

Late Life Psychosis & Schizophrenia

Tarek K. Rajji

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Canadian Coalition for Seniors' Mental Health
To promote seniors' mental health by connecting people, ideas and resources.

Coalition Canadienne pour la Santé Mentale des Personnes Âgées
Promouvoir la santé mentale des personnes âgées en reliant les personnes, les idées et les ressources.



Faculty/Presenter Disclosure

Faculty: Tarek K. Rajji

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Mitigating Potential Bias

The information presented in this CME program is based on recent information that is explicitly “evidence-based”.

This CME Program and its material is peer reviewed and all the recommendations involving clinical medicine are based on evidence that is accepted within the profession; and all scientific research referred to, reported, or used in the CME/CPD activity in support or justification of patient care recommendations conforms to the generally accepted standards





Late-Life Schizophrenia

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Objectives

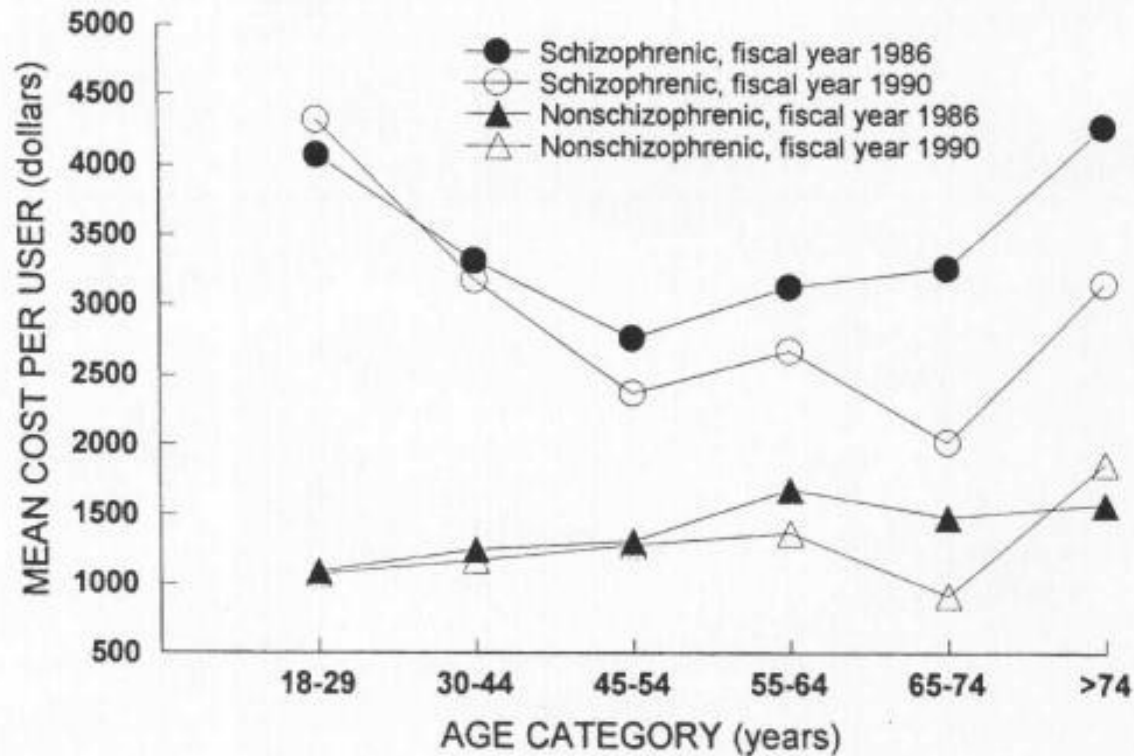
1. To describe the epidemiology and phenomenology of late-life schizophrenia
2. To describe the cognitive profiles of individuals with schizophrenia across the lifespan
3. To identify potential reversible factors that could reduce cognitive deficits in schizophrenia
4. To describe interventions that could enhance function in older individuals with schizophrenia

Growing Old with Schizophrenia

- 12% of persons with schizophrenia were age 50 or older in 2004
- 12% live in long-term homes
- 3% in hospitals
- 85% in the community
- 10 long-term studies with a total of 2,429 patients:
 - Follow-up: 20 to 37 years
 - Significant clinical improvement: 46% to 84% (median = 53%)
 - Social recovery: 21% to 77% (median = 49%)
 - About 20% remain institutionalized or quasi-institutionalized

Growing Old with Schizophrenia

FIGURE 1. Relation of Age and Schizophrenia Diagnosis to Mean Cost of Services in the San Diego County Public Mental Health System in Fiscal Years 1986 and 1990



Types of Schizophrenia in Late Life

Early-Onset Schizophrenia

- Onset before the age of 40
- Vast majority of older patients with schizophrenia

Late-Onset Schizophrenia

- Onset between age 40 and 60
- 23.5% of all patients with schizophrenia
- Incidence: 12.6 per 100, 000 population per year are diagnosed with schizophrenia with first onset after 44 years (van Os et al., 1995)

Very-Late-Onset Schizophrenia-Like Psychosis

- Onset after the age of 60
- 3% of all patients with schizophrenia

Early vs Late-Onset Schizophrenia

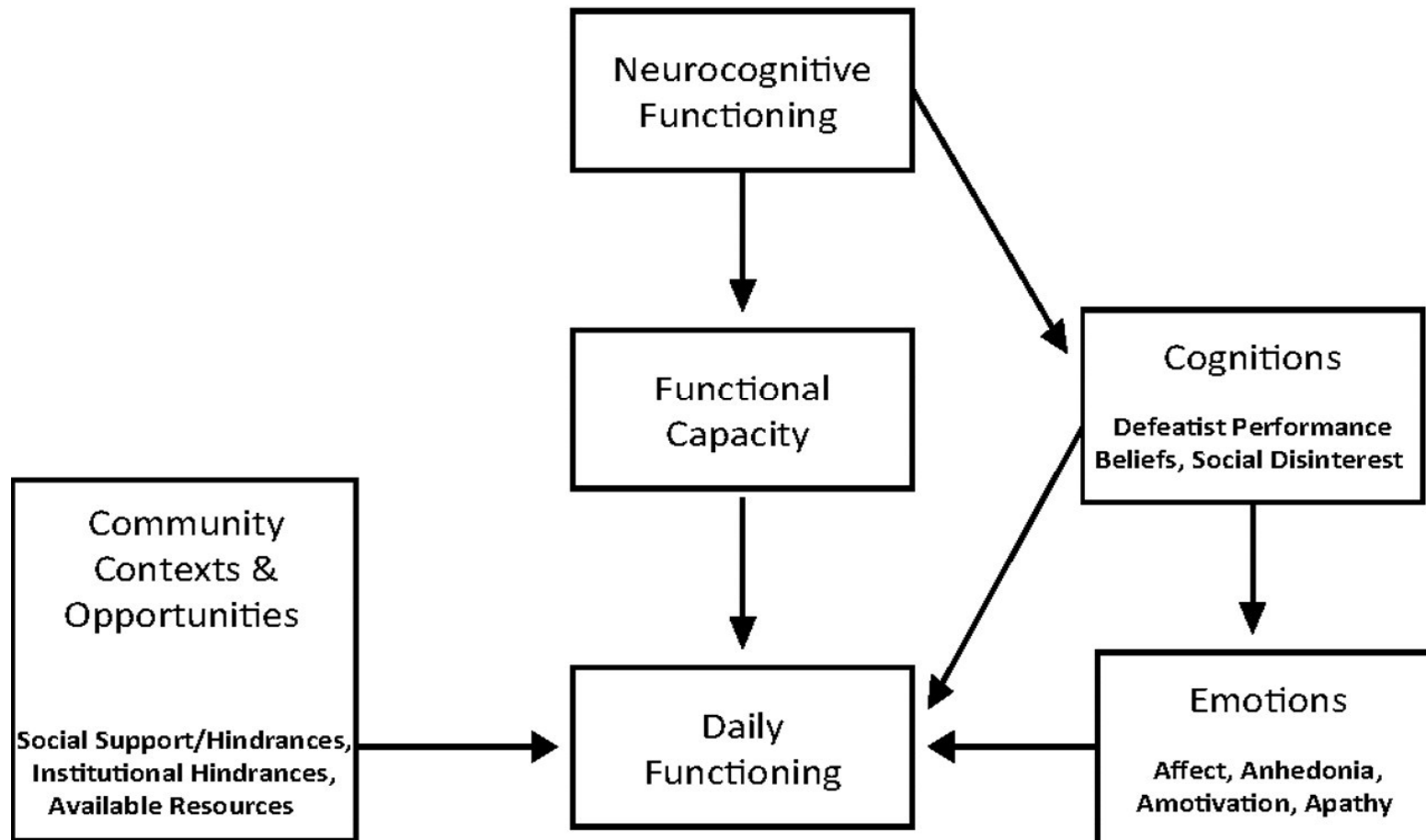
- More women among those with late-onset schizophrenia
- Late-onset schizophrenia is associated with positive rather than negative symptoms
- More variability in the profile of the cognitive deficits of patients with late-onset schizophrenia, with some domains less impacted than others; in contrast, those with early-onset schizophrenia tend to have a more generalized deficit
- Patients with late-onset schizophrenia tend to respond to lower doses of antipsychotics than those with early-onset

Alzheimer's Disease vs. Schizophrenia in Late Life

Symptoms	Alzheimer's Disease	Schizophrenia
Delusions Some one stealing thought control	+++ +/-	++ ++/+++
Hallucinations Auditory Visual	+/ ++/+++	++/+++ +
Family history	AD	Major mental illness
Course	Progressive decline	Variable
Social situation	Married, widowed, divorced, not socially isolated	Single, socially isolated

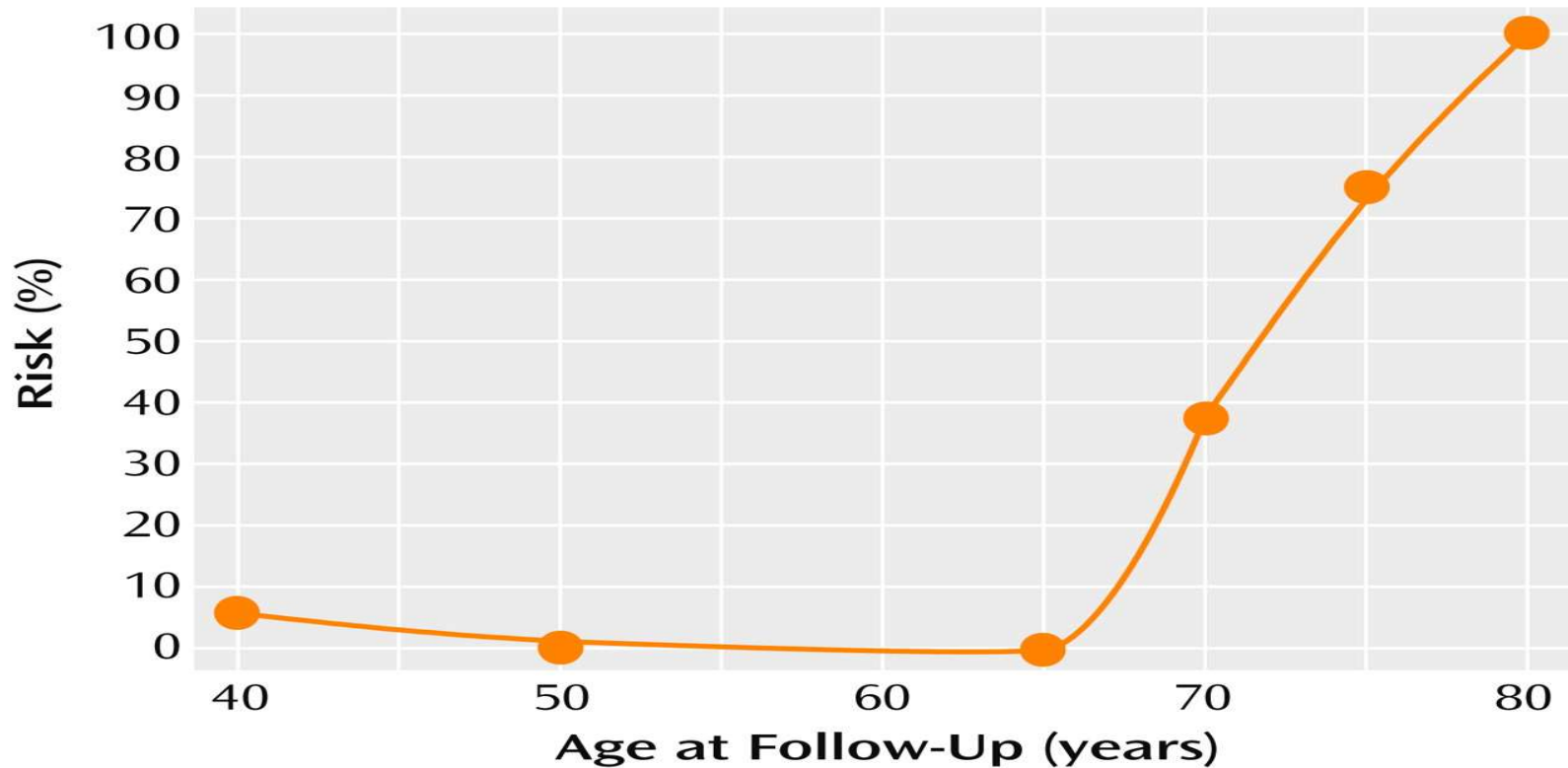
Cognition and Function in Schizophrenia

Model of Functional Outcome in Schizophrenia

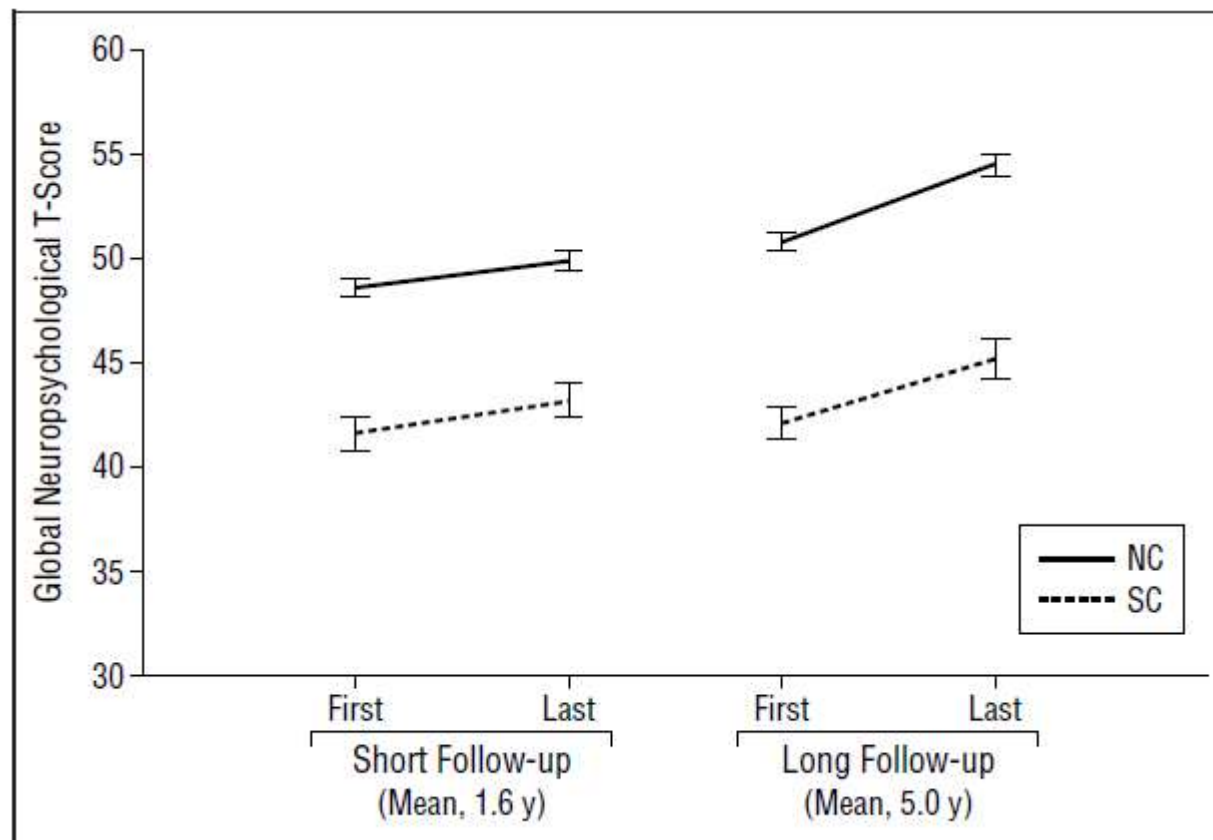


Institutionalized Older Patients with Schizophrenia

Risk of decline on the Clinical Dementia Rating scale from mild or no impairment at baseline to moderate or more severe impairment at 6-year follow-up

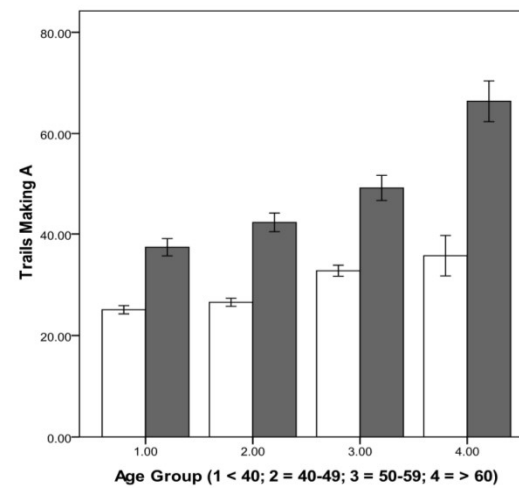
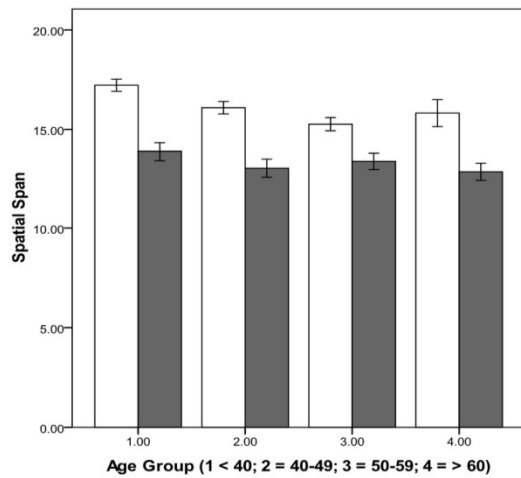
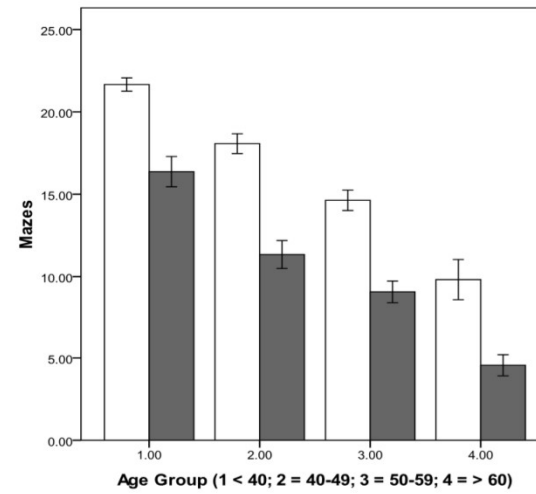
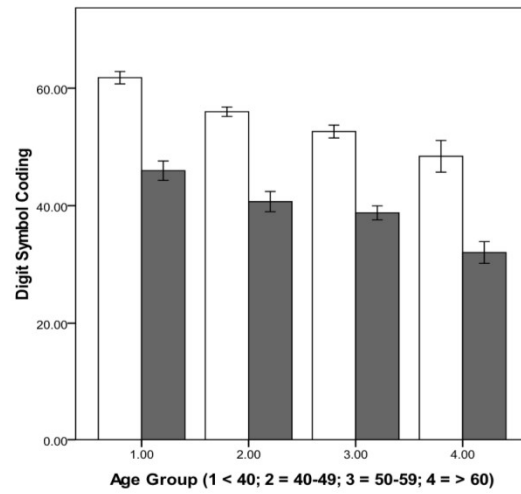
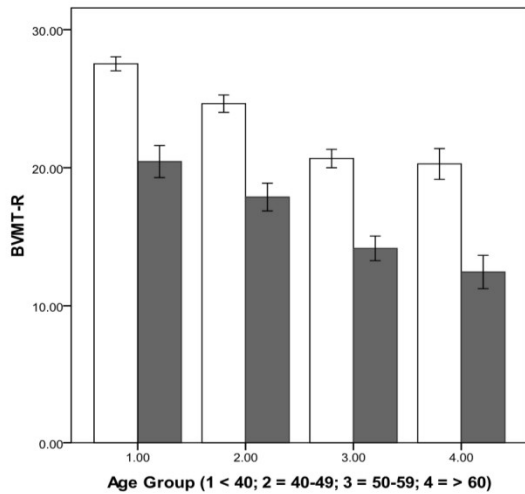


Community-Dwelling Older Patients with Schizophrenia

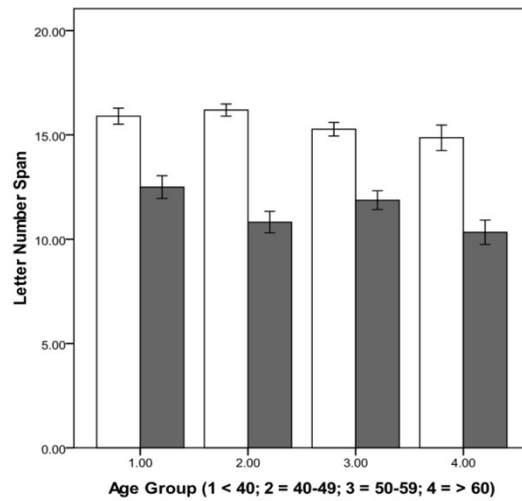
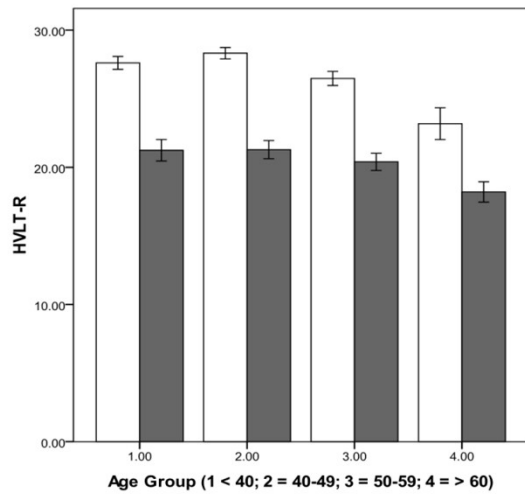
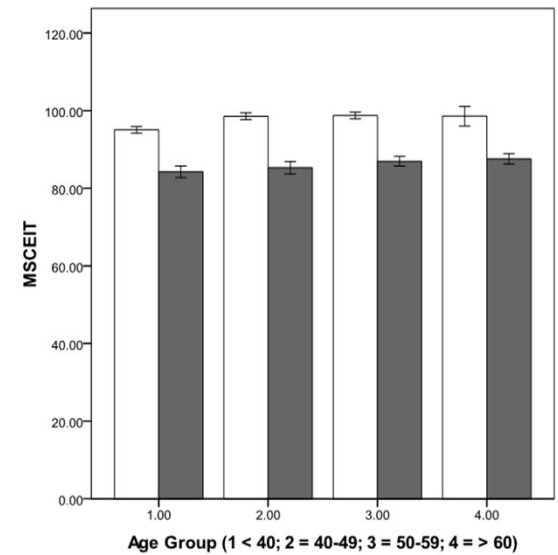
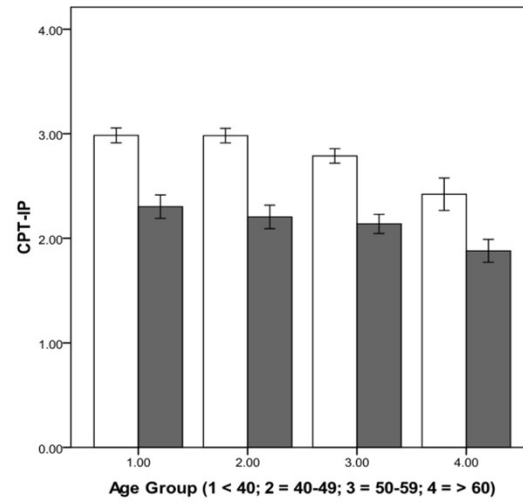
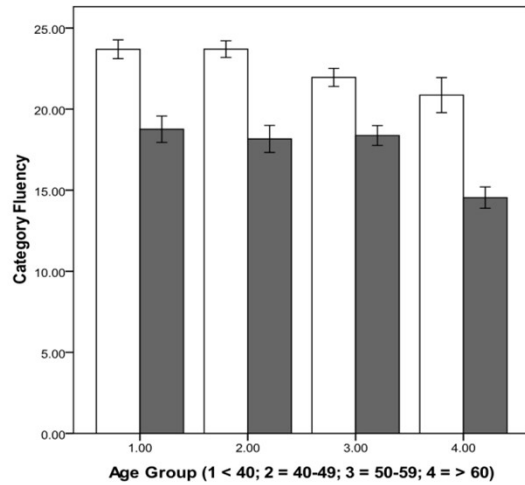


Heaton et al. Archives of General Psychiatry, 1995, 2001; Lowenstein et al. American Journal of Geriatric Psychiatry, 2012; Rajji et al. American Journal of Geriatric Psychiatry, 2013

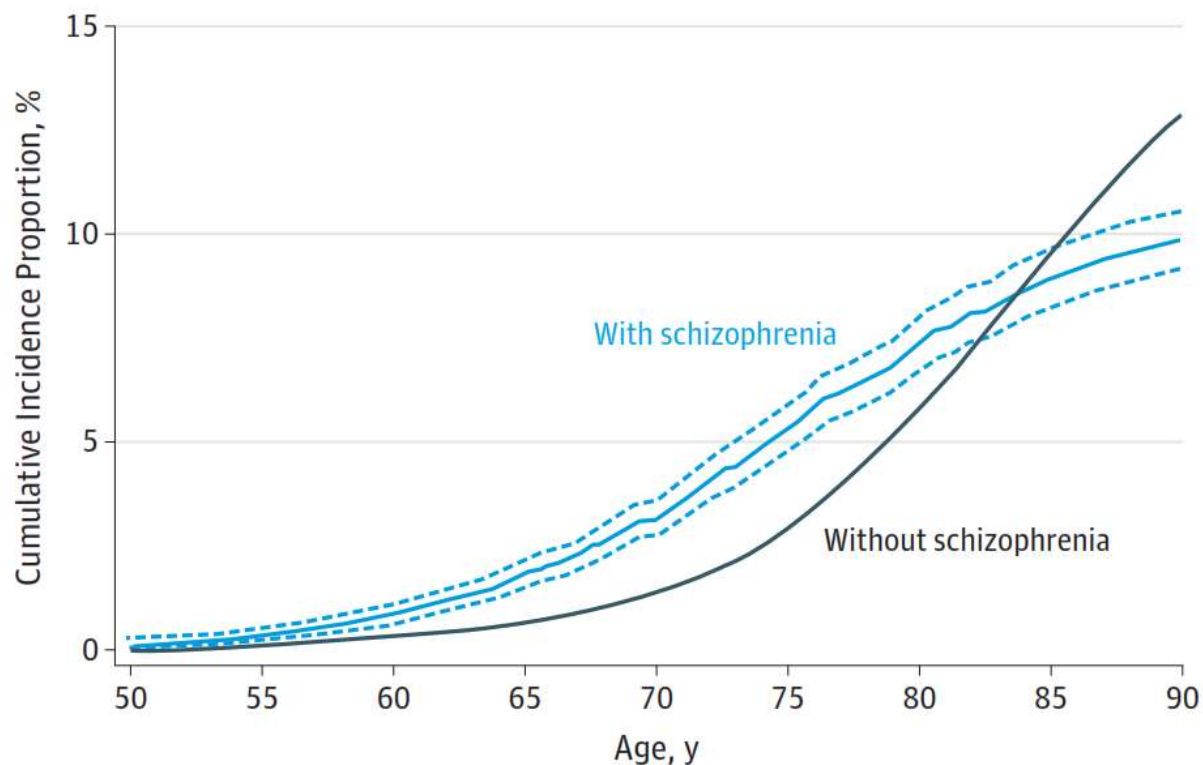
Cognition in Schizophrenia Across the Life Span



Cognition in Schizophrenia Across the Life Span



Older Patients with Schizophrenia in the General Population



The cumulative probability of dementia and corresponding 95% CIs (dashed lines) are presented as a function of age for persons with and without schizophrenia, taking competing risk of all-cause mortality into account. The 95% CIs are very narrow for persons without schizophrenia owing to the large sample size and thus are not discernible in this graph.

Cognition in Schizophrenia
Across the Life Span:

Focus on Anticholinergic Burden

Anticholinergic Load and Cognition

- High serum anticholinergic burden → **impaired cognition** among older community dwelling adults
- High anticholinergic medications use → increase **brain atrophy**
- High cumulative exposure to anticholinergic drugs → increased risk of **dementia**

In Schizophrenia

- High serum anticholinergic burden → deficits in **verbal working memory and learning and memory**
- High serum anticholinergic activity → impaired ability to benefit from **cognitive training**
- High anticholinergic burden → impaired ability to benefit from **psychosocial interventions** through its effect on cognition

Mulsant et al, Arch Gen Psychiatry, 2003; Vinogradov et al, Am J Psychiatry, 2009; Gray et al. JAMA Intern Med, 2015; O'Reilly et al, Psychol Med, 2016; Risacher et al. JAMA Neurol, 2016

Anticholinergic Burden and Cognition in Older Patients with Schizophrenia

Model and Variable	B	SE B	β	p
AD Composite Score: $R^2=0.24$, $F(5, 54)=3.41$, $p=0.009$				
Age	0.02	0.01	0.24	0.06
Gender	0.01	0.16	0.01	0.97
Education	-0.03	0.03	-0.15	0.23
PANSS Total	0.00	0.01	0.06	0.61
ACB Total Score	0.16	0.05	0.37	0.004
SOC Score: $R^2=0.15$, $F(5, 54)=1.97$, $p=0.10$				
Age	-0.08	0.05	-0.21	0.12
Gender	-0.23	0.64	-0.05	0.73
Education	0.17	0.11	0.20	0.13
PANSS Total	0.01	0.02	0.05	0.70
ACB Total Score	-0.34	0.21	-0.21	0.11
IED Score: $R^2=0.13$, $F(5,54)=1.54$, $p=0.20$				
Age	-0.34	0.79	-0.06	0.67
Gender	20.34	10.18	0.26	0.05
Education	0.81	1.68	0.07	0.63
PANSS Total	-0.58	0.37	-0.21	0.12
ACB Total Score	-2.44	3.34	-0.10	0.47
RBANS Total Score: $R^2=0.27$, $F(5,54)=4.35$, $p=0.002^*$				
Gender	-1.32	3.26	-0.05	0.69
Education	1.67	0.53	0.37	0.003
PANSS Total	0.10	0.12	0.10	0.44
ACB Total Score	-2.93	1.08	-0.32	0.007

Anticholinergic Burden and Function in Schizophrenia Across the Life Span

Participants, N	223
Age (years), Mean (SD)	49 (13.1)
Female, N (%)	68 (30%)
Education (years), Mean (SD)	12.4 (2.7)
ACB total score, Mean (SD)	3.0 (2.3)
Frequency (N, %)	
Score = 0	17 (7.6%)
Score = 1	59 (26.5%)
Score = 2	5 (2.2%)
Score ≥ 3	142 (63.7%)
Olanzapine Equivalence, Mean (SD)	14.7 (11.9)
BPRS 18, Mean (SD)	36.1 (10.4)
Negative symptoms score, Mean (SD)	8.5 (3.1)
Global Cognition (MCCB), Mean T-score (SD)	31.8 (11.2)
UPSA Functional Domains scores Mean (SD)	
Communication (0-20)	14.6 (4.4)
Finances (0-20)	17.8 (3.0)
Comprehension and Planning of Recreational Activities (0-10)	7.6 (2.0)
Transportation (0-20)	17.2 (4.3)
Household chores (0-20)	16.2 (4.5)
UPSA Total (0-90)	73.4 (12.7)

Model & Variable	B	SE B	β	p
Total UPISA: $R^2 = 0.52$, $F(6, 216) = 39.7$, $p < 0.0001$				
Age	-0.242	0.051	-0.250	<0.0001
Education	0.638	0.244	0.134	0.010
Negative Symptoms	-0.182	0.196	-0.045	0.355
Global Cognition	0.580	0.064	0.512	<0.0001
Olanzapine Equivalence	0.106	0.060	0.100	0.077
ACB Score	-0.865	0.313	-0.154	0.006

Khan et al. Schizophr Bull, 2020

Cognition in Schizophrenia Across the Life Span:

Focus on D2 Receptor Blockade

From: **Neurocognitive Effects of Antipsychotic Medications in Patients With Chronic Schizophrenia in the CATIE Trial**

Arch Gen Psychiatry. 2007;64(6):633-647. doi:10.1001/archpsyc.64.6.633

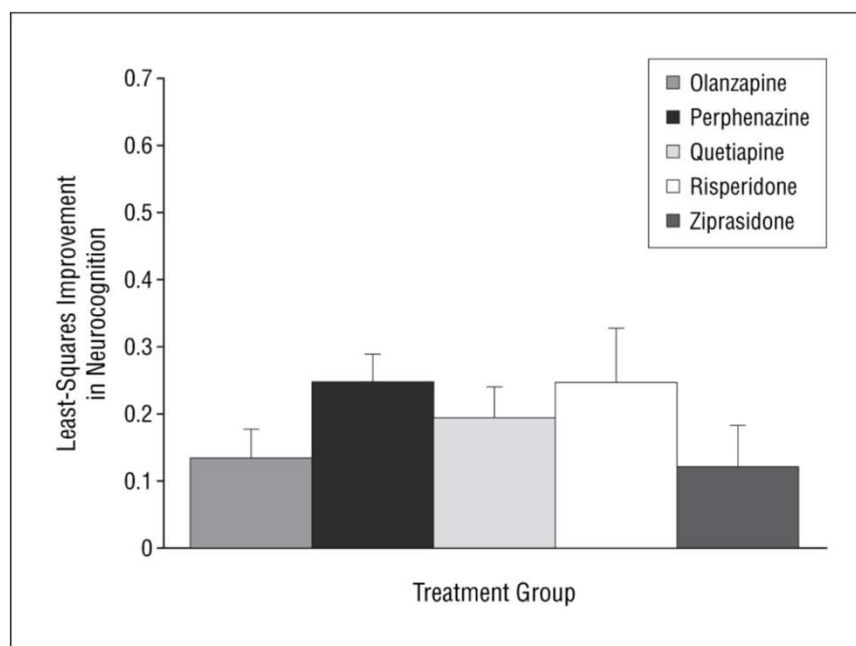


Figure Legend:

Least-squares mean improvement in neurocognitive composite score after 2 months of antipsychotic treatment, adjusted for baseline score and whether the patient required crisis stabilization in the 3 months prior to study entry. Patients with tardive dyskinesia were not included in the data presented in this figure (data set 1). Only the ziprasidone hydrochloride data were from data set 3, collected when ziprasidone became available, after 40% of the patients had already been entered into the study.

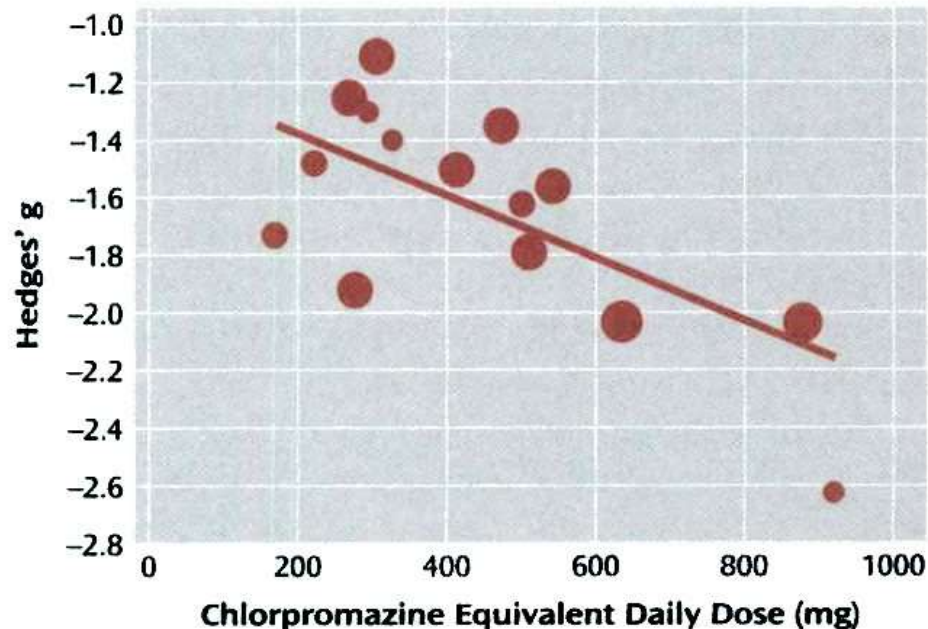
Quetiapine was given as quetiapine fumarate.

Date of download: 3/28/2015

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Antipsychotics and Cognition in Schizophrenia

FIGURE 3. Association Between Mean Chlorpromazine Equivalent Daily Dose and Coding Task Effect Size^a



^a The position of the point in the lower right-hand corner of the figure suggests that it might be an outlier; however, as indicated by the size of this data point, its contribution to the metaregression analysis was relatively small. When it is removed, the relationship remains significant (metaregression β coefficient = -0.001 , 95% CI = -0.002 to -0.00001 , $p=0.031$).

Stable schizophrenia

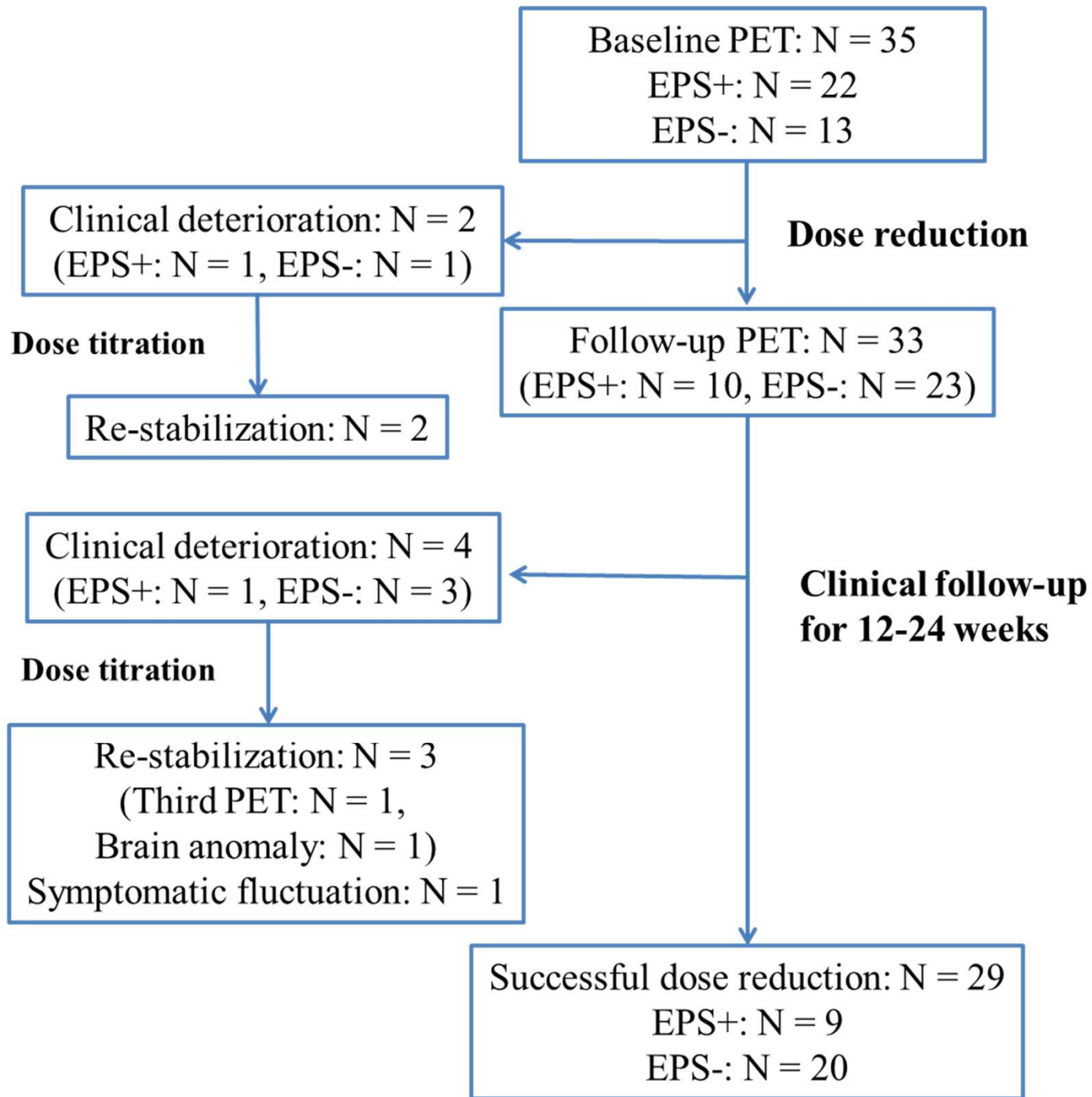
- Aged ≥ 50 years
- Stable for ≥ 6 months
- On the same dose of \geq RIS 2mg/day or OLZ 10mg/day

① [^{11}C]-raclopride-PET
② Clinical assessments

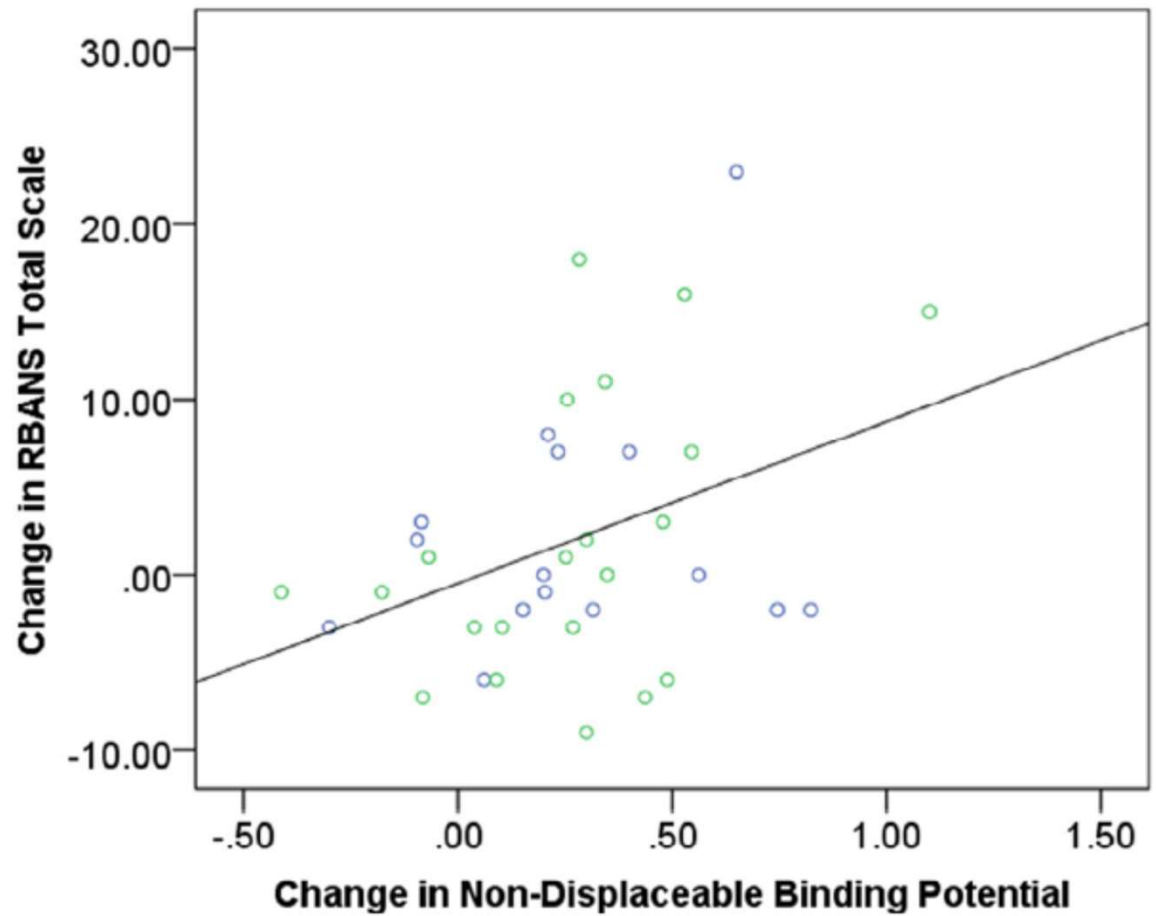
① Gradual dose reduction to 60% of the baseline dose by RIS 0.5mg/week or OLZ 2.5mg/week (Target dose \geq RIS 1.5mg/day, OLZ 7.5mg/day)
② Clinical assessments

① [^{11}C]-raclopride-PET
② Clinical assessments

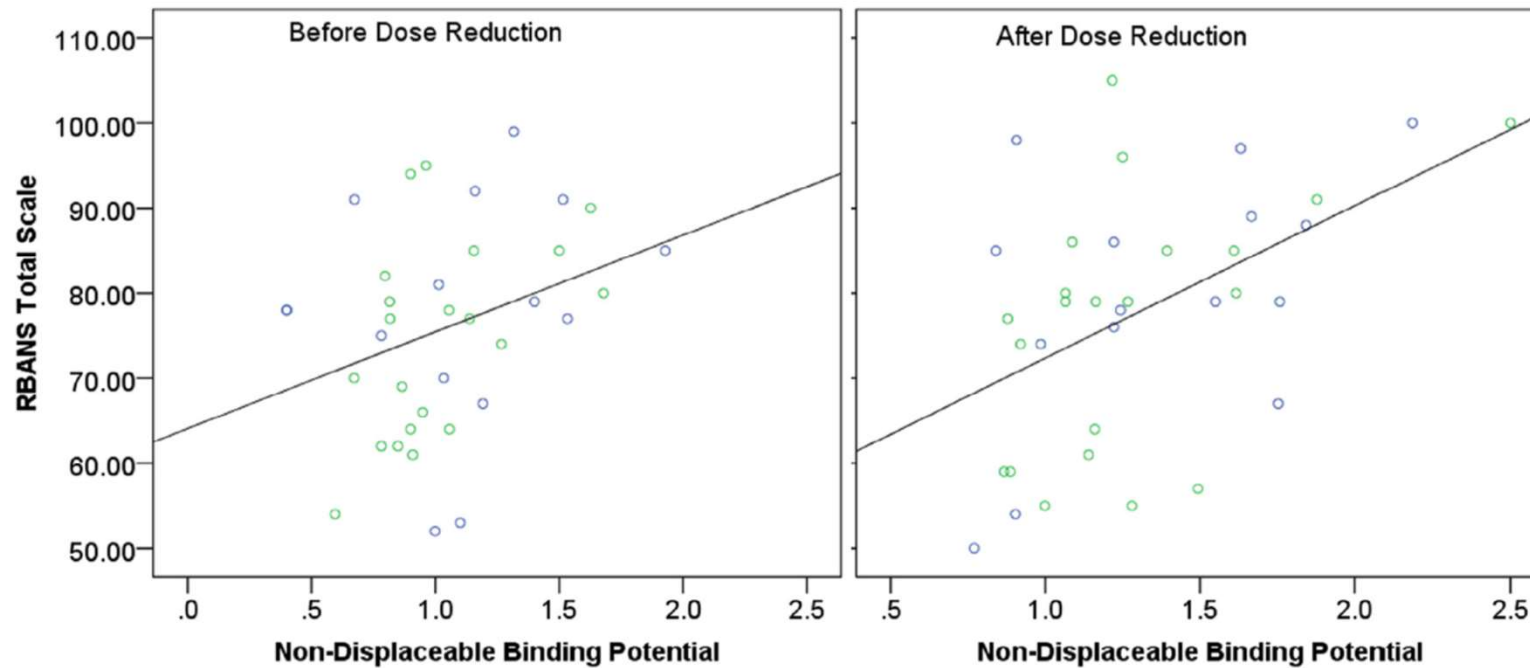
Clinical follow-up for 12-24 weeks



	Baseline PET visit	Follow-up PET visit	Final visit	df	F	p
Clinical symptoms			60.7 ±			
PANSS total score	61.3 ± 14.4	60.4 ± 14.6	16.5	1.19, 40.29	0.54	.49
BPRS total score	42.1 ± 9.2	42.0 ± 10.0	42.2 ± 10.7	1.56, 52.88	0.04	.93
AIMS total score	1.3 ± 2.3	1.1 ± 2.1	1.0 ± 1.9	1.57, 53.26	2.17	0.14
BAS total score	0.8 ± 1.5	0.3 ± 0.9	0.3 ± 0.8	1.34, 45.48	6.64	.008 ^c
SAS total score	3.5 ± 2.7	2.3 ± 2.2	1.9 ± 2.1	1.52, 51.81	23.35	< .001 ^d
	<u>Baseline PET visit</u>	<u>Follow-up PET visit</u>	-	-	<u>Z</u>	<u>p</u>
Serum prolactin concentrations (ug/L)	23.4 ± 31.3	15.8 ± 13.6			-3.99	< .001
D_{2/3}R occupancies (%)						
Putamen	65.1 ± 12.1	58.5 ± 11.5			-3.53	< .001
Caudate	68.6 ± 12.1	60.6 ± 11.1			-3.99	< .001
Ventral striatum	69.0 ± 12.0	64.3 ± 12.4			-2.76	.01
Whole striatum	67.6 ± 11.4	61.1 ± 11.0			-3.70	< .001



Model	Variable	<i>B</i>	<i>SE B</i>	β	<i>P</i>
Δ RBANS Total Scale $R^2 = 0.27, F_{(4,31)} = 2.84$ $p = 0.04$	Age	-0.30	0.17	-0.27	0.09
	Δ PANSS Total Score	-0.32	0.60	-0.09	0.57
	Δ BP _{ND}	-10.46	3.85	-0.43	0.011
	Baseline BP _{ND}	4.24	3.47	0.20	0.23



Before Dose Reduction

After Dose Reduction

Model	Variable	<i>B</i>	<i>SE B</i>	β	<i>P</i>	Model	<i>B</i>	<i>SE B</i>	β	<i>P</i>
RBANS Total Scale (Primary Analyses)										
$R^2 = 0.21, F_{(3,32)} = 2.85$	Age	0.22	0.31	0.12	0.48	$R^2 = 0.33, F_{(3,32)} = 5.14$	-0.13	0.35	-0.06	0.73
$p = 0.053$	PANSS	-0.32	0.15	-0.36	0.047 ^a	$p = 0.005$	-0.28	0.17	-0.27	0.11
	BP _{ND}	10.03	5.56	0.29	0.081		16.70	5.42	0.46	0.004 ^b

Care for Late-Life Schizophrenia

Chronic Care Model

- Medications management
- Mood and cognition monitoring
- Coordination of care with primary care providers
- Accessible services
- Social integration
- Social rehabilitation services

Antipsychotics

Best evidence is for olanzapine or risperidone

Consider risperidone as first line, given the high anticholinergic burden of olanzapine

Consider other atypical antipsychotics with low anticholinergic burden, e.g., aripiprazole and ziprasidone

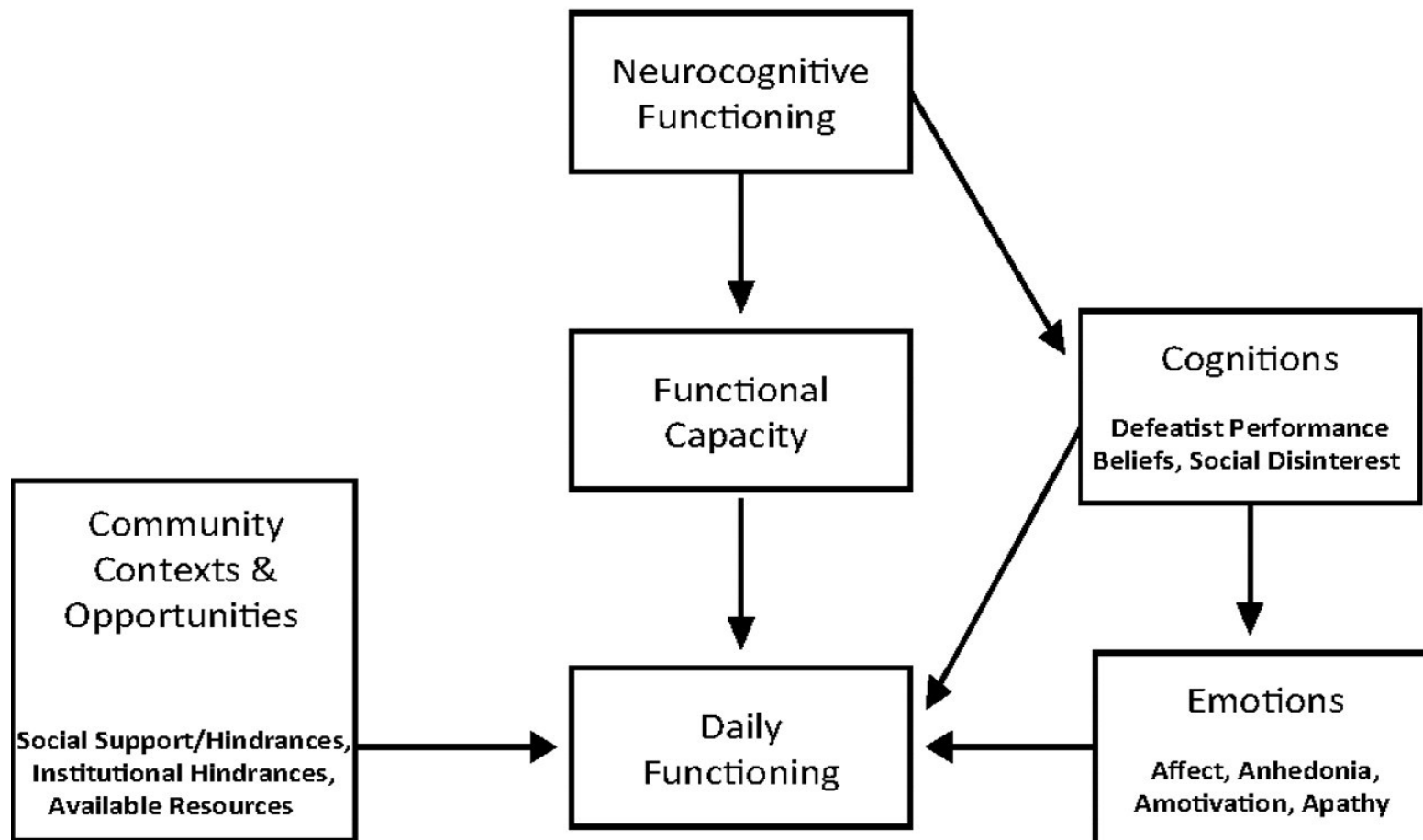
Most clozapine studies avoided older patients: Still, worth considering it in treatment-resistant patients instead of trying, for example, olanzapine, with equally high anticholinergic burden

Medication	Initial dose	Titration step	Maintenance target dose	Half-life (hours)
Aripiprazole	2–5	2–5	10–15	75
Clozapine	6.25–12.5	12.5–25	100–200	4–66
Olanzapine	2.5–5	2.5–5	5–20	21–54
Quetiapine	12.5–50	25–50	100–450	6
Risperidone	0.25–0.5	0.25–0.5	1–4	3–20

Focus on Function

Cognition and Function in Schizophrenia

Model of Functional Outcome in Schizophrenia



Functional Adaptation Skills Training (FAST)

- Manualized, group format, 24 weeks, 1x/week, 120 min each session
- 6 areas of everyday functioning:
 - medication management
 - social skills
 - communication skills
 - organization and planning
 - transportation
 - financial management

Helping Older People Experience Success (HOPES)

- Psychosocial Intervention:
 - Weekly classes for 1 year followed by booster sessions monthly for another year
 - Manualized
 - 7 modules: Communicating Effectively, Making and Keeping Friends, Making the Most of Leisure Time, Healthy Living, Using Medications Effectively, and Making the Most of a Health Care Visit
- Preventative Health Care :
 - Monthly meeting with a nurse embedded in mental health setting

Cognitive Behavioral Social Skills Training (CBSST)

- Group therapy tailored to Schizophrenia & Aging:
 - Memory deficits
 - Physical and mental health disability
 - Limited social support
 - Increased dependency:
 - Family
 - Social services
 - Health care providers
 - Ageism beliefs
- Manual based with a patient workbook

Thank You!