on negative symptoms was observed**

Roluperidone: Clinical Update

On May 11, 2021, the Company announced results of the open-label extension of the phase 3 trial of roluperidone for the treatment of negative symptoms of schizophrenia following the completion of the 40-week open-label extension period. Details are provided in that press release, and key results include:

- Continuous improvement in negative symptoms as measured by Positive and Negative Syndrome Scale (PANSS) Marder Negative Symptom Factor Score (NSFS) observed over one year (12-week double-blind and 40-week open-label periods) in patients receiving both 64 mg and 32 mg doses
- Continuous improvement in Personal and Social Performance (PSP) total score over one year, suggesting improvement in patients' everyday life functioning
- Favorable safety profile with few serious adverse events and no evidence of somnolence, extrapyramidal side effects or weight gain
- Limited number of relapses observed over one year.

Lumateperone (ITI-007)



- ITI-007 is an entirely novel first-in-class investigational drug which simultaneously modulates serotonin, dopamine, and glutamate neurotransmission in the brain

- Lumateperone (CAPLYTA) was FDA approved for the treatment of schizophrenia in December 2019

- Lumateperone is currently in Phase 3 clinical trials for bipolar depression and agitation associated with dementia

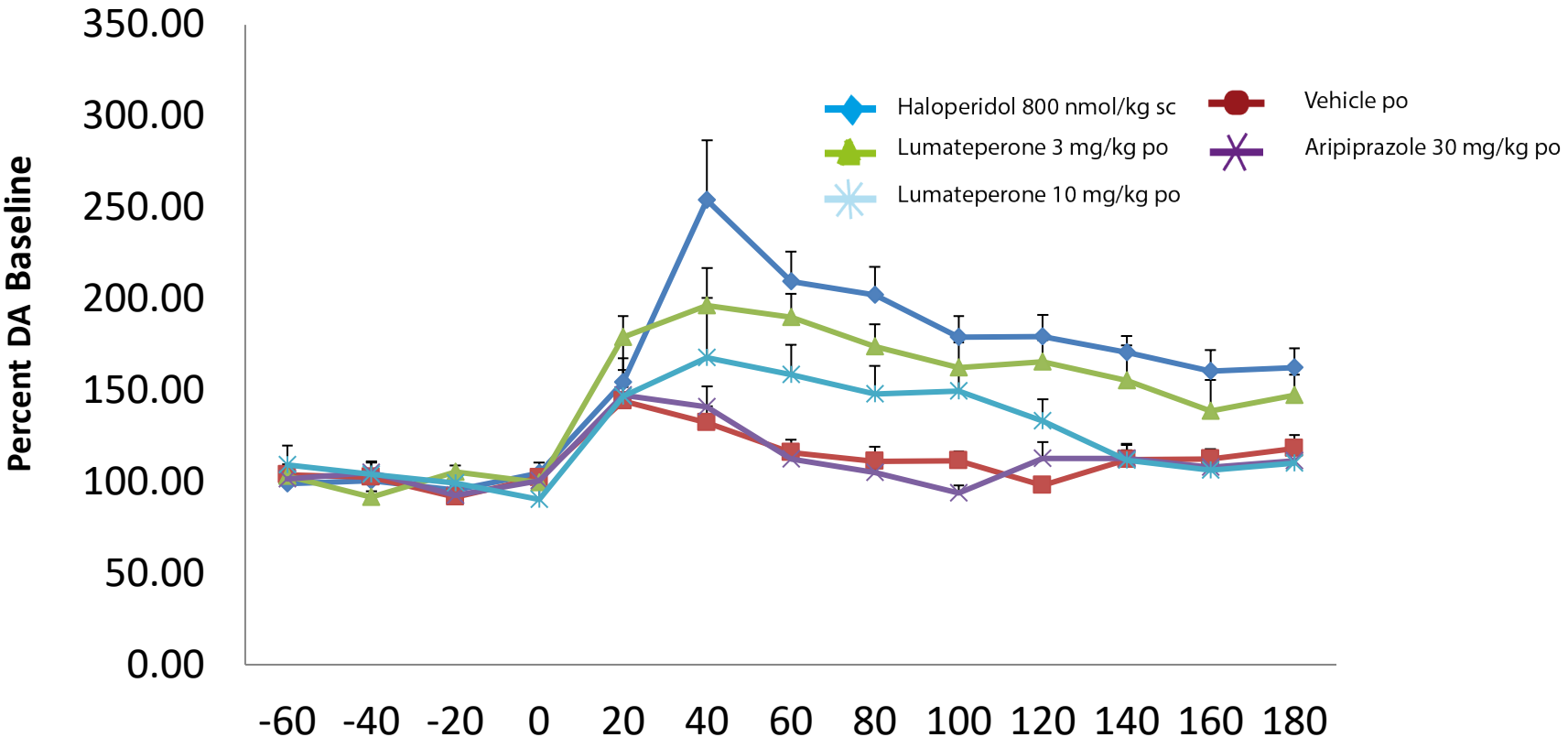
Snyder et al, Psychopharmacology 2015

Mechanism of Action

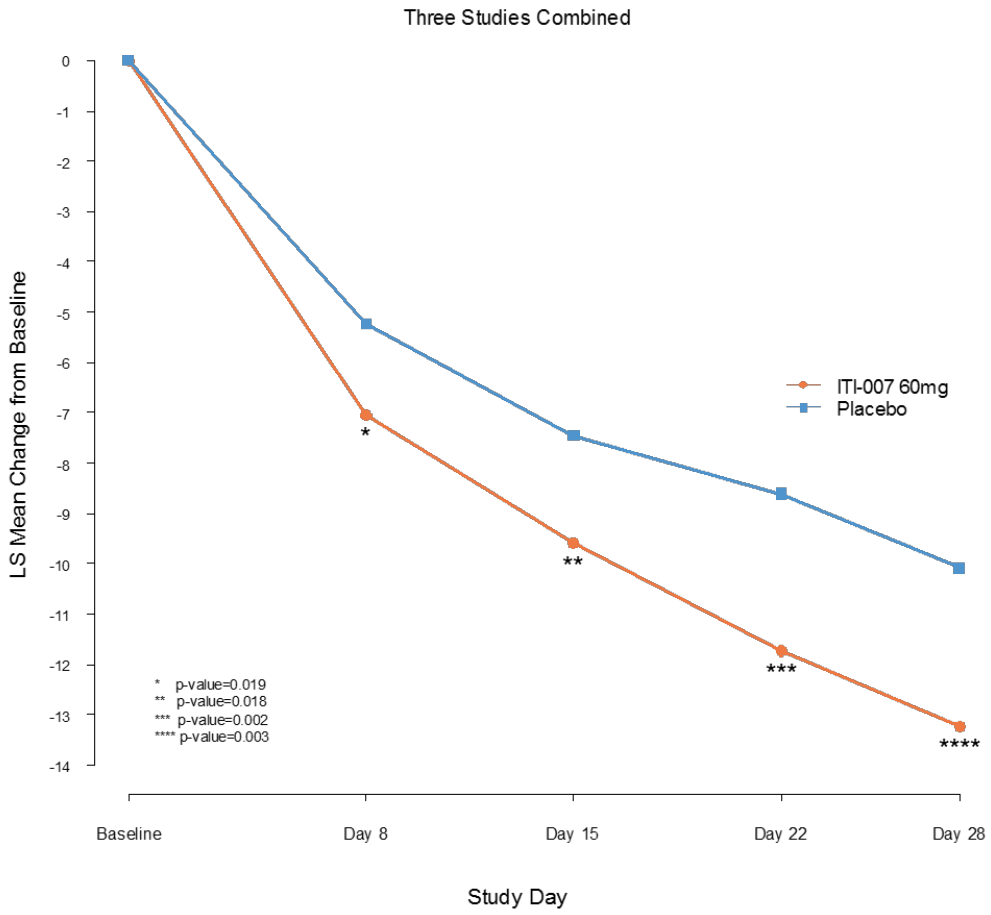
- Lumateperone (ITI-007) is a potent antagonist at **5-HT2A receptors** and, in contrast to all other antipsychotic drugs, also exhibits potent **serotonin reuptake inhibition**.
- ITI-007 also binds to dopamine **D1 and D2 receptors** acting as a mesolimbic/mesocortical dopamine phosphoprotein *modulator* (DPPM) with pre-synaptic partial agonism and post-synaptic antagonism at D2 receptors
- Furthermore, lumateperone is an indirect **glutamatergic** (GluN2B) phosphoprotein *modulator* with D1-dependent enhancement of both NMDA and AMPA currents in the prefrontal cortex via the mTOR pathway.

Snyder et al, Psychopharmacology 2015

ITI-007 Selectively Increases Dopamine Release in the Rat Prefrontal Cortex, But Not in the Striatum

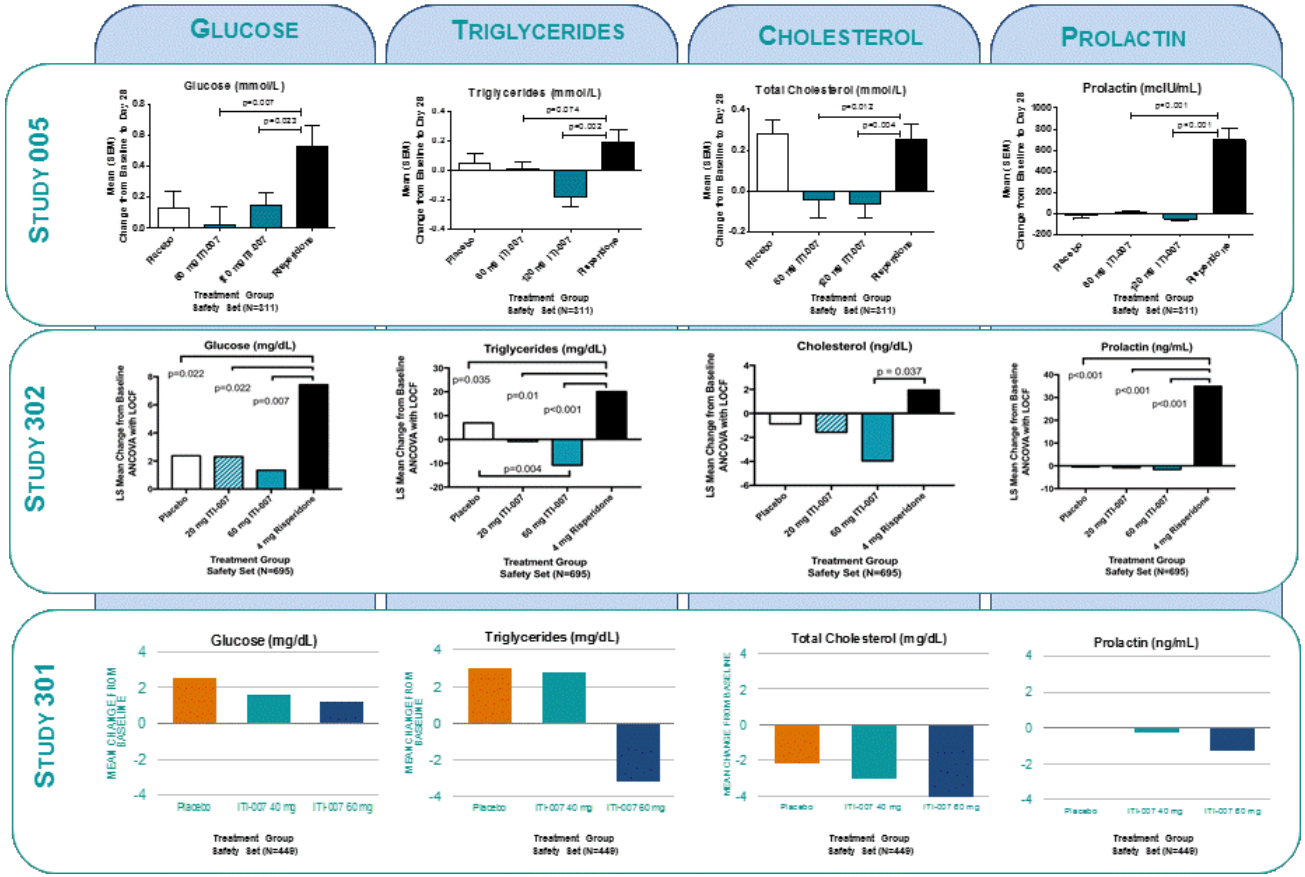


Lumateperone (60 mg) Demonstrates Early and Sustained Antipsychotic Activity



Lieberman et al, Biological Psychiatry 2016

Lumateperone Displays a Consistent Safety Profile and Superiority Over Risperidone on Key Parameters in Clinical Studies



BI 425809 Is a Novel Glyt1 Inhibitor That Increases The Concentration of Glycine in the Synaptic Cleft

- **Cognitive impairment** is a core feature of schizophrenia and a major determinant of poor functional outcome, but no pharmacological treatment is currently approved for this aspect of the disease[1,2]
- NMDA receptor hypofunction is known to be associated with **cognitive impairment** in schizophrenia[3]
- Glycine is an NMDA receptor co-agonist; inhibition of GlyT1 can increase synaptic glycine levels and may therefore improve NMDA receptor function[3]
- BI 425809 is a **novel GlyT1 inhibitor that increases the concentration of glycine[4,5] in the synaptic cleft**
- This on-going Phase II trial (NCT02832037) will test the effect of add-on treatment with BI 425809 to standard of care on cognitive impairments in patients with schizophrenia

GlyT1, glycine transporter 1; NMDA, *N*-methyl-D-aspartate

1. Schaefer J, et al. *Schizophr Res* 2013;150:42–50
2. Green MF, et al. *Schizophr Bull* 2000;26:119–136
3. Hashimoto K. *Open Med Chem J* 2010; 4:10–19
4. Moschetti V, et al. *Eur J Drug Metab Pharmacokinet* 2018;43:239–49
5. Moschetti V, et al. *Clin Drug Investig* 2018;38:737–50.

Mode of Action

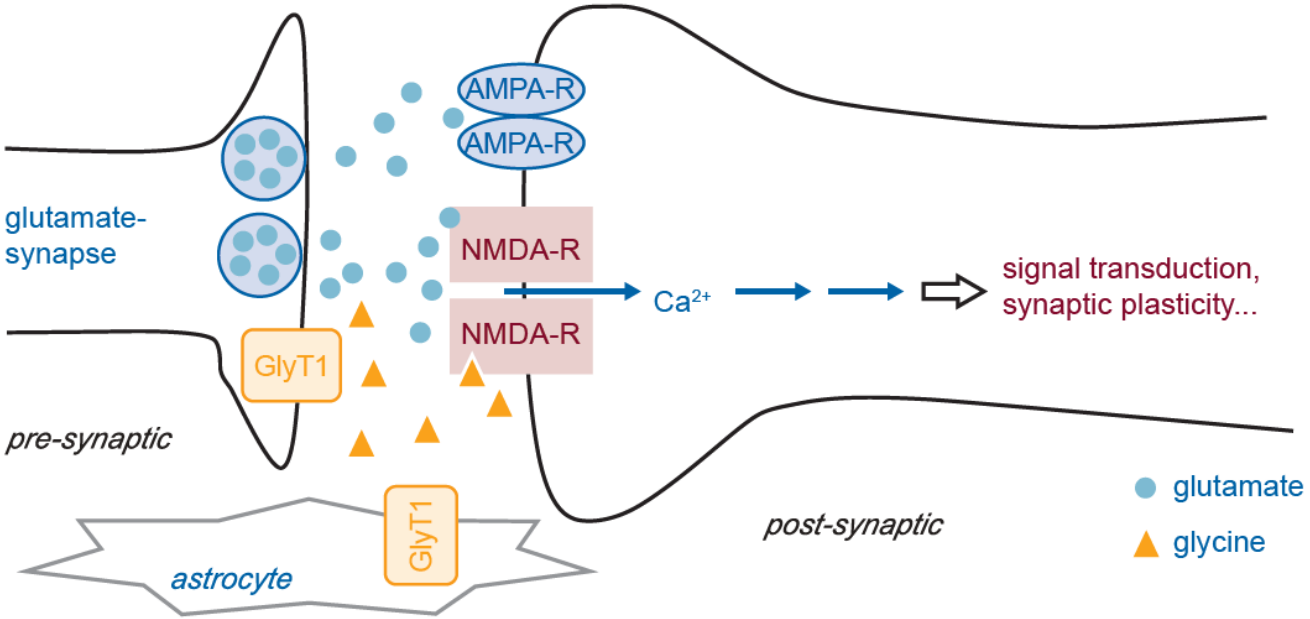


Figure adapted from Moschetti et al., 2016[1]

AMPA-R, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor; GlyT1, glycine transporter 1; NMDA, *N*-methyl-D-aspartate

1. Moschetti V, et al. *Brit J Clin Pharmacol* 2016; 82(5):1315–24

THE LANCET
Psychiatry

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Efficacy and safety of the novel glycine transporter inhibitor BI 425809 once daily in patients with schizophrenia: a double-blind, randomised, placebo-controlled phase 2 study

Prof W Wolfgang Fleischhacker, MD • Jana Podhorna, MD • Martina Gröschl, PhD • Sanjay Hake, MD • Yihua Zhao, PhD • Songqiao Huang, PhD • et al. Show all authors

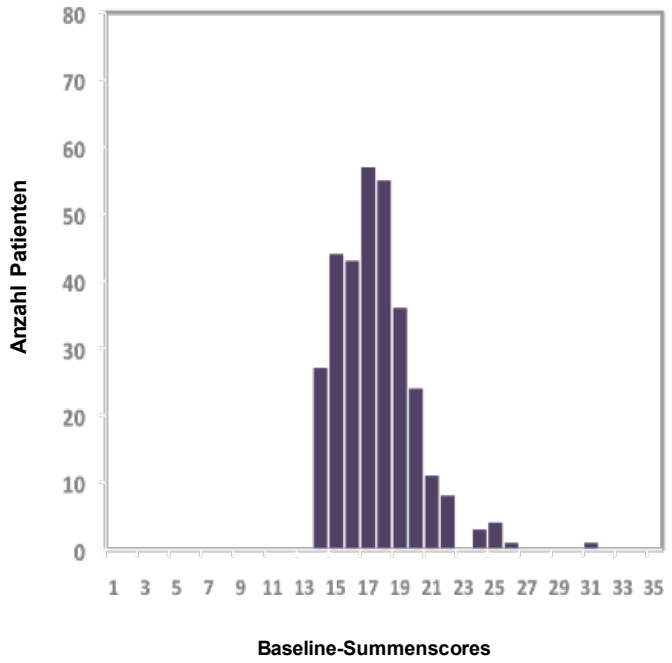
Published: March, 2021 • DOI: https://doi.org/10.1016/S2215-0366(20)30513-7 •

Phase II trial results demonstrated improvement in cognition with BI 425809 in adult patients with schizophrenia

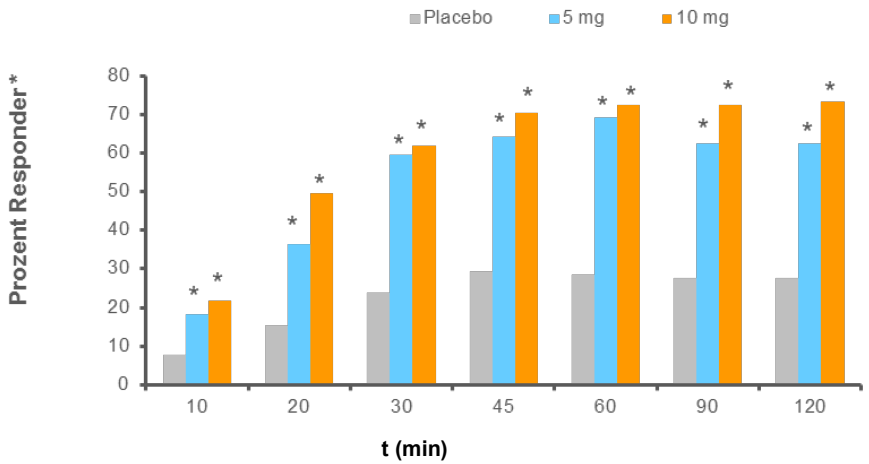
- Results presented at the 33rd ECNP Congress from a 12-week, placebo-controlled Phase II trial demonstrated BI 425809 has met its primary endpoint[1,2]
- Trial results, together with an ongoing combination Phase II study of BI 425809 and adjunctive computerized cognitive training, add to the body of evidence for Boehringer Ingelheim's schizophrenia research program[3]
- Cognitive impairment associated with schizophrenia (CIAS) has a significant negative impact on daily functioning and remains a focus for Boehringer Ingelheim's research across several neuropsychiatric disorders

Loxapin (via inhalation) for Agitation in Schizophrenia (or Bipolar Disorder)

PANSS Excitement Component (PEC)
for measurement of degree of agitation



*Response defined as at least. 40% Improvement in Total Score



Loxapine (ADASUVE for inhalation)

Gil E, et al (2018) *BMJ Open* 8(10): e020242
Kasper S et al (2015) *CliniCum neuropsy* Sonderausgabe

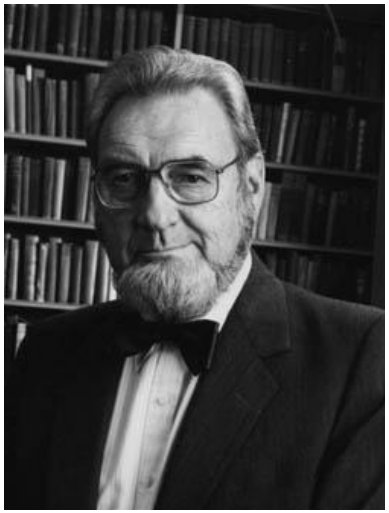
Matching Pharmacology to Patient

- An understanding of multiple treatment factors could improve selection of antipsychotic therapy for individual patients
  - Different efficacy profiles[1]
  - Different tolerability profiles[1]
  - Individual patient characteristics that may influence the pharmacological actions of an antipsychotic[2]
  - Individual patient preference[2]

Understanding the relationship between antipsychotic pharmacology and clinical effects could inform personalised (precison) treatment[2]

1. Leucht et al. Lancet 2013;382(9896):951–962
2. Barnes et al. J Psychopharmacol 2011;25(5):567–620

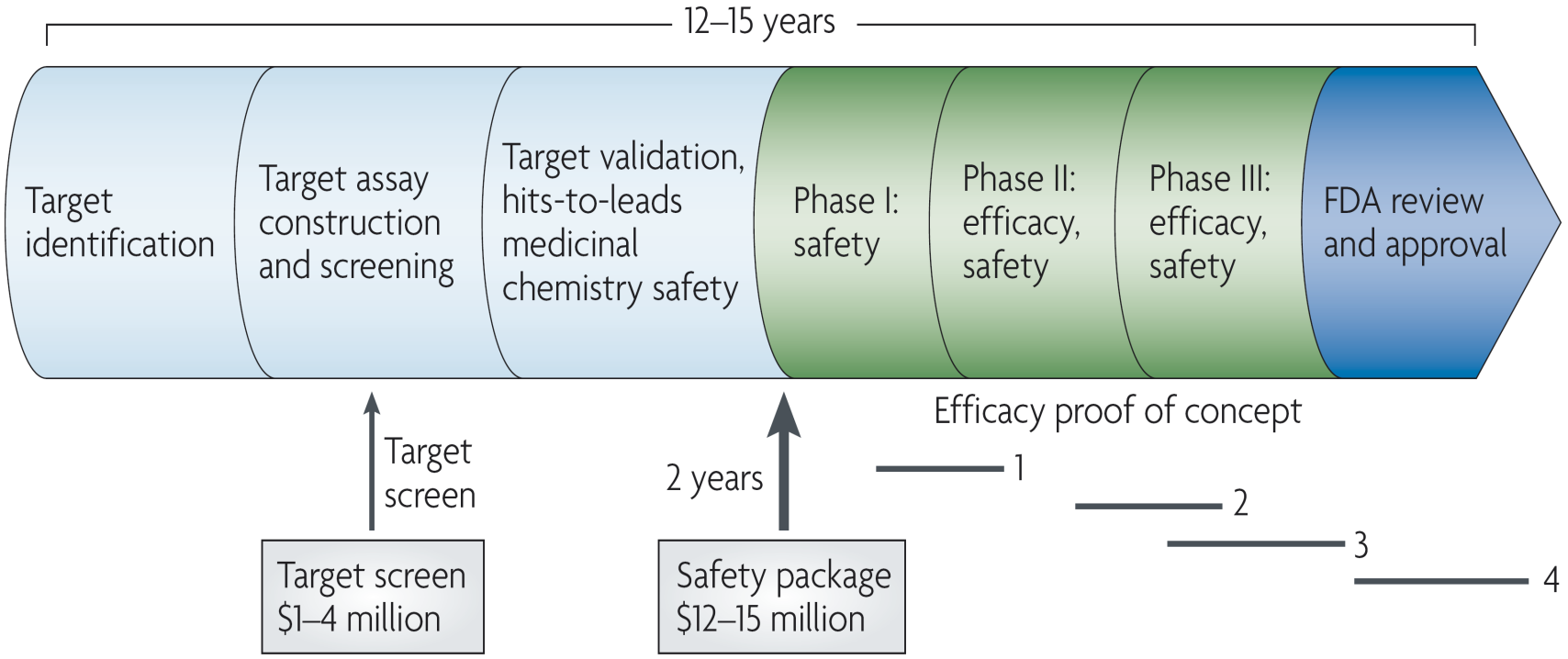
> **“Drugs don’t work in patients who don’t take them.” (C. Everett Koop, MD)**



C. Everett Koop (*1916-2013)

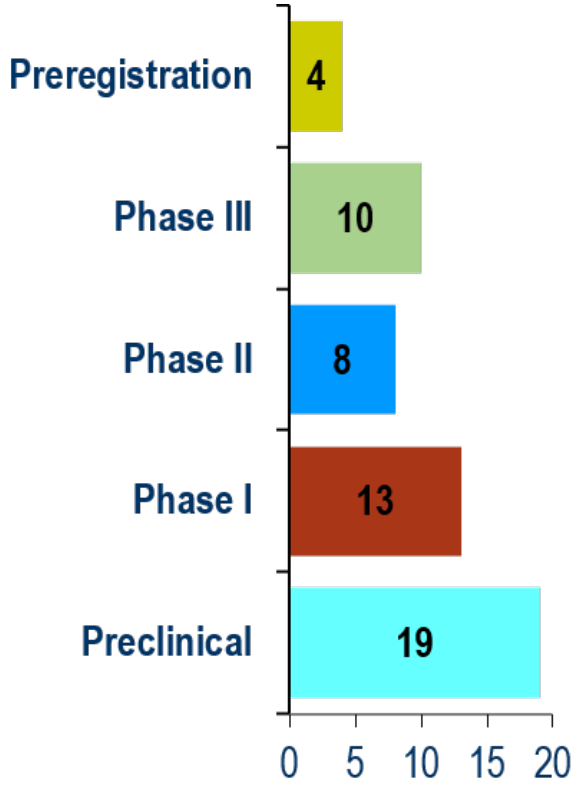
Surgeon General of the United States
(Leiter des öffentlichen Gesundheitsdienstes) 1982-1989

From Targets to Drugs

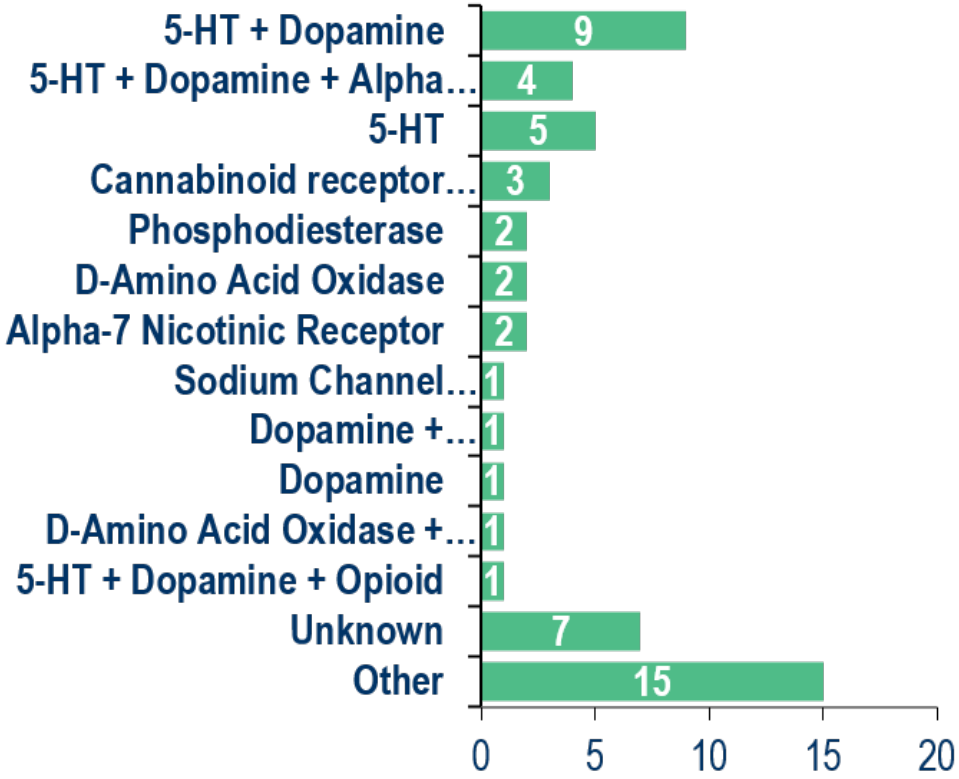


Roses, 2008

Schizophrenia Pipeline by Phase



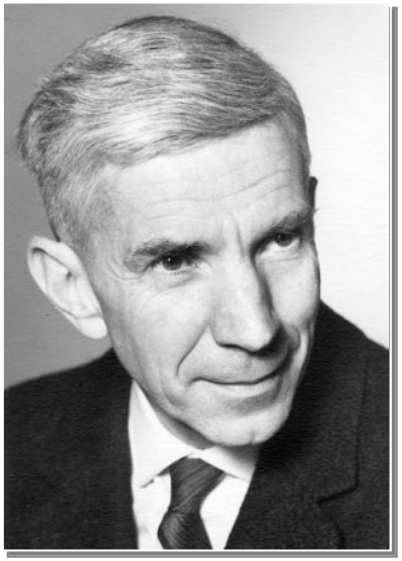
Pipeline by Mechanism of Action



Careful Clinical Observations Have Led to the Discovery of Antipsychotics and Antidepressants

JEAN DELAY
(1907-1987)

PIERRE DENIKER
(1917-1998)



ROLAND KUHN
(1912-2005)

Thank You for Your Attention!

siegfried.kasper@meduniwien.ac.at