Università Magna Graecia di Catanzaro
Dipartimento di Scienze della Salute
U.O. e Scuola di Specializzazione in Psichiatria

La Terapia Antipsicotica e la ricaduta sugli Interventi Riabilitativi

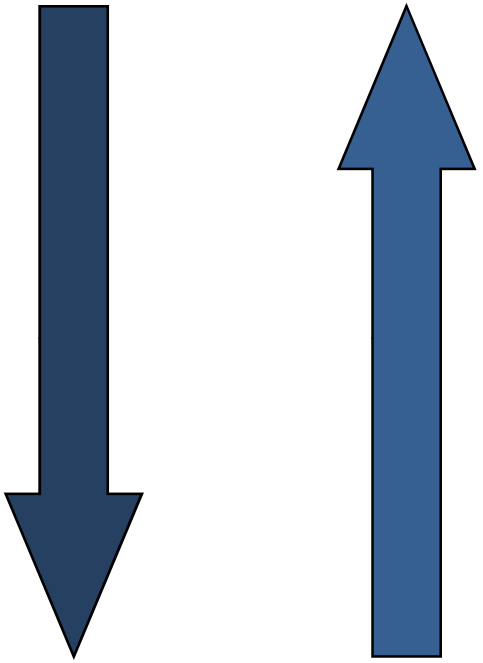
P. De Fazio

Catanzaro, 14 novembre 2015

Quali sono gli outcome a lungo termine nella schizofrenia?

Riduzione di:

- sintomi[1]
- impatto del problema sulla famiglia e sugli amici del paziente[1]
- ricaduta[2]
- ospedalizzazione[2]



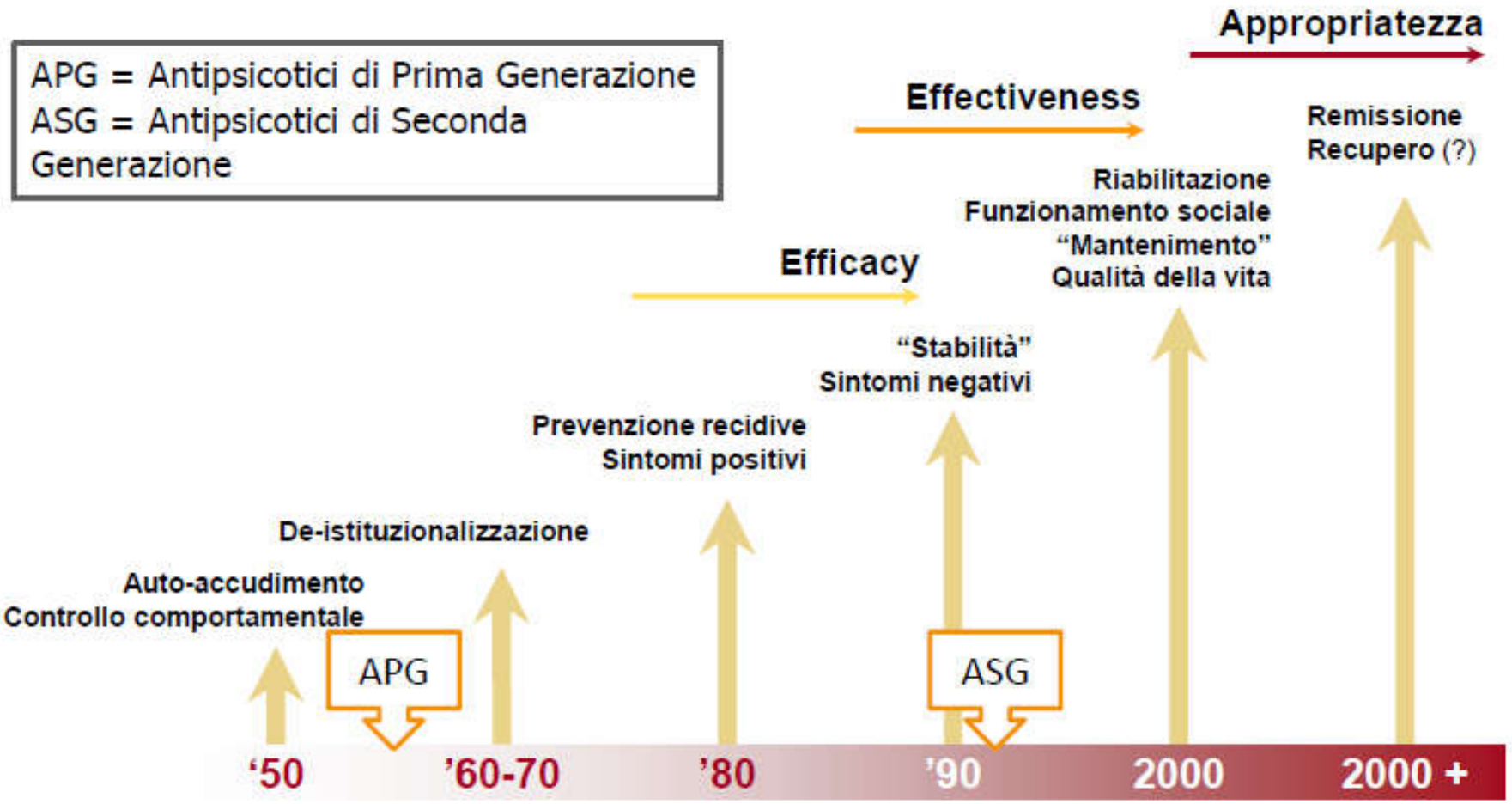
Aumento di:

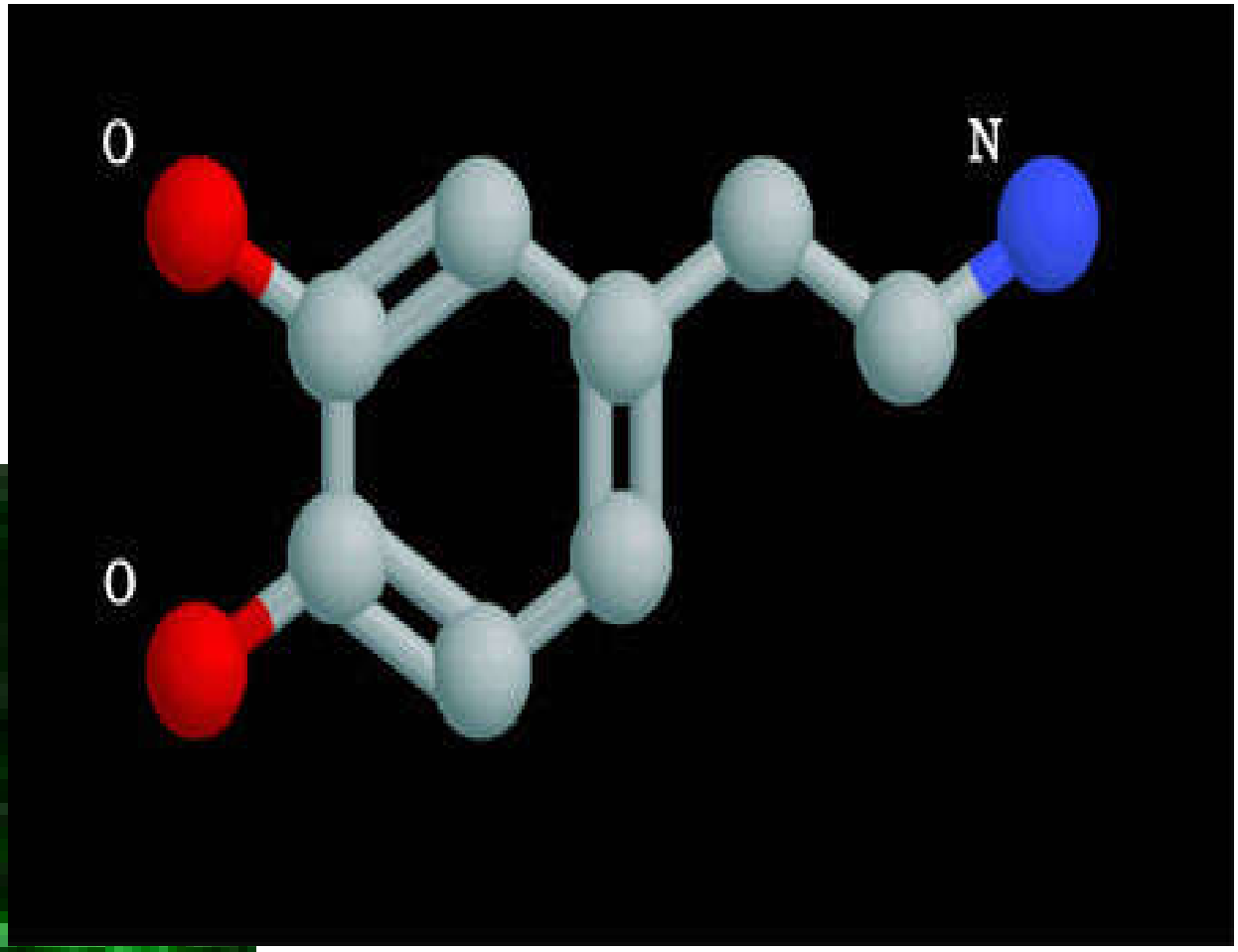
- aderenza alla terapia[3]
- funzionamento sociale[1]
- grado di soddisfazione del paziente[4]
- qualità della vita[5]

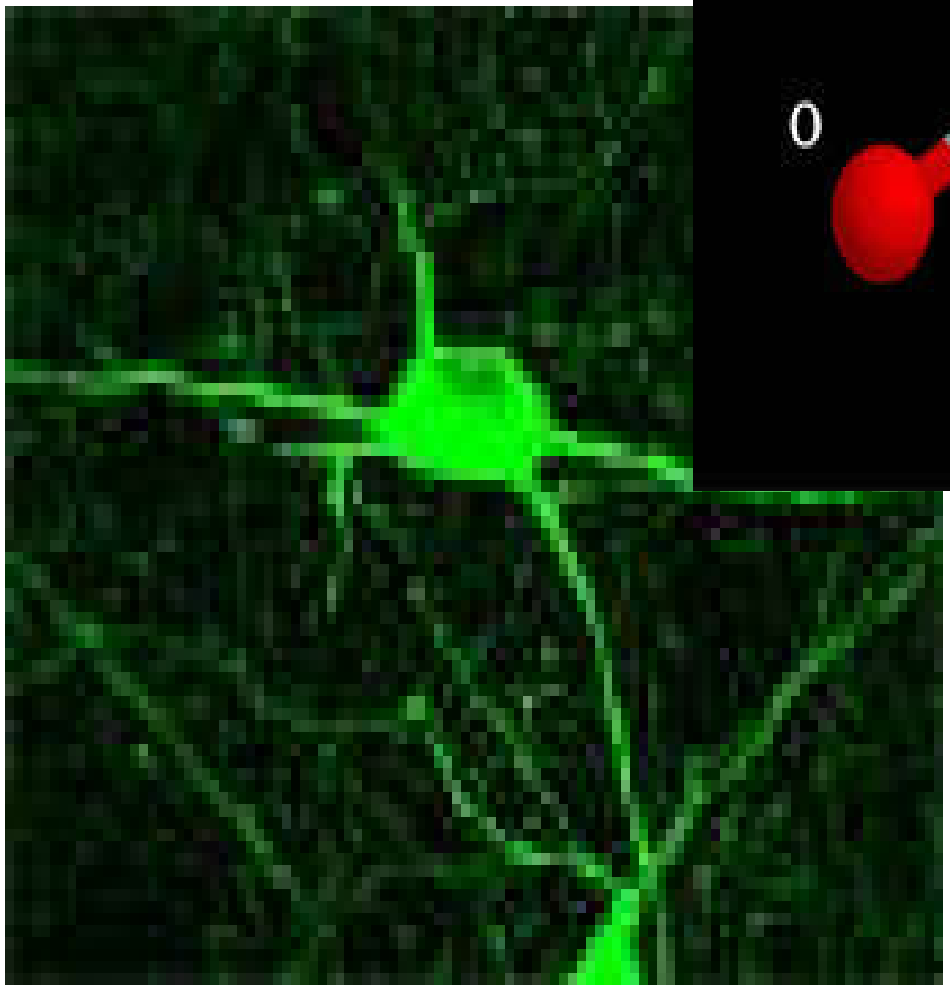
1. Andreasen et al., Am J Psychiatry 2005: 162:441-449
2. Schooler J Clin Psychiatry 2003; 64:14-17
3. Llorca et al., Psychiatry Res 2008; 161:235-247
4. Gharawab et al., BMC Psychiatry 2006; 6: 45
5. Eack & Newhill, Schizophr bull 2007; 33: 125-1237

Outcomes della schizofrenia

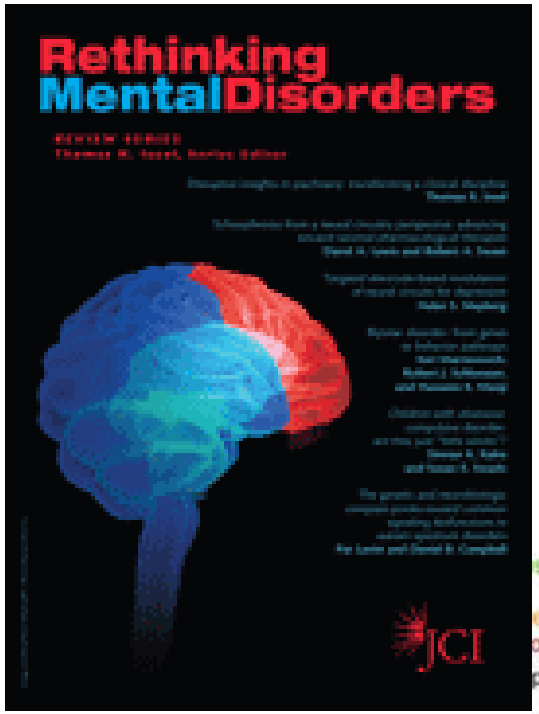
APG = Antipsicotici di Prima Generazione
ASG = Antipsicotici di Seconda Generazione

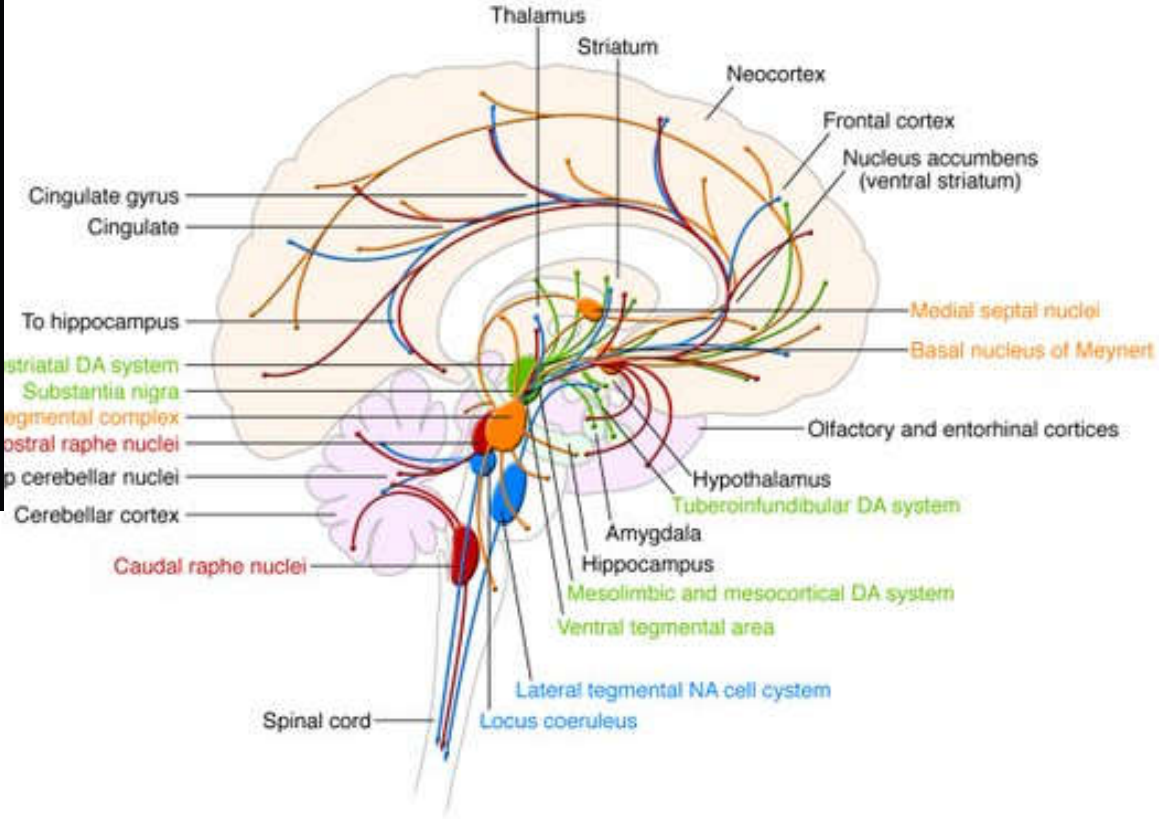






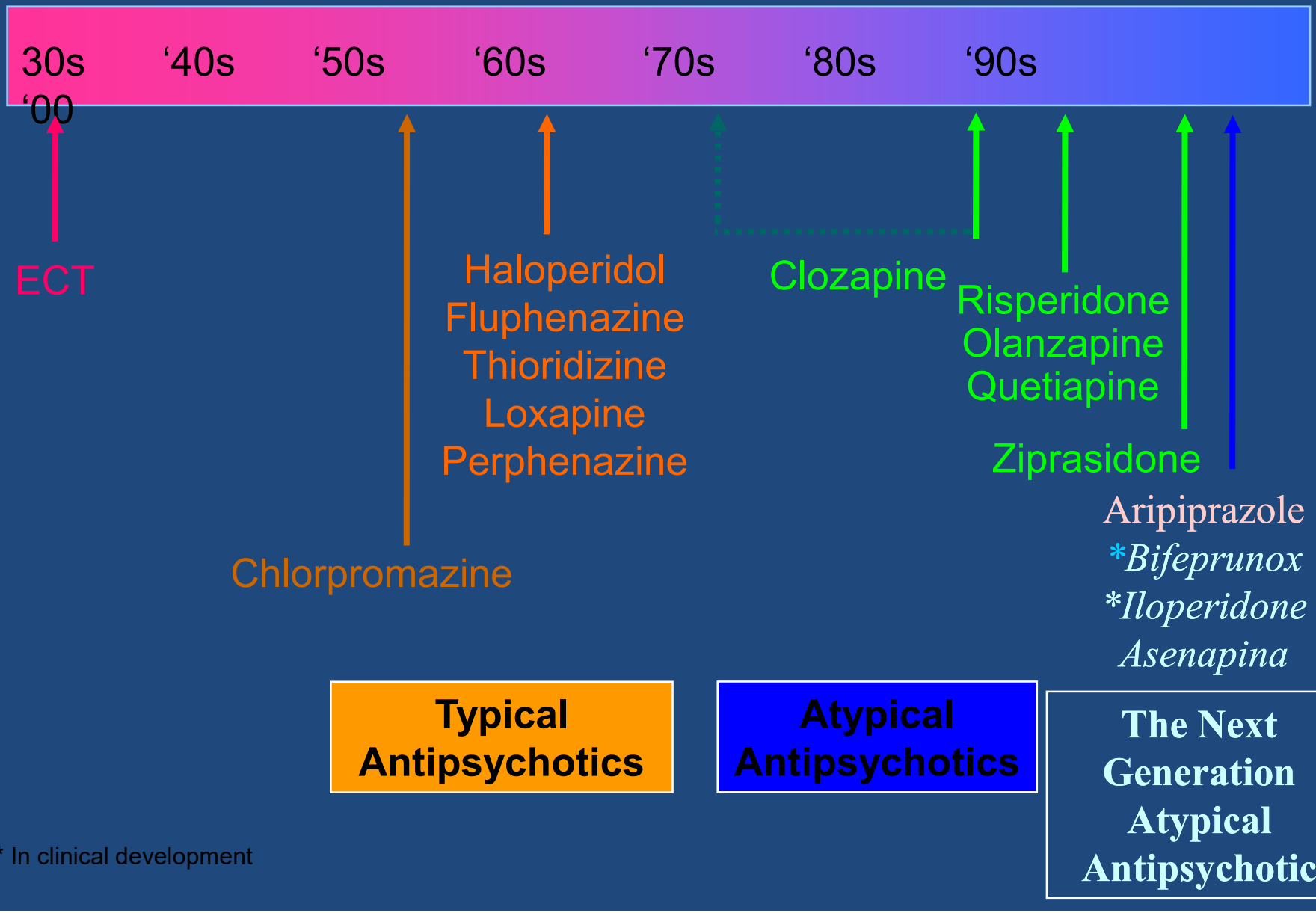
DOPAMINA





Locations of the monoaminergic nuclei within the brain as well as the projections from these nuclei throughout the brain.
Nuclei as well as their projections are color coded: yellow, cholinergic; green, dopaminergic; blue, noradrenergic; red, serotonergic

Developments in Medical Treatments for Psychotic Disorders



* In clinical development

Remission in Schizophrenia: Proposed Criteria and Rationale for Consensus

Nancy C. Andreasen, M.D., Ph.D.

William T. Carpenter, Jr., M.D.

John M. Kane, M.D.

Robert A. Lasser, M.D.

Stephen R. Marder, M.D.

Daniel R. Weinberger, M.D.

New advances in the understanding of schizophrenia etiology, course, and treatment have increased interest on the part of patients, families, advocates, and professionals in the development of consensus-defined standards for clinical status and improvement, including illness remission and recovery. As demonstrated in the area of mood disorders, such standards provide greater clarity around treatment goals, as well as an improved framework for the design and comparison of investigational trials and the subsequent evaluation of the effectiveness of interventions. Unlike the approach to mood disorders, however, the novel application of the concept of standard outcome criteria to schizophrenia must reflect the wide heterogeneity of its long-term course and outcome, as well as the variable effects of different treatments on schizophrenia symptoms. As an initial step in developing operational criteria, an expert working group reviewed available definitions and assessment instruments to provide a conceptual framework for symptomatic, functional, and cognitive domains in schizophrenia as they relate to remission of illness. The first consensus-based operational criteria for symptomatic remission in schizophrenia are based on distinct thresholds for reaching and maintaining improvement, as opposed to change criteria, allowing for alignment with traditional concepts of remission in both psychiatric and nonpsychiatric illness. This innovative approach for standardizing the definition for outcome in schizophrenia will require further examination of its validity and utility, as well as future refinement, particularly in relation to psychosocial and cognitive function and dysfunction. These criteria should facilitate research and support a positive, longer-term approach to studying outcome in patients with schizophrenia.

(Am J Psychiatry 2005; 162:441–449)

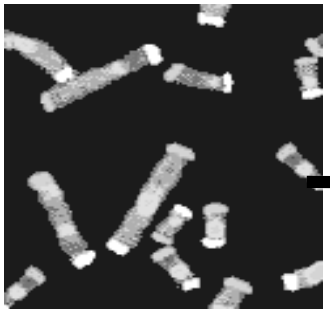
Sfide della terapia della Schizofrenia

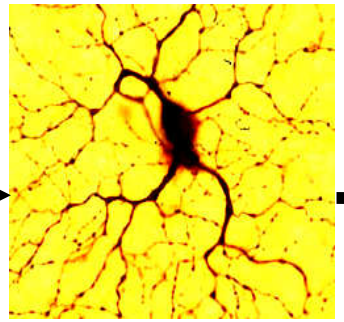
- Sintomi Negativi
- Sintomi cognitivi
- Stigma
- “Insight” alterato
- “Compliance” alterata
- Abuso di sostanze
- Rischio di comportamento violento
- Rischio suicidario
- Problemi medici frequenti e misconosciuti

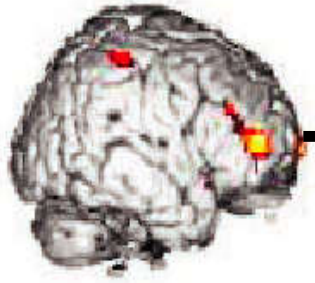
Environmental factors

Low SES Substance Abuse Urbanicity Perinatal Complications Elderly father

Dysbindin-1
COMT
NRG-1







Abnormal
Emotional regulation
Attention
Memory
Perception

Genes:
Multiple susceptibility genes each of small effect

Cells:
Abnormalities in enzymes
DA signal/noise
Nicotine or cannabinoid receptors

Systems:
Abnormal cortical micro-circuits neural connections & information processing

Abnormal
Thought, speech, cognitive performanc e

Abnormal
Behavior

A continuum of symptoms clusters of various severity

Psychiatric Diagnosis

Adapted from D Weinberger

Effect of COMT Val$^{108/158}$ Met genotype on frontal lobe function and risk for schizophrenia

Michael F. Egan*†, Terry E. Goldberg*, Bhaskar S. Kolachana*, Joseph H. Callicott*, Chiara M. Mazzanti‡, Richard E. Straub§, David Goldman‡, and Daniel R. Weinberger*

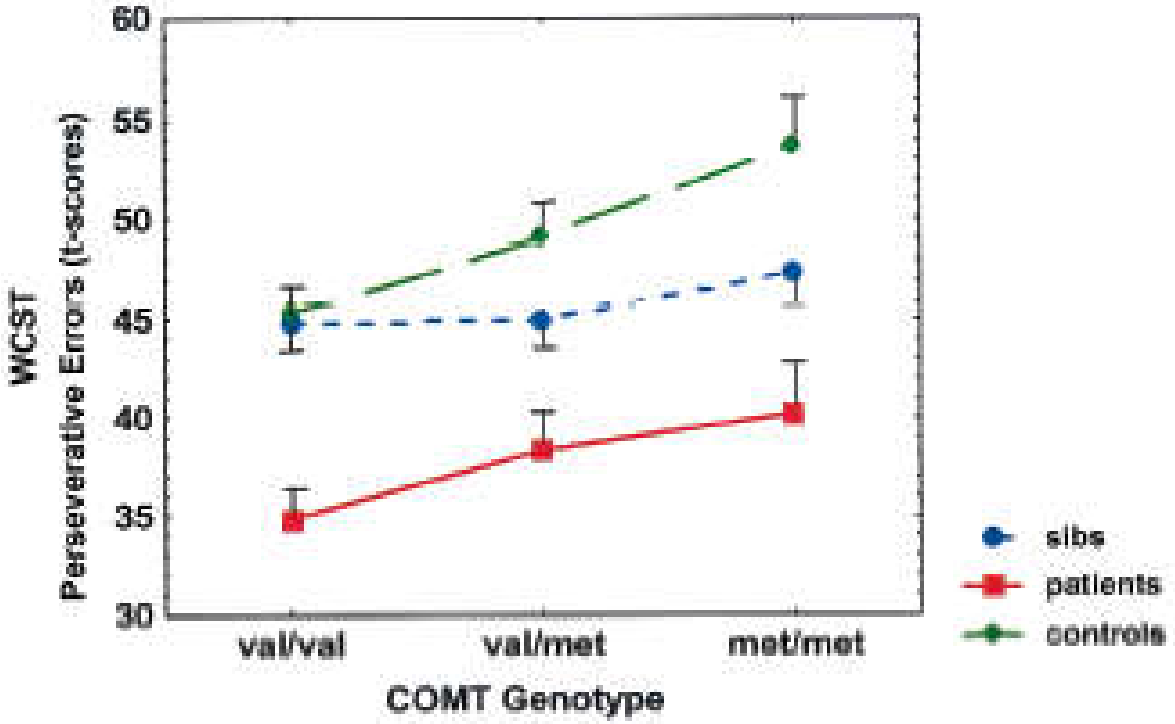


Fig. 1. WCST perseverative error *t* scores (± SE) by genotype for each group (population mean = 50, SD = 10, lower scores indicate worse performance). Main effect of genotype: $F = 4.93$, df = 2,224, $P = 0.008$.

Schizophrenia Bulletin vol. 35 no. 3 pp. 549–562, 2009
doi:10.1093/schbul/sbp006
Advance Access publication on March 26, 2009

The Dopamine Hypothesis of Schizophrenia: Version III—The Final Common Pathway

Oliver D. Howes[2,3] and Shitij Kapur[1,2]

[2]Positron Emission Tomography (PET) Psychiatry Group, Medical Research Council (MRC) Clinical Sciences Centre, Faculty of Medicine, Imperial College London, Hammersmith Hospital Campus, London W12 0NN, UK; [3]Institute of Psychiatry, King's College London, London SE5 8AF, UK

cus on identifying and manipulating the upstream factors that converge on the dopaminergic funnel point.

Key words: psychosis/biology/etiology, cause/brain/imaging, pathophysiology/risk factors/treatment

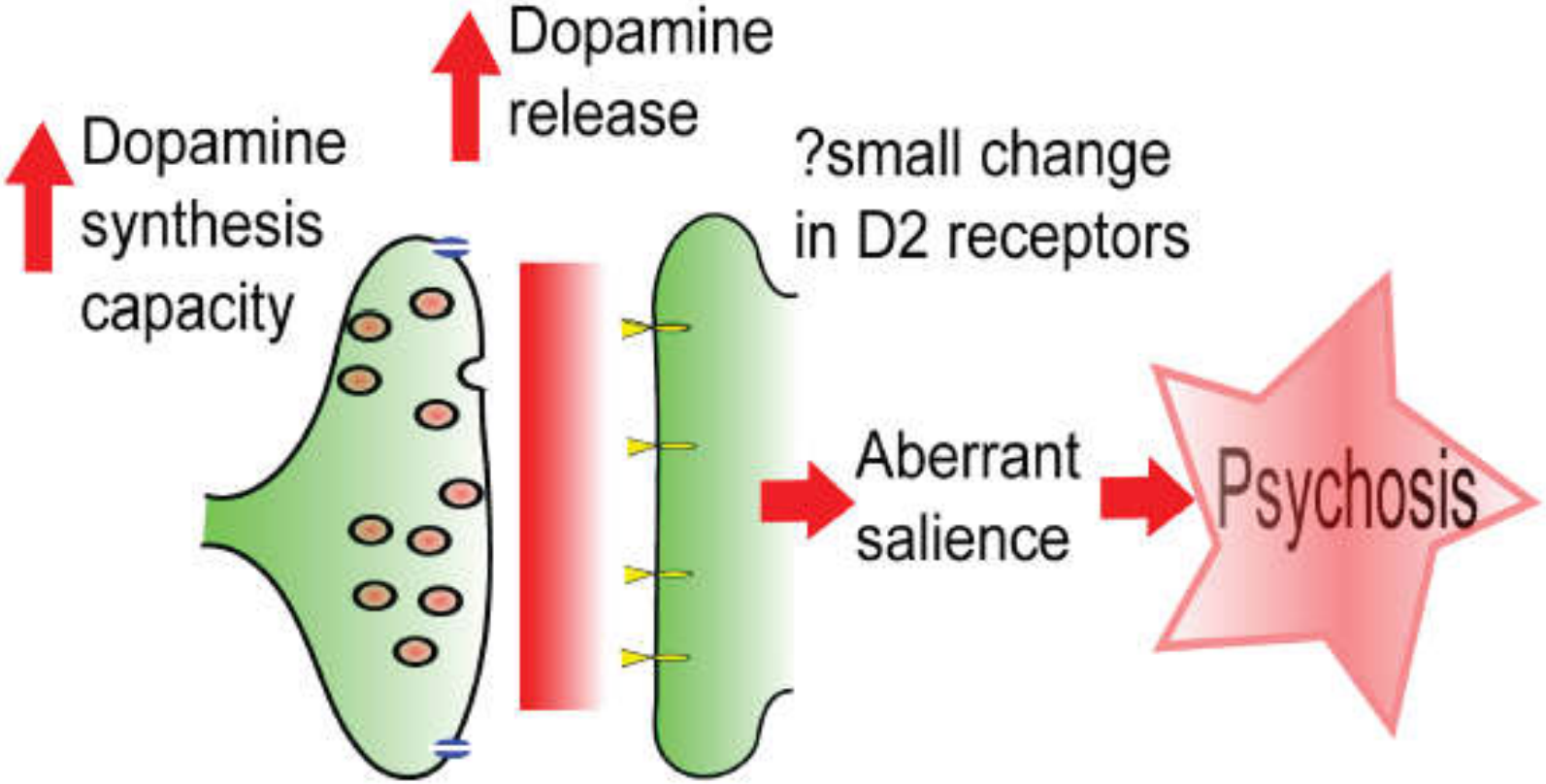


Figure 1.
Showing the main dopaminergic abnormalities in schizophrenia and the proposed mechanism linking these to psychotic symptoms

Cosa succede nella realtà?

- Gli outcome clinici ottenuti per il paziente affetto da schizofrenia sono mediocri[1].
- Tra questi:
  - elevata frequenza di ricadute[1]
  - parziale/mancata aderenza alla terapia[1]
  - perdita di autostima[2]
  - perdita di funzionalità[2]
  - burden family e alienazione dalla famiglia[2]

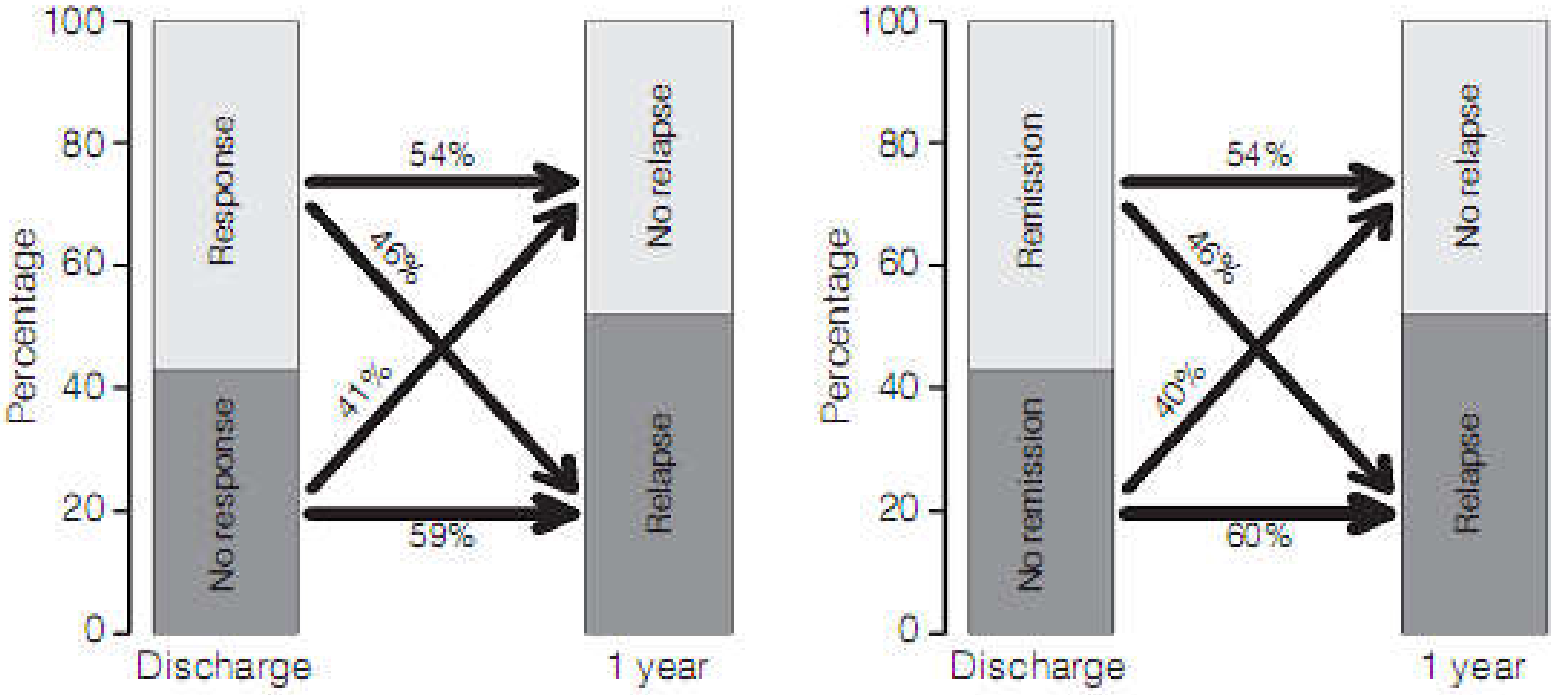
Circa il 42% dei pazienti con schizofrenia in trattamento con antipsicotici orali è riospedalizzato 1 anno dopo la dimissione[1]

1. Schooler J Clin Psychiatry 2003; 64:14-17
2. Kane CNS Spectr 2007; 12(10 suppl); 17:21-26

Predictors of Relapse in the Year After Hospital Discharge Among Patients With Schizophrenia

Rebecca Schennach, M.D.
Michael Obermeier
Sebastian Meyer
Markus Jäger, M.D.
Max Schmauss, M.D.
Gerd Laux, M.D.
Herbert Pfeiffer, M.D.
Dieter Naber, M.D.
Lutz G. Schmidt, M.D.
Wolfgang Gaebel. M.D.
Joachim Klosterkötter, M.D.
Isabella Heuser, M.D.
Wolfgang Maier, M.D.
Matthias R. Lemke, M.D.
Eckart Rüther, M.D.
Stefan Klingberg, M.D.
Markus Gastpar, M.D.
Florian Seemüller, M.D.
Hans-Jürgen Möller, M.D.
Michael Riedel, M.D.

Relapse during the year after hospital discharge among 200 patients, by whether their symptoms had responded to treatment or were in remission at discharge



Schizophrenia Bulletin vol. 40 suppl. no. 3 pp. S165–S194, 2014
doi:10.1093/schbul/sbu006

Schizophrenia—Time to Commit to Policy Change

W. Wolfgang Fleischhacker*[,1], Celso Arango[2], Paul Arteel[3], Thomas R. E. Barnes[4], William Carpenter[5], Ken Duckworth[6], Silvana Galderisi[7], Lisa Halpern[8], Martin Knapp[9], Stephen R. Marder[10], Mary Moller[11], Norman Sartorius[12], and Peter Woodruff[13]

Antipsychotic medication is effective in treating acute psychotic episodes and improves symptoms of early schizophrenia in 85% of patients[7]; long-term therapy can reduce the risk of psychotic relapses by 60%,[8] and it has also been shown to reduce suicidal behavior.[9] Currently available drugs, however, have limited effects on the most disabling "negative" symptoms and on cognitive impairment, which are associated with decreased social function.[10] The authors strongly support the rationale for research and development of new treatments to address this unmet need.

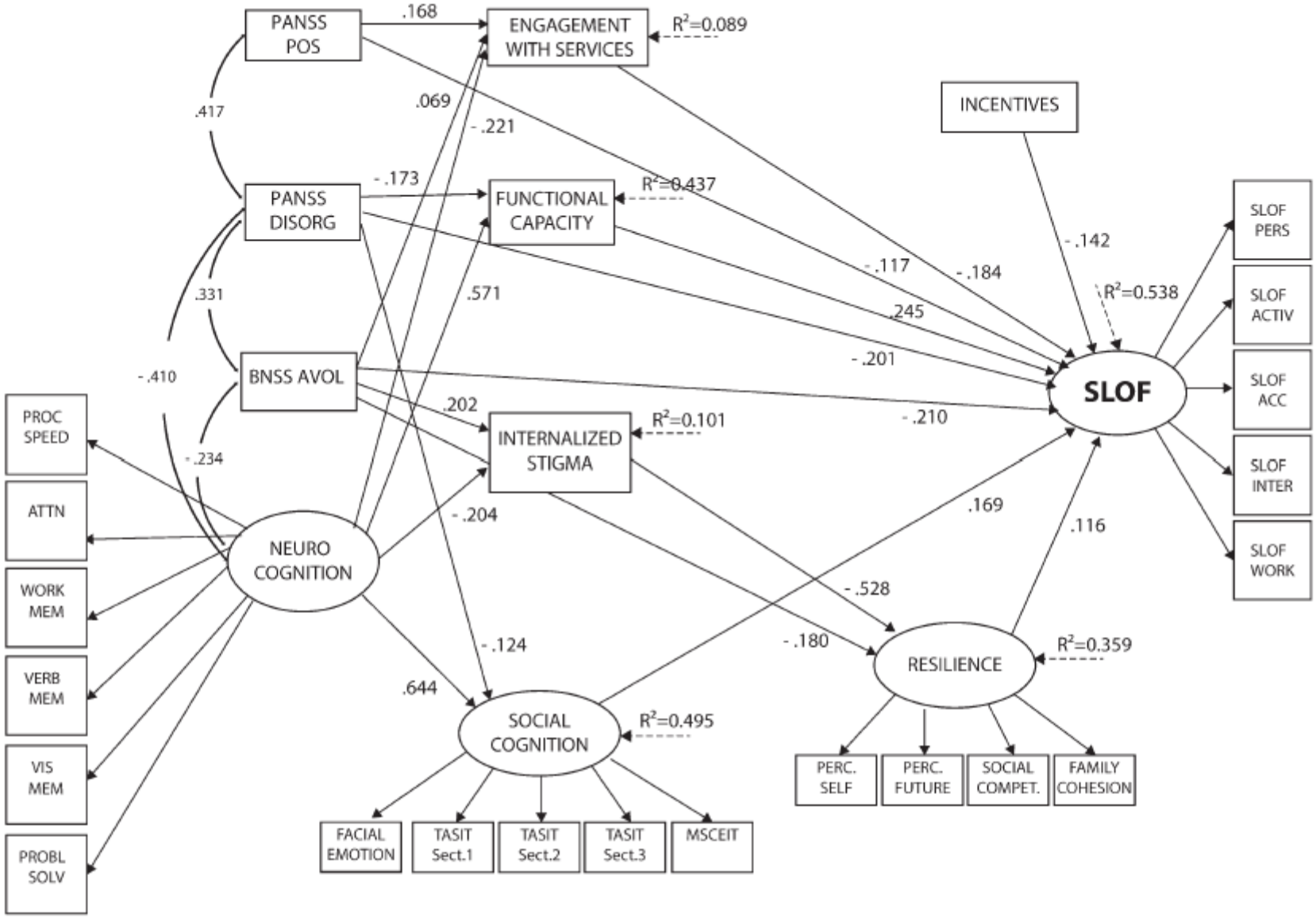
Table 1. Potential Benefits and Limitations of Current Antipsychotic Medication

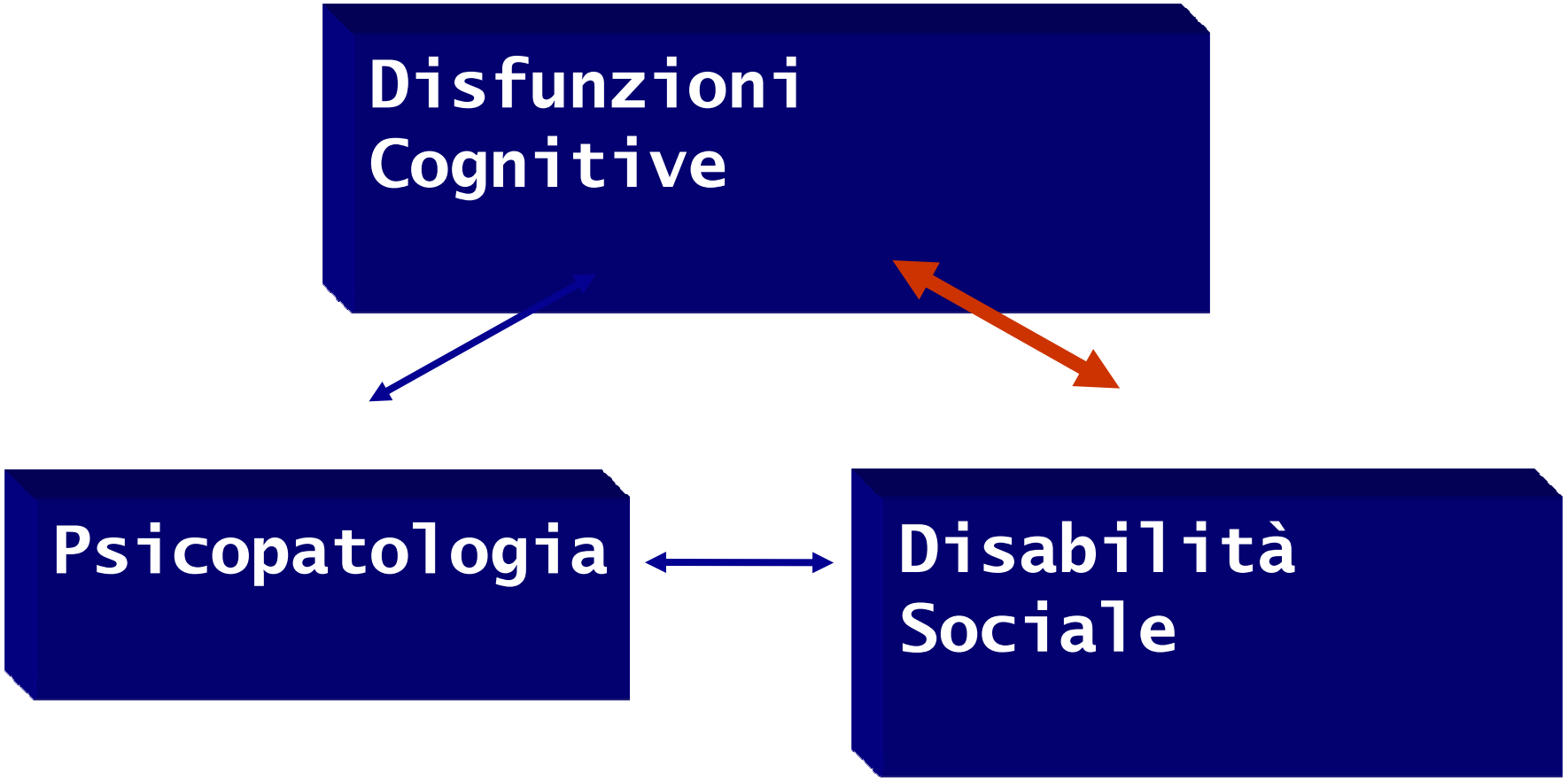
Benefits	Limitations
• Reduction of positive symptoms	• Limited efficacy against negative symptoms
• Treatment of acute episodes	• Inadequate treatment of cognitive impairment
• Reduced risk of relapse	• Troubling side effects or tolerability issues
• Provision of stability and a platform for other treatments	• Low acceptability to some patients
• Reduction of aggression and hostility	– Poor adherence
• Reduced suicidal behavior	– Negative perceptions

RESEARCH REPORT

The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia

Silvana Galderisi[1], Alessandro Rossi[2], Paola Rocca[3], Alessandro Bertolino[4], Armida Mucci[1], Paola Bucci[1], Paola Rucci[5], Dino Gibertoni[5], Eugenio Aguglia[6], Mario Amore[7], Antonello Bellomo[8], Massimo Biondi[9], Roberto Brugnoli[10], Liliana Dell'Osso[11], Diana De Ronchi[12], Gabriella Di Emidio[2], Massimo Di Giannantonio[13], Andrea Fagiolini[14], Carlo Marchesi[15], Palmiero Monteleone[16], Lucio Oldani[17], Federica Pinna[18], Rita Roncone[19], Emilio Sacchetti[20], Paolo Santonastaso[21], Alberto Siracusano[22], Antonio Vita[20], Patrizia Zeppegno[23], Mario Maj[1];
Italian Network For Research on Psychoses*


PANSS POS
PANSS DISORG
BNSS AVOL
ENGAGEMENT WITH SERVICES
FUNCTIONAL CAPACITY
INTERNALIZED STIGMA
INCENTIVES
SLOF
SLOF PERS
SLOF ACTIV
SLOF ACC
SLOF INTER
SLOF WORK
NEURO COGNITION
SOCIAL COGNITION
RESILIENCE
PROC SPEED
ATTN
WORK MEM
VERB MEM
VIS MEM
PROBL SOLV
FACIAL EMOTION
TASIT Sect.1
TASIT Sect.2
TASIT Sect.3
MSCEIT
PERC. SELF
PERC. FUTURE
SOCIAL COMPET.
FAMILY COHESION
.168
.069
-.221
.417
-.173
.331
.571
-.410
.202
-.234
-.204
.644
-.124
.245
-.117
-.184
-.201
-.210
-.142
.169
.116
-.528
-.180
R²=0.089
R²=0.437
R²=0.101
R²=0.538
R²=0.495
R²=0.359


Disfunzioni
Cognitive
Psicopatologia
Disabilità
Sociale

Neurocognizione e schizofrenia

- Sono stati identificati per la schizofrenia 8 domini separabili di deficit cognitivo:

- (7 neurocognitivi + cognizione sociale):

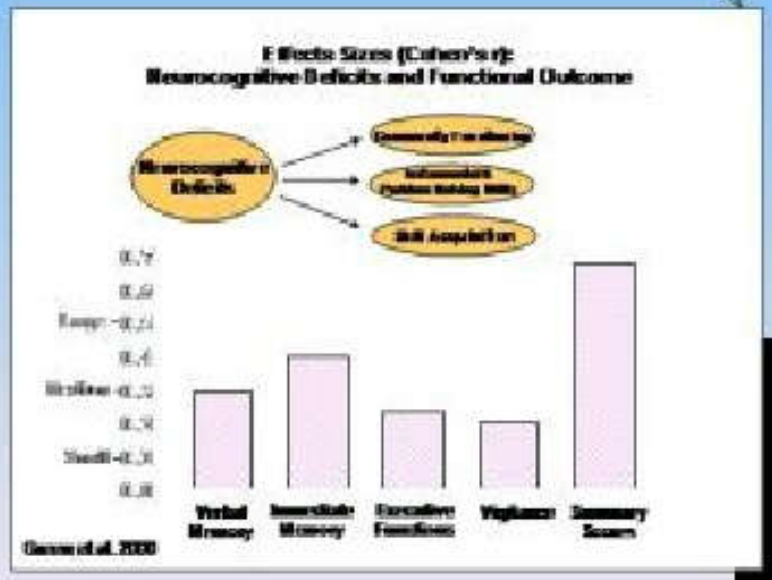
  - velocità di elaborazione
  - memoria di lavoro
  - attenzione / vigilanza
  - apprendimento e memoria verbale
  - apprendimento e memoria visiva
  - ragionamento e problem solving
  - comprensione verbale

(Green et al., 2004)

Neurocognizione e schizofrenia

Positive symptoms
(40-50 %)
Hallucinations
Delusions
Loose associations

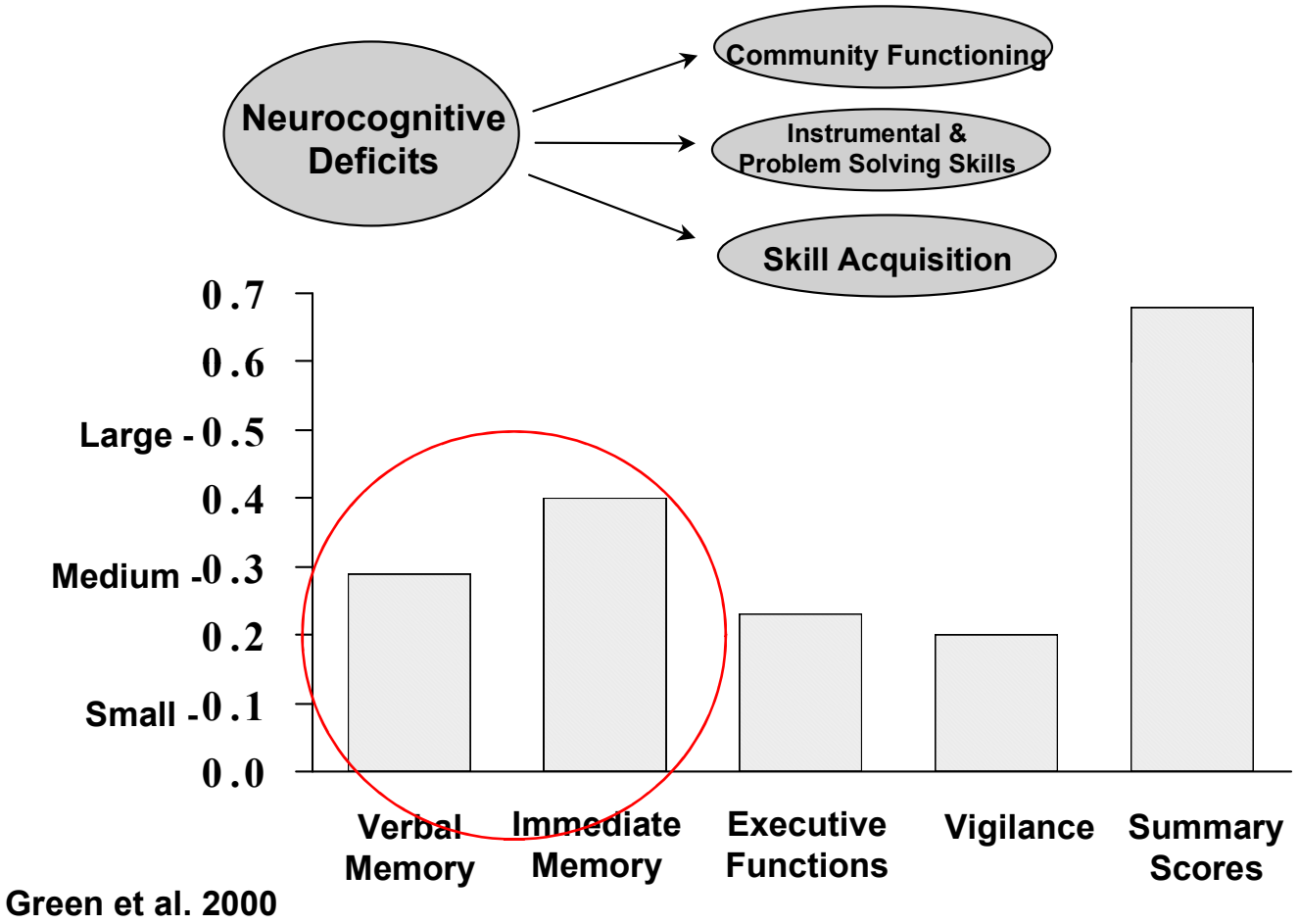
Cognitive
(80-90%)
Working memory
Selective attention



Functional
Impairment

Negative symptoms
(60-70 %)
Avolition
Anhedonia
Anergia
Asociality
Alogia

Effects Sizes (Cohen's r):
Neurocognitive Deficits and Functional Outcome



Green et al. 2000

Schizophr Res. 2010 June ; 119(1-3): 47–51. doi:10.1016/j.schres.2009.12.035.

Decreased BDNF in Patients with Antipsychotic Naïve First Episode Schizophrenia

Ripu D. Jindal, M.D[1], **Anilkumar Pillai, PhD**[2], **Sahebrao P. Mahadik, PhD**[2], **Kevin Eklund, BSN**[1], **Debra M. Montrose, PhD**[1], and **Matcheri S. Keshavan, M.D**[1,3]

[1] University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

[2] Medical College of Georgia, Augusta, GA, USA

[3] Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

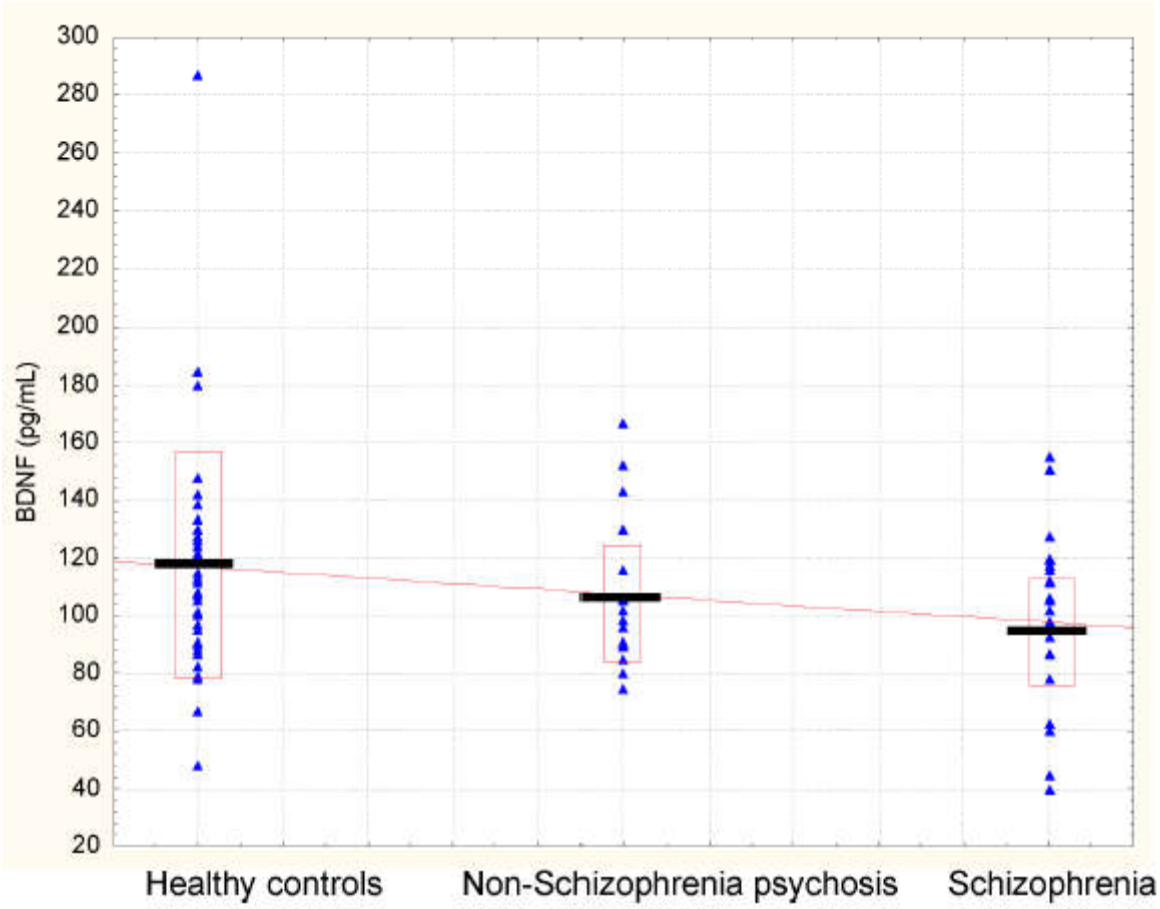


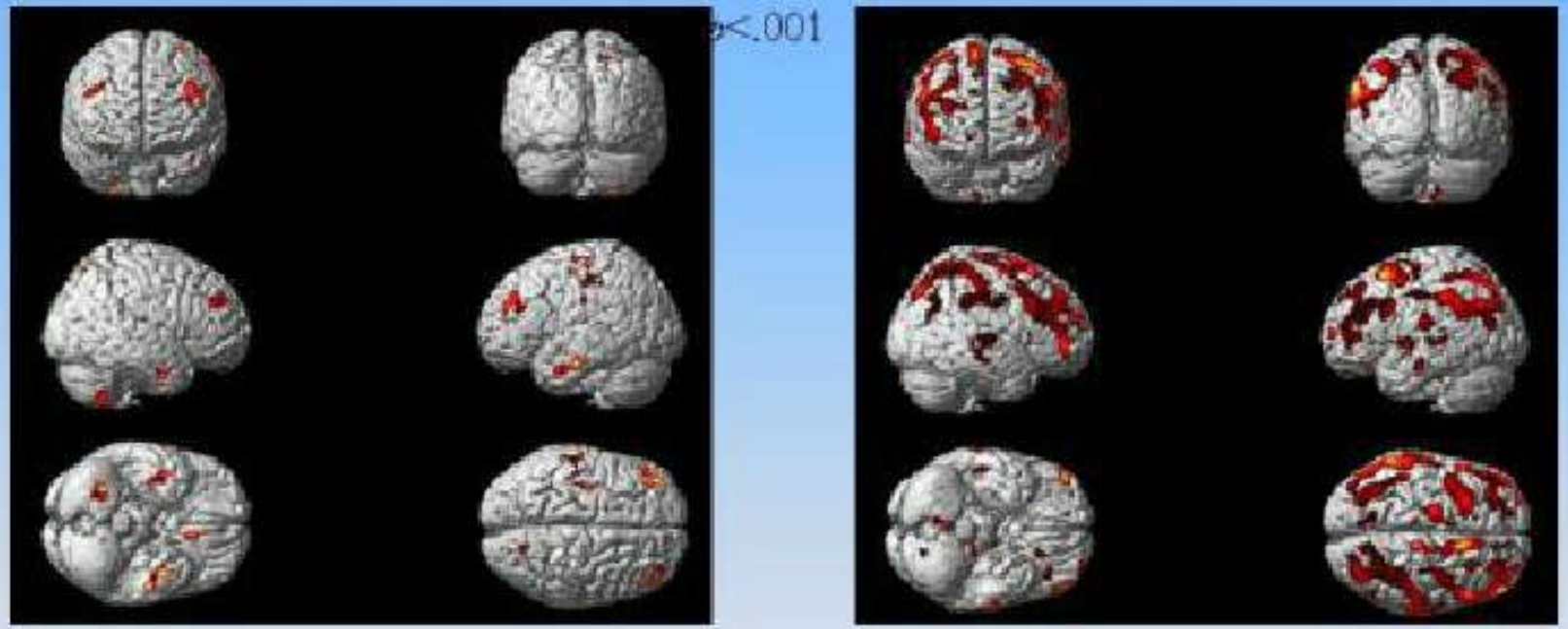
Figure 1.
Scatterplot showing serum BDNF levels (pg/mL) in first episode schizophrenia, healthy controls and non-schizophrenia psychosis patients. Boxes represent standard deviations.

Brain changes may be seen before onset of schizophrenia in teenagers at risk

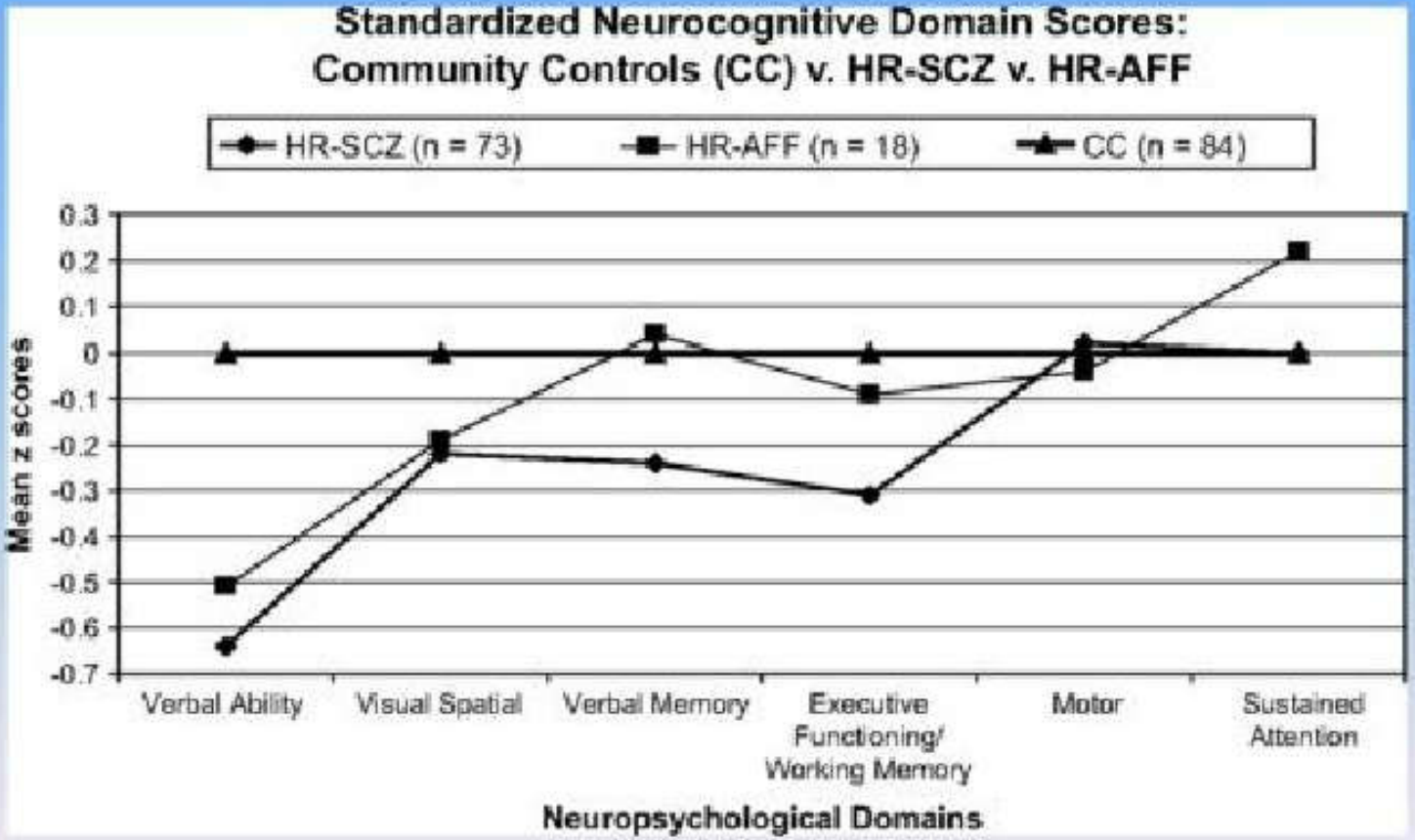
Gray matter loss during follow-up

Healthy teenagers (n=14)

High Risk offspring (n=16)

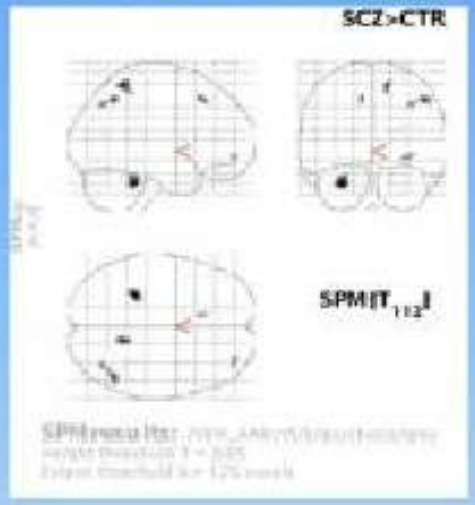


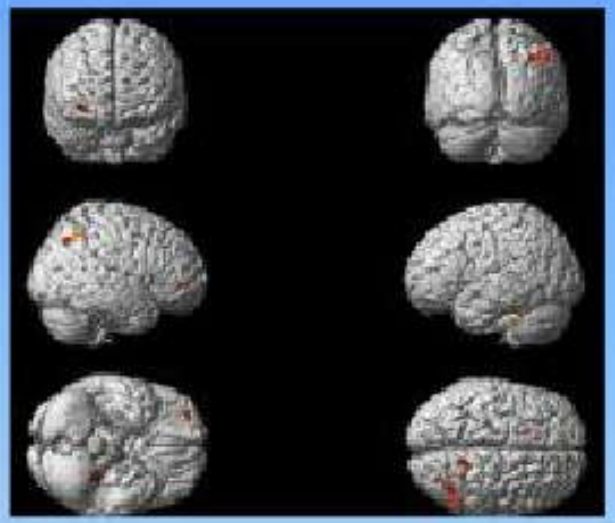
Cognitive Impairments Begin Early

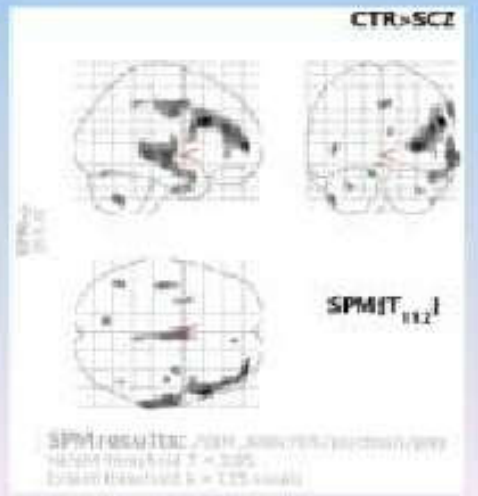


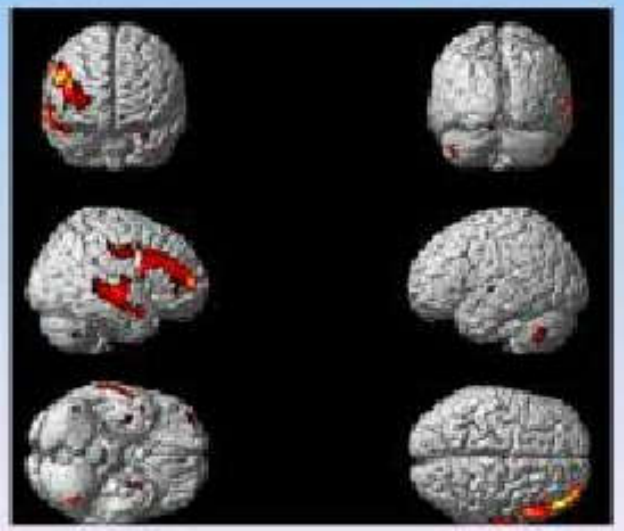
Seidman et al., 2006

Frontal and temporal gray matter loss in early schizophrenia

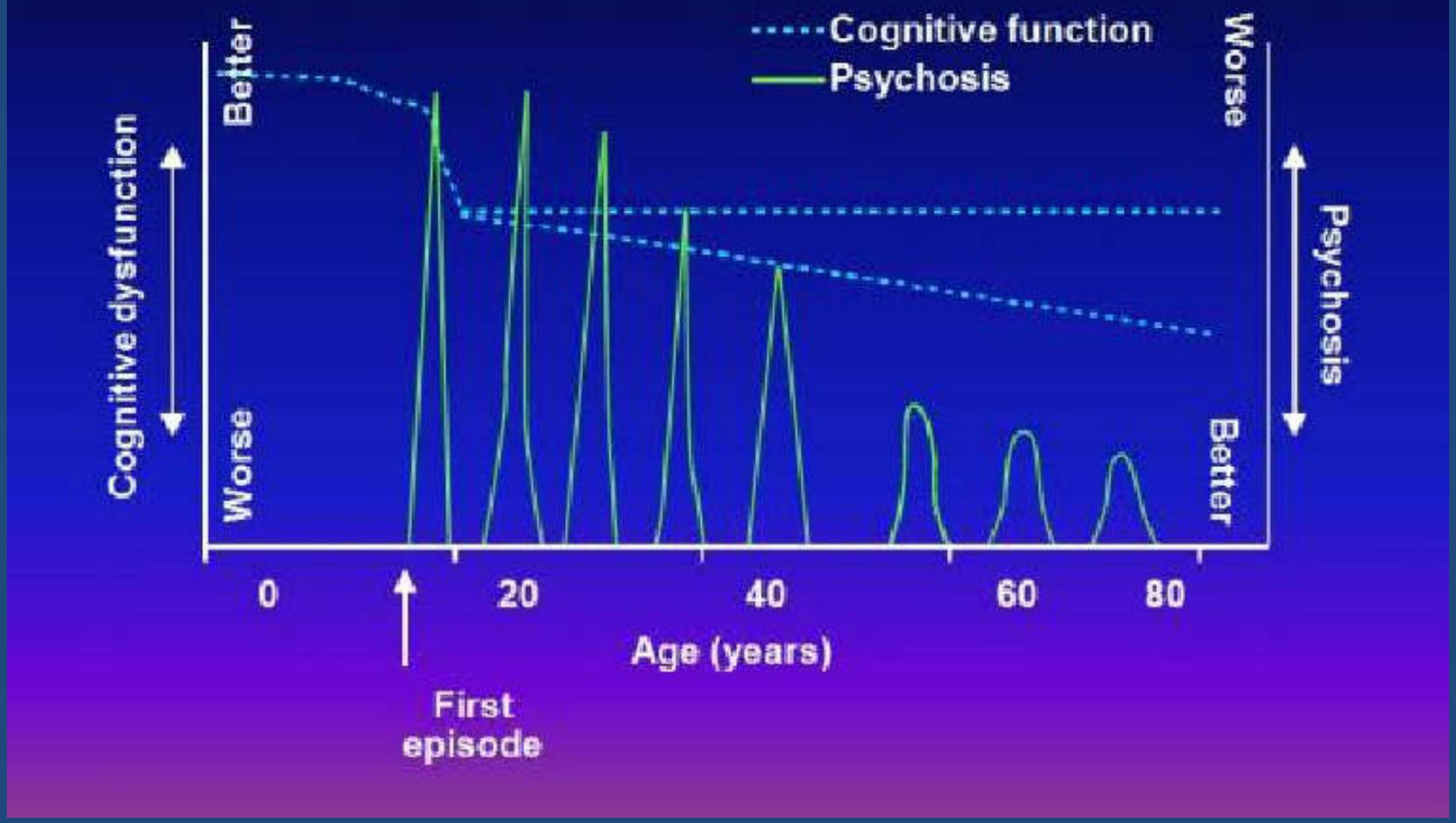








Cognitive dysfunction is a lasting feature of schizophrenia



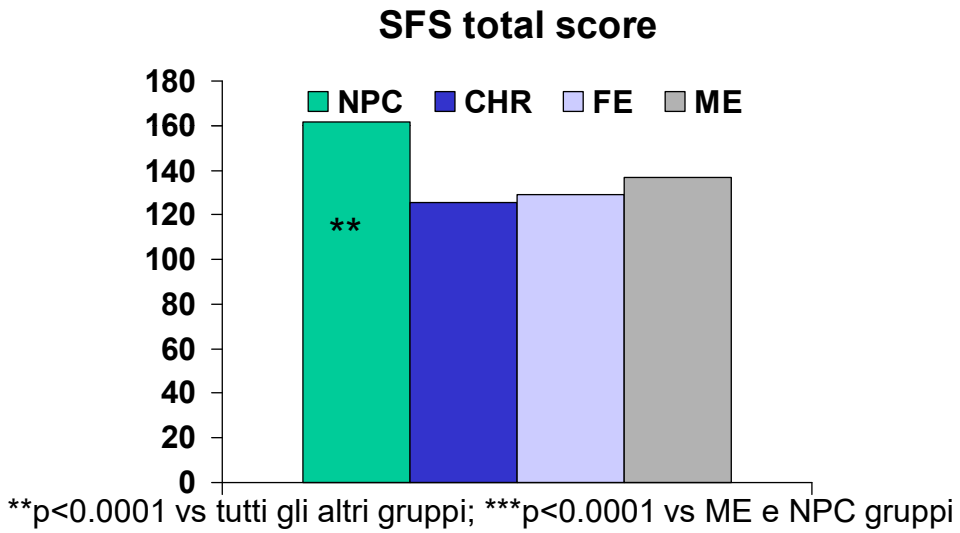
Cognizione sociale e schizofrenia

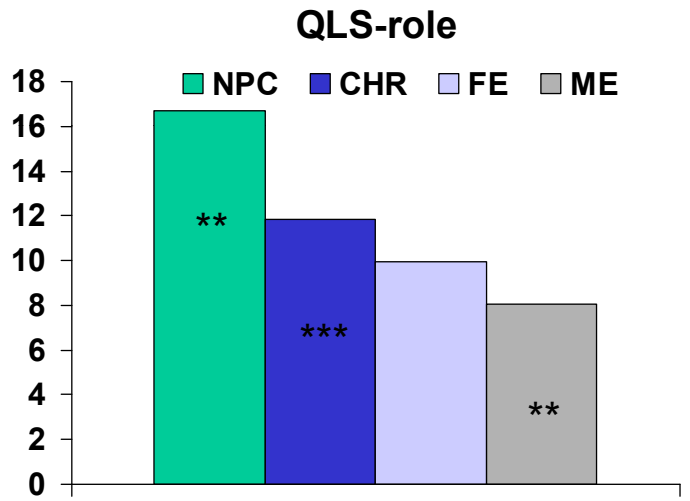
- La Cognizione sociale (SC), è stato identificata come un dominio aggiuntivo e raggruppa le operazioni mentali alla base del comportamento sociale, come l'interpretazione delle intenzioni o delle emozioni di un'altra persona.
- SC è un costrutto multidimensionale che comprende funzioni come:
  - elaborazione emotiva
  - percezione e conoscenza sociale
  - teoria della mente
  - attribuzione AS

[Bellack et al., 2007], [Green et al., 2008], [Penn et al., 1997] ,[Penn et al., 2008]).

I deficit sociali sono presenti prima che inizino i sintomi psicotici

- Valutazione prospettica del funzionamento sociale in:
  - Gruppo di controllo non-psichiatrico (NPC)
  - Soggetti ad alto rischio clinico di sviluppare psicosi (CHR)*
  - Pazienti al primo episodio (FE)
  - Pazienti con episodi multipli (ME)





**p<0.0001 vs tutti gli altri gruppi; ***p<0.0001 vs ME e NPC gruppi

*Individui nella fase prodromica della malattia, valutata con i criteri degli stati prodromici usando la Structured Interview for Prodromal Syndromes (SIPS)

SFS, Social Functioning Scale; QLS, Quality of Life Scale

Addington et al. Schizophr Res 2008;99:119–124

Schizophrenia Bulletin vol. 32 no. S1 pp. S44–S63, 2006
doi:10.1093/schbul/sbl029
Advance Access publication on August 17, 2006

The Functional Significance of Social Cognition in Schizophrenia: A Review

Shannon M. Couture, David L. Penn[1], and David L. Roberts

Department of Psychology, University of North Carolina at Chapel Hill, CB #3270, Davie Hall, Chapel Hill, NC 27599-3270

been used to apply to self- or other report of interper
behaviors, behavior in community settings (eg, skil
ings while shopping), skills of independent living
self-care skills, grooming, financial skills, etc), ra
of social skill in laboratory settings (eg, role-play t

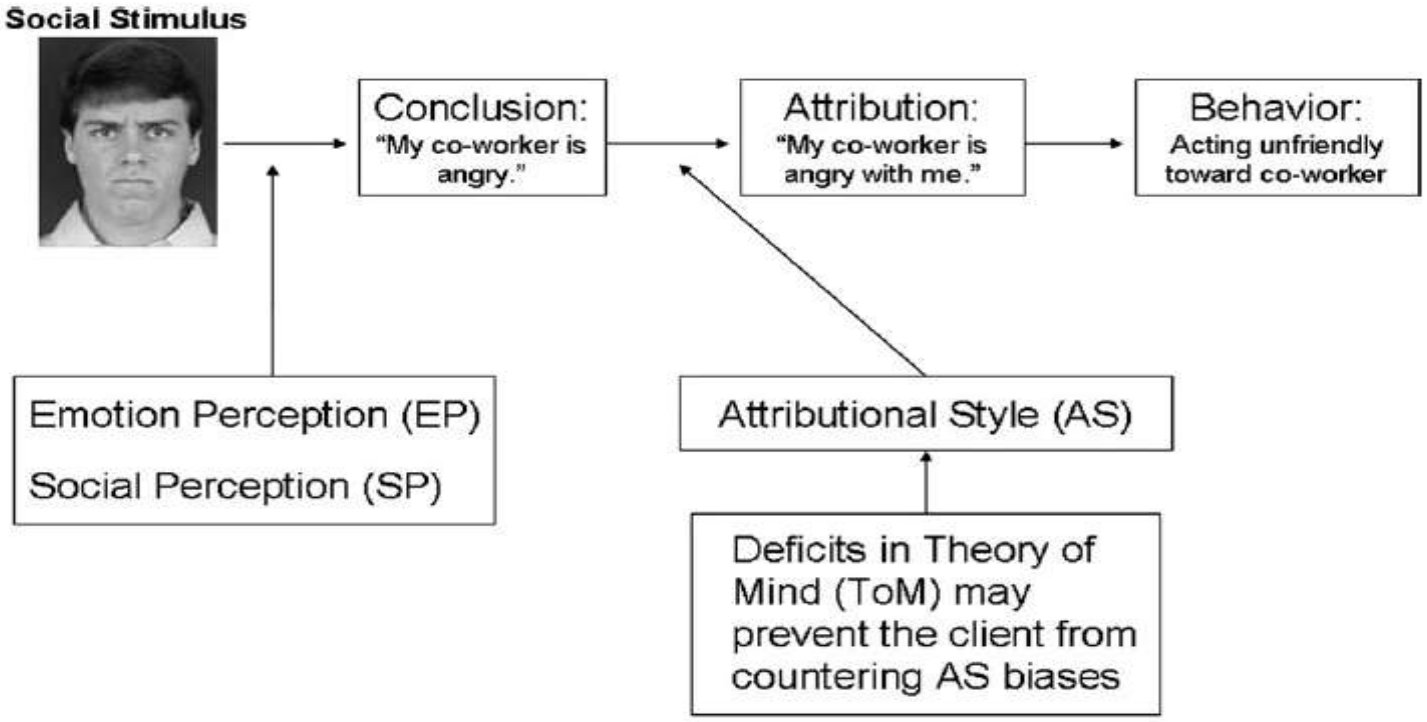
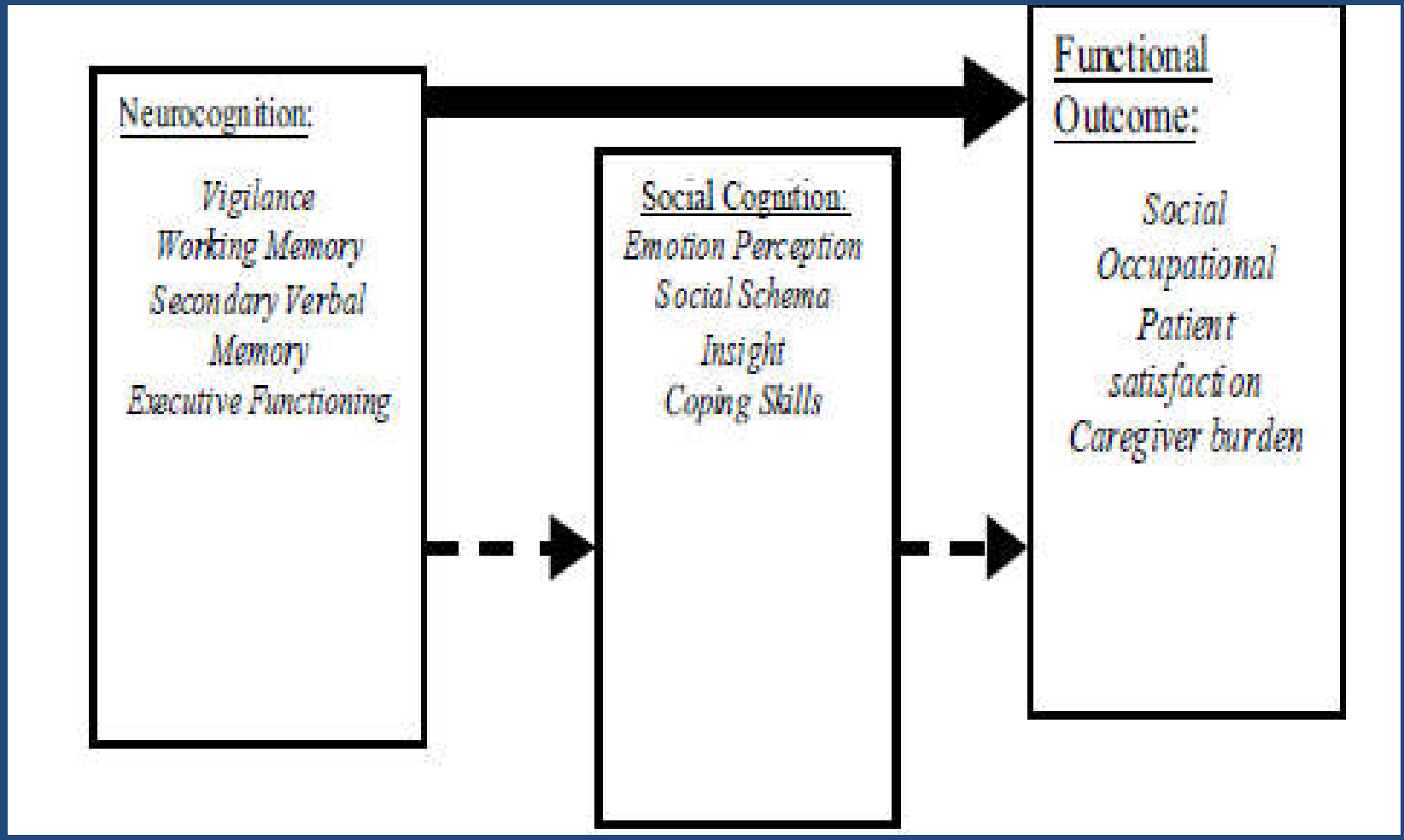
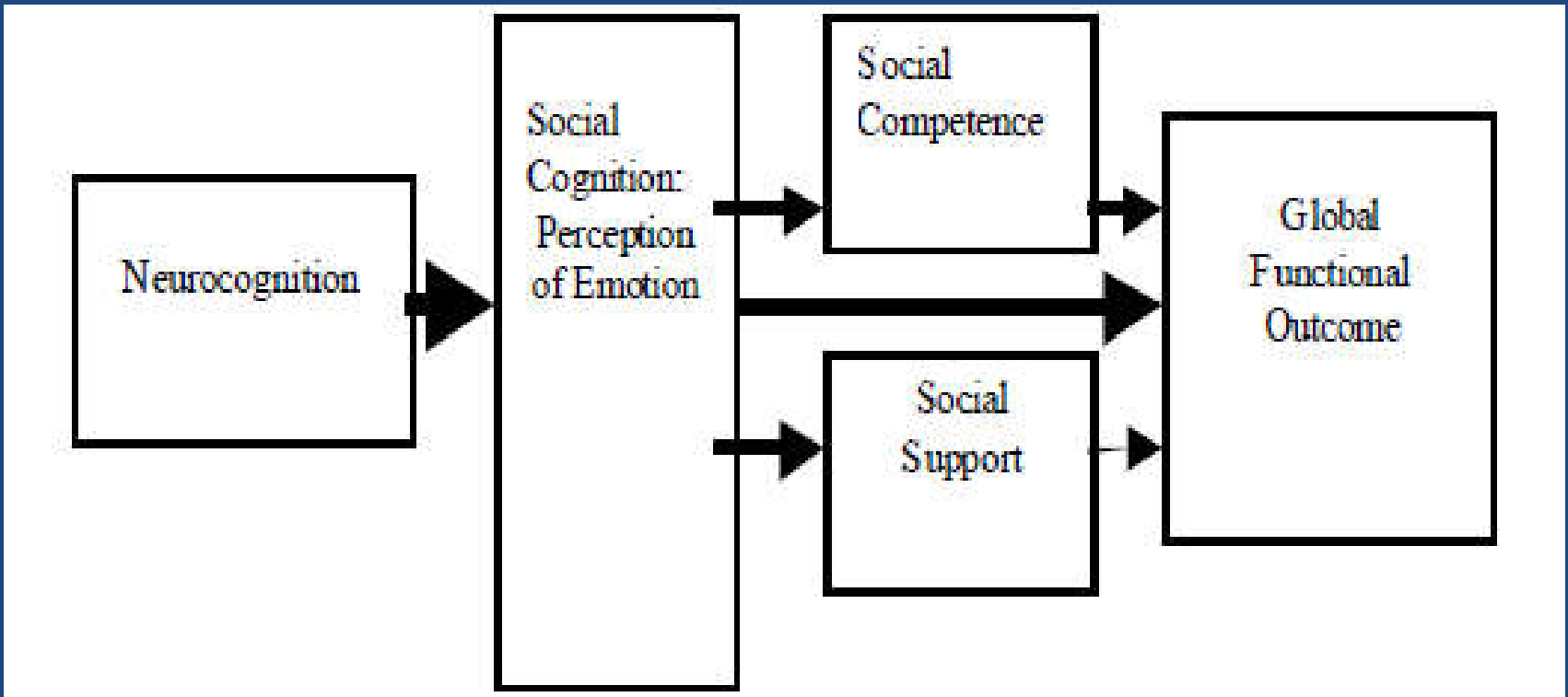


Fig. 1. Conceptual Framework for Understanding the Interplay Between Social Cognition and Social Functioning.

Modello di Green e Nuechterlein, 1999



Modello di Brekke, 2005



Neurocognitive Deficits and Functional Outcome in Schizophrenia: Are We Measuring the "Right Stuff"?

by Michael Foster Green, Robert S. Kern, David L. Braff, and Jim Mintz

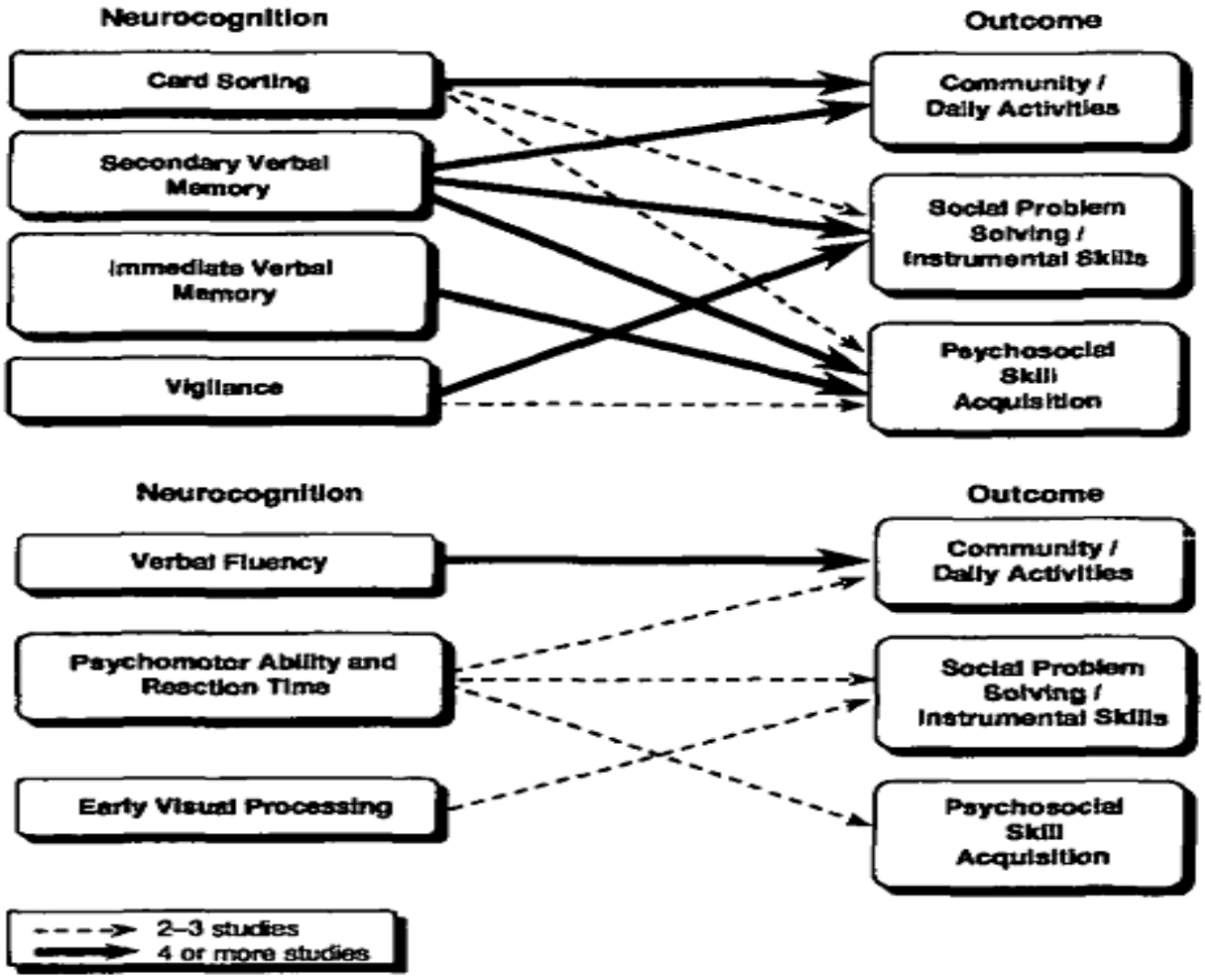
Abstract

There has been a surge of interest in the functional consequences of neurocognitive deficits in schizophrenia. The published literature in this area has doubled in the last few years. In this paper, we will attempt to confirm the conclusions from a previous review that certain neurocognitive domains (secondary verbal memory, immediate memory, executive functioning as measured by card sorting, and vigilance) are associated with functional outcome. In addition to surveying the number of replicated findings and tallying box scores of results, we will approach the review of the studies in a more thorough and empirical manner by applying a meta-analysis. Lastly, we will discuss what we see as a key limitation of this literature, specifically, the relatively narrow selection of predictor measures. This limitation has constrained identification of mediating variables that may explain the mechanisms for these relationships.

Keywords: Schizophrenia, neurocognition, functional outcome, social cognition, learning potential.

Schizophrenia Bulletin, 26(1):119–136, 2000.

Figure 1. Neurocognitive prediction of functional outcome



Biol Psychiatry. 2008 March 1; 63(5): 505–511.

Predicting Schizophrenia Patients' Real World Behavior with Specific Neuropsychological and Functional Capacity Measures

Christopher R. Bowie, PhD[1,2], Winnie W. Leung, PhD[1,2,3], Abraham Reichenberg, PhD[1], Margaret M. McClure, PhD[1,2,3], Thomas L. Patterson, PhD[4], Robert K. Heaton, PhD[4], and Philip D. Harvey, PhD[1,3]

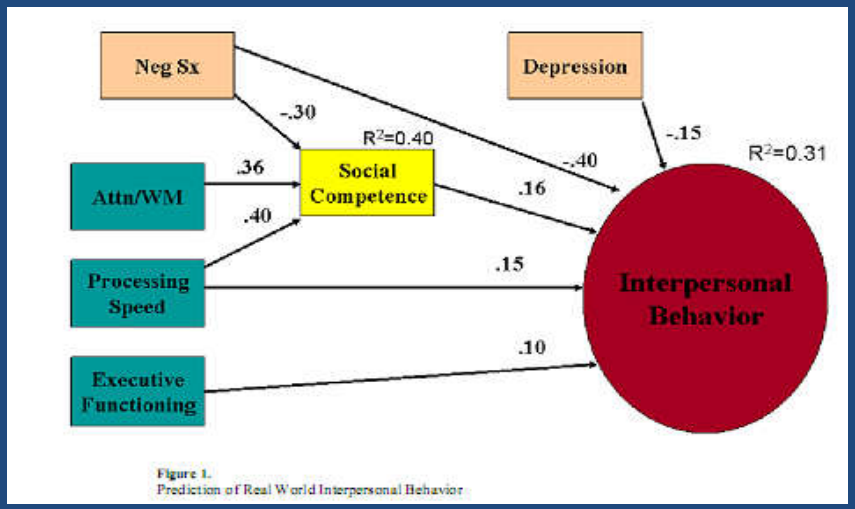


Figure 1.
Prediction of Real World Interpersonal Behavior

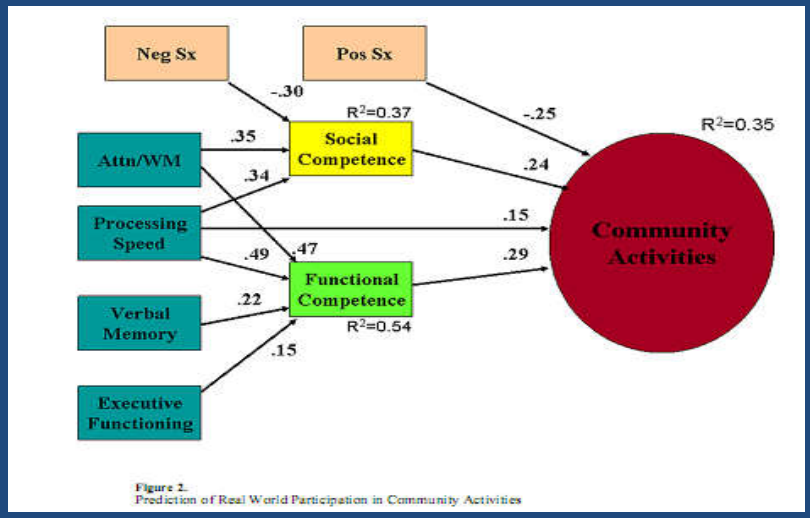


Figure 2.
Prediction of Real World Participation in Community Activities

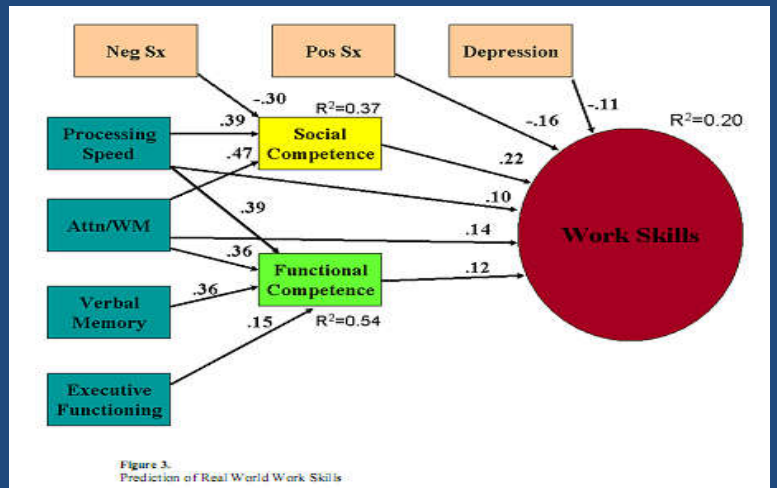


Figure 3.
Prediction of Real World Work Skills

Cognizione ed Outcome Funzionale nella Schizofrenia

- I deficit cognitivi sono correlati all'outcome funzionale e sono in grado di predirlo
- La correlazione è media per specifici deficit ma è ampia per il complesso delle funzioni
- La relazione tra deficit cognitivi e outcome funzionale è più forte di quella tra sintomi psicotici ed outcome funzionale.
- I deficit cognitivi inflenzano ampiamente il successo della riabilitazione psichiatrica

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Adjunctive psychosocial therapies for the treatment of schizophrenia

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Available online 15 January 2008

Domains of improvement with psychosocial therapies

Intervention	Domains most consistently improved	Domains less consistently improved
Cognitive-behavioral therapy (CBT)	Psychopathology, residual symptoms	Adherence, social function
Family intervention therapy (FIT)	Adherence, relapse, hospitalization, disease burden	Residual symptoms, social function
Social skills therapy (SST)	Social function, activities of daily life	Adherence, residual symptoms
Cognitive remediation therapy (CRT)	Cognitive function	Residual symptoms, social function
Integrated therapies	Social function, residual symptoms	Adherence, relapse

Psychosocial Treatments for Schizophrenia

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[3]Department of Psychology, University of North Carolina, Chapel Hill, North Carolina 27599-3270; email: dpenn@email.unc.edu

Annu. Rev. Clin. Psychol. 2013. 9:465–97

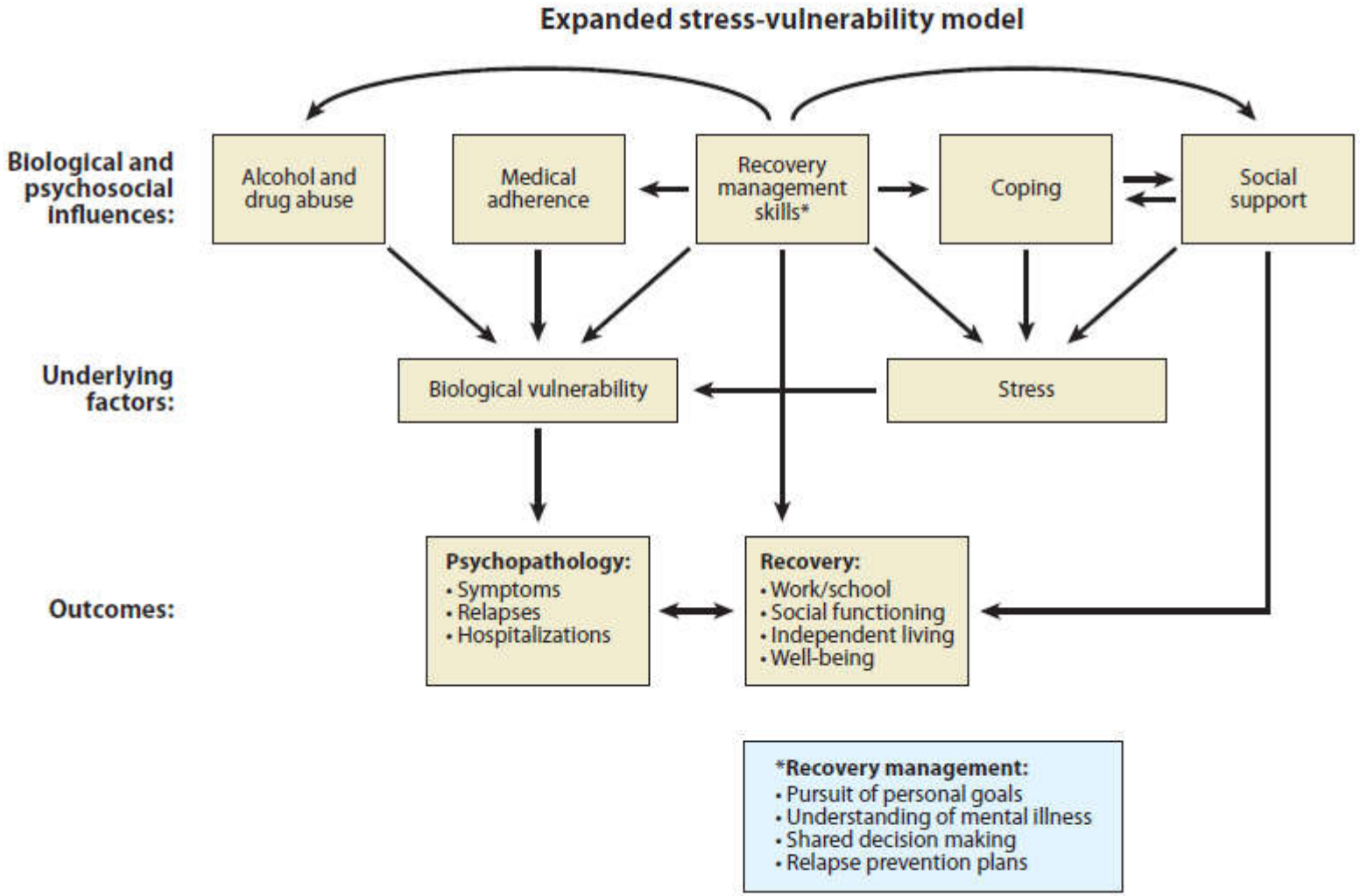

Figure 1

Components of the expanded stress vulnerability model, including recovery management.

Trattamenti Evidence-Based

- Il termine "pratica basata sulle evidenze" si riferisce agli interventi che si sono dimostrati essere efficaci nel migliorare il corso o l'outcome di una malattia specifica sulla base di studi di ricerca condotti con rigore. Nel caso della Schizofrenia ci riferiamo a :
  - Assertive Community Treatment
  - Cognitive Behavior Therapy for Psychosis
  - Cognitive Remediation
  - Family Psychoeducation
  - Illness Self-Management Training
  - Social Skill Training
  - Supported Employment

Trattamenti Promettenti

Non tutte le aree sono state oggetto di studio; sono infatti escluse quelle troppo onerose o perché troppo di nicchia. Tra le pratiche più promettenti non EBM-based ci sono:

- CAT (Cognitive Adaptive Therapy)
- CBT for post-traumatic stress disorder
- Chronic Illness Self-Managment Training
- First-episode psychosis intervention
- Healthy Lifestyle Interventions
- Integrated treatment for co-occurring disorders
- Interventions targeting older individuals
- Peer support services
- Prodromal Stage Intervention
- Social cognition training
- Supported Education
- Supported Housing

Table 1 Primary domains targeted by psychosocial interventions for schizophrenia

	Core psychopathology		Psychosocial functioning				Comorbid conditions		
	Symptoms/ relapses	Cognitive impair- ment	Overall	Work/ school	Social/ leisure	Self-care	Substance abuse	Trauma/ PTSD	Physical disease
Evidence-based treatments									
CBT for psychosis	X		X						
Cognitive remediation		X							
Family psychoed- ucation	X		X						
Illness self- management training	X		X						
Social skills training			X		X	X			
Supported employment				X					
Promising practices									
Cognitive adaptive therapy	X					X			
CBT for PTSD								X	
Healthy lifestyle interventions									X
Integrated treatments for co-occurring disorders							X		
Physical disease management									X
Social cognition training		X			X				
Supported education				X					

Table 2 Primary targets of psychosocial interventions for schizophrenia

	Human service system gap	Stage of illness	Specific age group
Evidence-based treatments			
Assertive community treatment	X		
Promising treatments			
First-episode psychosis intervention		X	
Interventions targeting older individuals			X
Peer support services	X		
Prodromal stage intervention		X	
Supported housing	X		

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journal homepage: www.elsevier.com/locate/schres

Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domains in schizophrenia: A prospective study in a real-world setting

Antonio Vita [a,b,*], Luca De Peri [a], Stefano Barlati [b], Paolo Cacciani [b], Giacomo Deste [a], Roberto Poli [c], Emilia Agrimi [c], Bruno M. Cesana [a,d], Emilio Sacchetti [a,b,e]

[a] University of Brescia, School of Medicine, Brescia, Italy

Table 3
Neurocognitive variables before and after 24 weeks of treatment.

		IPT-Cog ($n=26$)	CACR ($n=30$)	REHAB ($n=28$)	p
Mean processing speed	T0	−0.49 ± 1.05	−0.08 ± 1.24	−0.15 ± 0.72	0.028
	T6	0.019 ± 0.57	0.09 ± 0.91	−0.18 ± 0.94	
	Change[a]	0.51 ± 0.81	0.18 ± 0.66	−0.02 ± 0.73	
Mean working memory	T0	−1.34 ± 1.08	−0.89 ± 1.07	−0.79 ± 1.0	0.020
	T6	−0.82 ± 1.08	−0.56 ± 1.18	−1.12 ± 1.32	
	Change[b]	0.51 ± 0.81	0.32 ± 0.73	−0.33 ± 1.03	
Mean memory	T0	−2.64 ± 1.27	−2.29 ± 1.58	−2.20 ± 1.43	0.632
	T6	−1.74 ± 1.45	−1.12 ± 1.78	−0.98 ± 1.93	
	Change	0.89 ± 0.95	1.17 ± 1.23	1.21 ± 1.32	
Man executive functions	T0	−0.73 ± .93	−0.52 ± 0.92	−0.70 ± 0.74	0.702
	T6	−0.66 ± 1.02	−0.31 ± 0.93	−0.64 ± 1.23	
	Change	0.06 ± 0.48	0.21 ± 0.58	0.05 ± 0.96	
Mean Global Cognitive Composite score	T0	−1.30 ± 0.85	−0.95 ± 0.96	−0.96 ± 0.73	0.281
	T6	−0.80 ± 0.82	−0.47 ± 1.02	−0.73 ± 1.12	
	Change	0.49 ± 0.43	0.47 ± 0.45	0.22 ± 0.74	

[a] IPT-cog vs REHAB, $p=0.008$ (ES = 0.69); CACR vs REHAB, $p=0.086$ (ES = 0.28); IPT-cog vs CACR, $p=0.252$. Test for parallelism: $p=0.052$; for linearity $p<0.001$.
[b] IPT-cog vs REHAB, $p=0.010$ (ES = 0.91); CACR vs REHAB, $p<0.021$ (ES = 0.73); IPT-cog vs CACR, $p=0.653$. Test for parallelism: $p=0.391$; for linearity $p<0.001$.

Table 2
Psychopathologic variables before and after 24 weeks of treatment.

		IPT-Cog ($n=25$)	CACR ($n=30$)	REHAB ($n=28$)	p
CGI-S	T0	5.0 ± 0.63	4.67 ± 0.75	4.71 ± 0.93	0.025
	T6	4.04 ± 0.87	3.87 ± 0.81	4.36 ± 0.91	
	Change[a]	−0.96 ± 0.72	−0.80 ± 0.76	−0.36 ± 0.78	
PANSS Pos	T0	19.0 ± 4.45	18.97 ± 5.91	19.68 ± 6.67	<0.001
	T6	14.0 ± 3.12	13.50 ± 4.18	17.89 ± 6.47	
	Change[b]	−5.0 ± 3.40	−5.47 ± 4.92	−1.79 ± 4.33	
PANSS Neg	T0	28.73 ± 6.65	22.27 ± 7.95	21.18 ± 7.33	<0.001
	T6	21.77 ± 5.20	17.37 ± 6.70	21.21 ± 6.22	
	Change[c]	−6.96 ± 5.67	−4.90 ± 6.31	0.04 ± 4.13	
PANSS Tot	T0	91.96 ± 12.74	88.07 ± 20.16	84.61 ± 19.94	<0.001
	T6	70.31 ± 13.17	67.27 ± 18.09	80.89 ± 19.89	
	Change[d]	−21.65 ± 15.40	−20.80 ± 18.35	−3.71 ± 14.68	

[a] IPT-cog vs REHAB, $p=0.011$ (Effect Size (ES) = −0.80); CACR vs REHAB, $p=0.031$ (ES = −0.57); IPT-cog vs CACR, $p=0.642$. Test for parallelism, $p=0.313$; for linearity, $p<0.001$.
[b] IPT-cog vs REHAB, $p<0.001$ (ES = −0.83); CACR vs REHAB, $p<0.001$ (ES = −0.79); IPT-cog vs CACR, $p=0.975$. Test for parallelism, $p=0.436$; for linearity, $p<0.001$.
[c] IPT-cog vs REHAB, $p<0.001$ (ES = −129); CACR vs REHAB, $p<0.001$ (ES = −0.94); IPT-cog vs CACR, $p=0.645$. Test for parallelism, $p=0.836$; for linearity, $p<0.001$.
[d] IPT-cog vs REHAB, $p<0.001$ (ES = −1.19); CACR vs REHAB, $p<0.001$ (ES = −1.03); IPT-cog vs CACR, $p=0.477$. Test for parallelism, $p=0.447$; for linearity, $p<0.001$.

Table 4
Functional outcome variables before and after 24 weeks of treatment.

		IPT-Cog ($n=26$)	CACR ($n=30$)	REHAB ($n=28$)	p
GAF	T0	45.62 ± 9.28	47.40 ± 11.71	50.11 ± 11.06	0.079
	T6	54.19 ± 9.56	55.63 ± 8.26	52.71 ± 10.16	
	Change[a]	8.58 ± 5.78	8.23 ± 9.02	2.61 ± 7.33	
HoNOS	T0	18.85 ± 5.27	17.53 ± 5.34	14.71 ± 5.42	<0.001
	T6	14.35 ± 6.23	8.20 ± 5.58	11.64 ± 6.05	
	Change[ab]	−4.50 ± 3.15	−9.33 ± 5.14	−3.07 ± 2.86	

[a] IPT-cog vs REHAB, $p=0.055$ (ES = 0.91); CACR vs REHAB, $p=0.043$ (ES = 0.68); IPT-cog vs CACR, $p=$ ns. Test for parallelism, $p=0.120$; for linearity, $p<0.001$.
[b] IPT-cog vs REHAB, $p=0.919$; CACR vs REHAB, $p<0.001$ (ES = −1.56); IPT-cog vs CACR, $p=0.001$ (ES = 1.16). Test for parallelism, $p=0.130$; for linearity, $p<0.001$.

ORIGINAL ARTICLE

Neuroprotective Effects of Cognitive Enhancement Therapy Against Gray Matter Loss in Early Schizophrenia

Results From a 2-Year Randomized Controlled Trial

Shaun M. Eack, PhD; Gerard E. Hogarty, MSW†; Raymond Y. Cho, MD; Konasale M. R. Prasad, MD; Deborah P. Greenwald, PhD; Susan S. Hogarty, MSN; Matcheri S. Keshavan, MD

Context: Cognitive rehabilitation has shown efficacy in improving cognition in patients with schizophrenia but the underlying neurobiologic changes that occur during these treatments and support cognitive improvement are not well known.

Objective: To examine differential changes in brain morphology in early course schizophrenia during cognitive rehabilitation vs supportive therapy.

Design: Randomized controlled trial.

Setting: An outpatient research clinic at a university-based medical center that provides comprehensive care services for patients with severe mental illness.

Patients: A total of 53 symptomatically stable but cognitively disabled outpatients in the early course of schizophrenia or schizoaffective disorder.

Interventions: A 2-year trial with annual structural magnetic resonance imaging and cognitive assessments. Cognitive enhancement therapy is an integrated approach to the remediation of cognitive impairment in schizophrenia that uses computer-assisted neurocognitive training and group-based social-cognitive exercises. Enriched supportive therapy is an illness management approach that provides psychoeducation and teaches applied coping strategies.

Main Outcome Measures: Broad ar
temporal gray matter change were ana
tudinal, voxel-based morphometry met
effects models followed by volumetr
gions that demonstrated significant di
between treatment groups.

Results: Patients who received cogni
therapy demonstrated significantly grea
gray matter volume over 2 years in the
parahippocampal gyrus, and fusiform
cantly greater gray matter increases in th
corrected $P<.04$) compared with those
riched supportive therapy. Less gray ma
parahippocampal and fusiform gyrus an
ter increases in the left amygdala wer
lated to improved cognition and media
cognitive effects of cognitive enhancem

Conclusion: Cognitive enhancement
fer neurobiologic protective and enhanc
schizophrenia that are associated wit
term cognitive outcomes.

Trial Registration: clinicaltrials
NCT00167362

Arch Gen Psychiatry. 2010;67(7):674-6

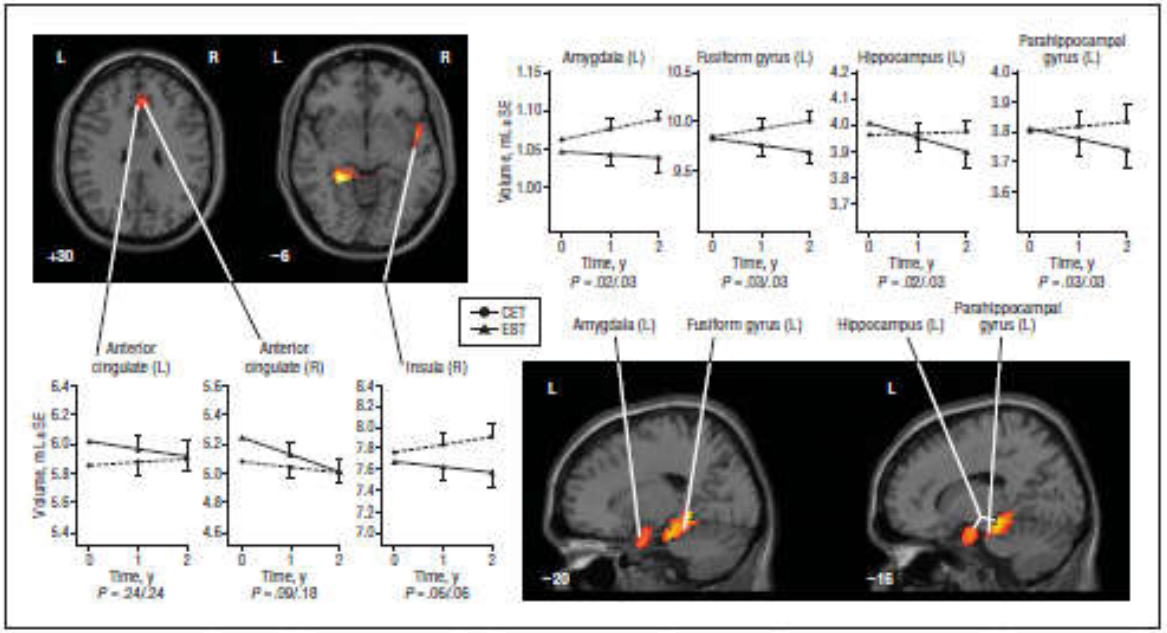


Figure 2. Regions of differential gray matter change among participants who received cognitive enhancement therapy vs enriched supportive therapy. *P* values to the right of the slash reflect Hochberg's correction. L indicates left; R, right; SE, standard error.

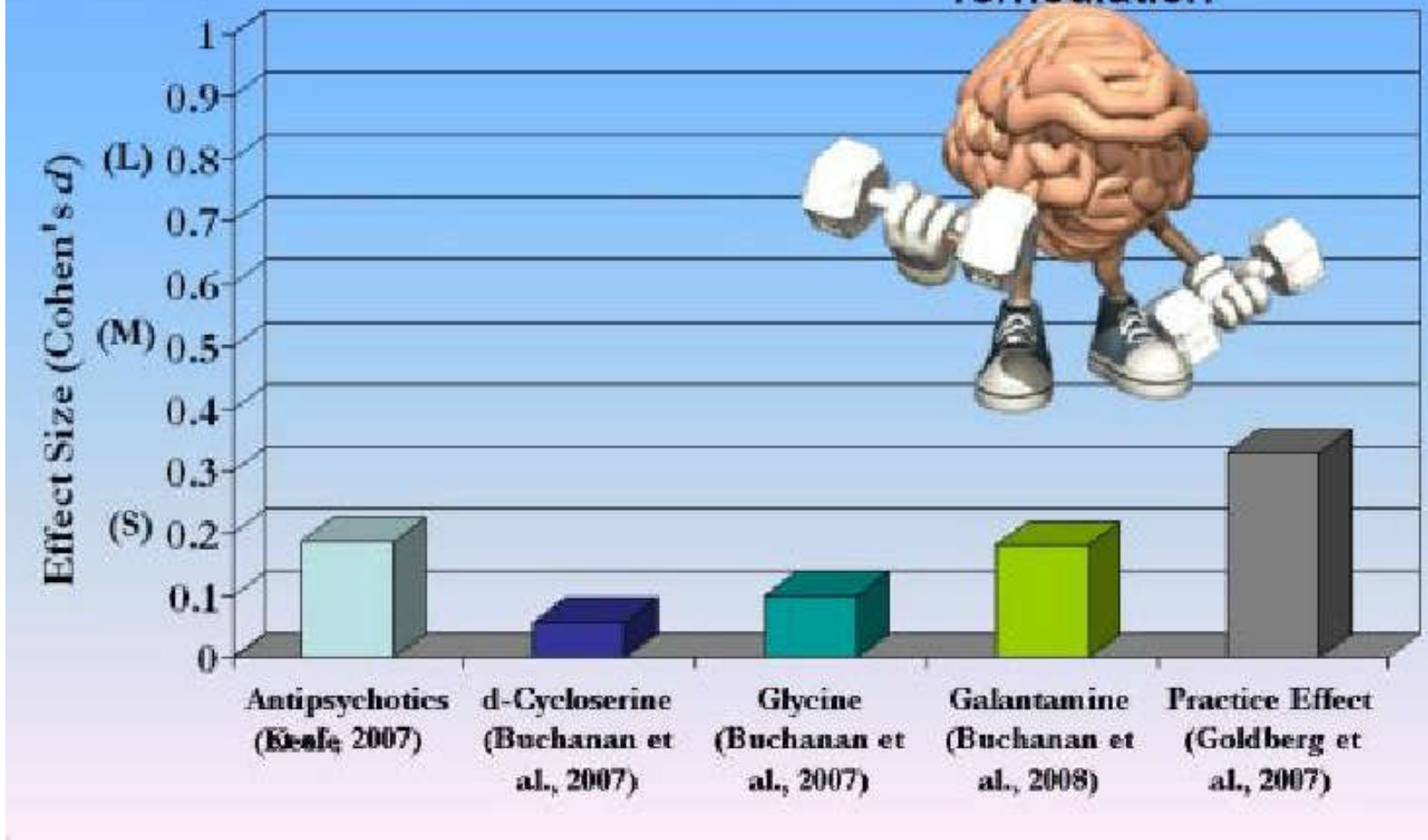
Table 2. Changes in Gray Matter Volume During 2 Years of Cognitive Enhancement Therapy or Enriched Supportive Therapy

	Mean (SD) Gray Matter Volume, cm³						Between-Group Effect		
	CET (n=30)			EST (n=23)					
Site/Cluster	Baseline	Year 1	Year 2	Baseline	Year 1	Year 2	*t*	*P* Value	*P* Value[a]
Frontal									
Left anterior cingulate	5.85 (0.83)	5.88 (0.82)	5.90 (0.88)	6.02 (0.99)	5.97 (1.17)	5.92 (0.89)	1.17	.24	.24
Right anterior cingulate	5.08 (0.72)	5.04 (0.71)	5.00 (0.74)	5.25 (0.85)	5.13 (1.00)	5.01 (0.74)	1.72	.09	.18
Medial temporal									
Left amygdala	1.06 (0.13)	1.08 (0.11)	1.09 (0.12)	1.05 (0.13)	1.04 (0.15)	1.04 (0.12)	2.36	.02	.03
Left fusiform gyrus	9.84 (1.11)	9.92 (1.00)	10.00 (1.08)	9.83 (1.36)	9.76 (1.37)	9.69 (1.18)	2.23	.03	.03
Left hippocampus	3.96 (0.35)	3.97 (0.33)	3.97 (0.35)	4.01 (0.46)	3.95 (0.50)	3.90 (0.46)	2.28	.02	.03
Left parahippocampal gyrus	3.80 (0.46)	3.82 (0.38)	3.83 (0.43)	3.81 (0.49)	3.78 (0.49)	3.74 (0.36)	2.16	.03	.03
Temporal									
Right insula	7.76 (1.03)	7.84 (0.93)	7.91 (0.99)	7.67 (1.10)	7.62 (1.30)	7.57 (0.94)	1.91	.06	NA

Abbreviations: CET, cognitive enhancement therapy; EST, enriched supportive therapy; NA, not applicable.
[a] *P* Values are adjusted for multiple inference testing within each cluster of results using Hochberg's correction.

Pharmacological Treatments for Cognition

Enter: Cognitive remediation



PSYCHIATRIC REHABILITATION SKILLS 1999 Vol. 3, No. 1, 124-147

Therapeutic Synergism: Optimal Pharmacotherapy and Psychiatric Rehabilitation to Enhance Functional Outcome in Schizophrenia

Steven B. Schwarzkopf, John F. Crilly and Steven M. Silverstein
University of Rochester

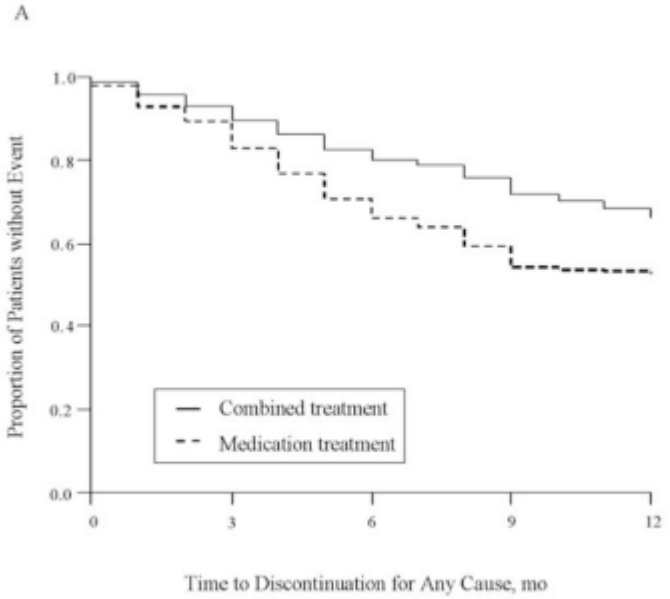
Arch Gen Psychiatry. 2010 September ; 67(9): 895–904. doi:10.1001/archgenpsychiatry.2010.105.

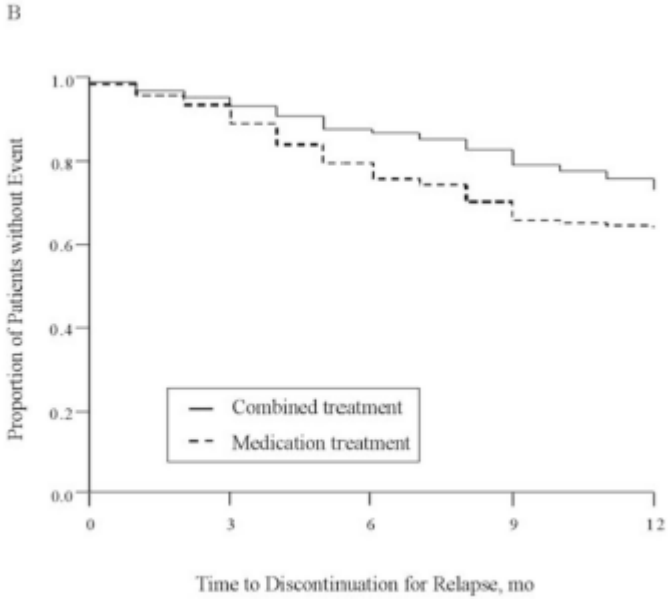
Antipsychotic Medication Alone versus Combined with Psychosocial Intervention on Outcomes of Early Stage Schizophrenia: A Randomized, One-year Study

Xiaofeng Guo, MD[*], **Jinguo Zhai, MD**[*], **Zhening Liu, MD**, **Maosheng Fang, MD**, **Bo Wang, MD**, **Chuanyue Wang, MD**, **Bin Hu, MD**, **Xueli Sun, MD**, **Luxian Lv, MD**, **Zheng Lu, MD**, **Cui Ma, MD**, **Xiaolin He, MD**, **Tiansheng Guo, MD**, **Shiping Xie, MD**, **Renrong Wu, MD**, **Zhimin Xue, MD**, **Jindong Chen, MD**, **Elizabeth W. Twamley, PhD**, **Hua Jin, MD**, and **Jingping Zhao, MD, PhD**

Design, Setting, and Participants—Randomized controlled trial of a clinical sample of 1268 patients with early stage schizophrenia, conducted at 10 clinical sites in China from 2005–2007.

Intervention—Patients were randomly assigned to antipsychotic medication treatment only or antipsychotic medication plus 12 months of psychosocial intervention, consisting of psycho-education, family intervention, skills training and cognitive-behavioral therapy, administered over 48 group sessions.





Assessment	Mean (95% CI)						Analyses [b]	
	baseline		6 months		12 months		Group-by-Time Interaction Effect	
	CT (n=580)	MT (n=604)	CT (n=512)	MT (n=472)	CT (n=406)	MT (n=338)	F	p
PANSS	44.6(43.5–45.7)	45.3(44.2–46.5)	37.3(36.5–38.1)	38.8(38.0–39.7)	34.7(34.2–35.2)	36.4(35.7–37.1)	0.406	0.81
ITAQ	12.8(12.4–13.2)	12.7(12.2–13.1)	17.9(17.5–18.3)	14.2(13.7–14.8)	19.5(19.1–19.8)	15.9(15.4–16.5)	25.945	<0.001
GAS	74.1(73.2–75.1)	74.2(73.2–75.1)	79.8(78.9–80.6)	77.9(77.0–78.8)	82.9(82.0–83.7)	80.8(79.9–81.8)	4.332	0.002
ADL	17.2(17.0–17.4)	17.2(17.0–17.4)	15.7(15.5–15.8)	16.6(16.5–16.8)	15.4(15.3–15.5)	16.4(16.3–16.5)	12.699	<0.001
SF-36								
Physical Functioning	90.8(89.7–91.8)	90.6(89.5–91.6)	92.9(91.8–93.9)	92.3(91.3–93.2)	95.2(94.3–96.1)	94.9(94.1–95.7)	0.121	0.87
Role-Physical	54.1(50.8–57.3)	57.3(54.1–60.6)	67.1(63.9–70.2)	65.8(62.5–69.2)	78.1(74.9–81.3)	73.4(69.6–77.1)	5.129	0.006
Bodily Pain	77.2(74.7–79.8)	78.8(76.4–81.2)	83.0(80.5–85.6)	84.4(81.9–86.9)	89.9(87.9–91.9)	89.3(87.0–91.6)	2.795	0.06
General Health	61.7(60.3–63.2)	63.5(62.1–65.0)	67.5(66.1–69.0)	65.8(64.2–67.4)	71.3(69.8–72.8)	67.9(66.2–69.7)	11.094	<0.001
Vitality	59.5(58.0–61.1)	58.0(56.4–59.5)	65.6(64.1–67.1)	60.1(58.4–61.9)	66.7(65.0–68.4)	60.5(58.4–62.7)	5.327	0.005
Social Functioning	74.5(72.5–76.5)	74.5(72.6–76.4)	82.2(80.4–84.0)	81.2(79.3–83.0)	86.5(84.5–88.4)	85.0(82.9–87.1)	1.003	0.37
Role-Emotional	57.5(54.2–60.7)	56.5(53.1–59.8)	68.0(64.7–71.2)	63.8(60.2–67.4)	80.1(76.9–83.2)	72.1(68.1–76.1)	3.985	0.02
Mental Health	65.2(63.8–66.6)	64.5(63.2–65.8)	69.1(67.7–70.6)	67.2(65.8–68.6)	71.9(70.4–73.5)	70.2(68.5–71.8)	1.573	0.21

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Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

The beneficial effects of combining pharmacological and psychosocial treatment on remission and functional outcome in outpatients with schizophrenia

M. Valencia [a, *], A. Fresan [b], F. Juárez [a], R. Escamilla [c], R. Saracco [c]

At the end of the study, 80% of the patients fulfilled the criteria for Symptomatic remission: 62 patients (91.2%) in the social skills training group in contrast to 34 patients (66.7%) in the TAU group.

Functional improvement criteria were accomplished by 41 patients (34.5%) at the endpoint of the study. Forty of these patients (58.8%) belonged to social skills training and one patient to customary treatment (c2 ¼ 41.7, df 1, p < 0.001) and when criteria for symptomatic remission and functional improvement were combined, 39 patients (97.5%) of the social skills training group and one patient (1.9%) of the customary treatment group achieved functional outcome.

International Journal of Neuropsychopharmacology (2005), **8**, 457–472. Copyright © 2005 CINP
doi:10.1017/S146114570500516X

A meta-analysis of neuropsychological change to clozapine, olanzapine, quetiapine, and risperidone in schizophrenia

Neil D. Woodward[1], Scot E. Purdon[2], Herbert Y. Meltzer[3] and David H. Zald[1]

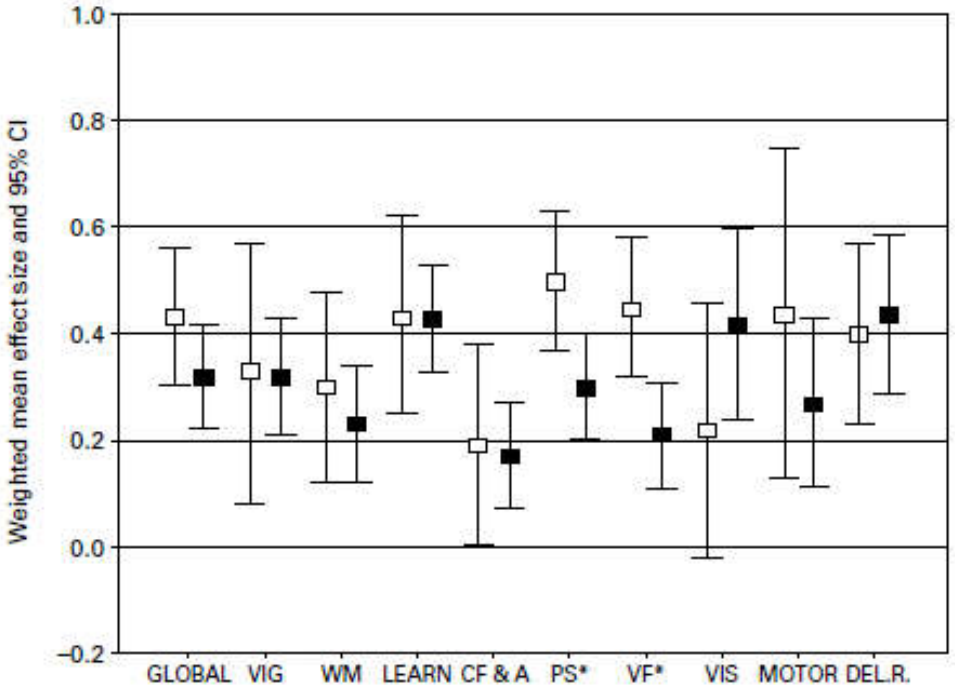


Figure 1. Neuropsychological change to atypical antipsychotic drugs: controlled (■) vs. uncontrolled studies (□). * Indicates significant differences between controlled and uncontrolled trials ($p < 0.05$). For abbreviations see Table 1.

Table 3. Neuropsychological change with atypical antipsychotic drugs: Analysis 1

	Number of effect sizes (k) and number of subjects (n)										Overall weighted ES			
	Clozapine		Olanzapine		Risperidone		Quetiapine		Total					
	k	n	k	n	k	n	k	n	k	n	ES	95% CI	Z statistic	p value
Global Cognitive Index	3	73	6	254	5	116	4	71	18	514	0.24	0.11 to 0.37	3.67	<0.001
Vigilance and Selective Attention	2	43	3	122	4	92	3	59	12	316	0.12	−0.04 to 0.28	1.43	0.152
Working Memory	2	53	3	135	4	87	1	11	10	286	0.05	−0.12 to 0.22	0.60	0.546
Learning	2	54	4	220	4	97	4	71	14	442	0.24	0.10 to 0.38	3.44	<0.001
Processing Speed	3	71	5	233	4	93	3	54	15	451	0.21	0.07 to 0.35	3.02	0.003
Cognitive Flexibility and Abstraction	3	72	6	243	3	62	2	28	14	405	0.04	−0.10 to 0.18	0.55	0.581
Verbal Fluency	3	72	5	242	3	65	4	71	15	449	0.16	0.02 to 0.30	2.26	0.024
Visuospatial Processing	2	43	4	134	3	65	1	11	10	253	0.00	−0.18 to 0.18	0.02	0.988
Motor Skill	1	24	4	222	3	65	1	11	9	322	0.21	0.05 to 0.37	2.56	0.010
Delayed Recall	3	72	3	201	2	58	2	43	10	374	0.13	−0.02 to 0.28	1.69	0.091

ES, Effect size; CI, confidence interval.

Table 4. Neuropsychological change with atypical antipsychotic drug (APDs): Analysis 2

	Number of effect sizes (k), number of subjects (n), mean effect size (ES)														
	Clozapine			Olanzapine			Risperidone			Quetiapine			All atypical APDs combined		
	k	n	ES	k	n	ES	k	n	ES	k	n	ES	k	n	ES
Global Cognitive Index	17	344	0.29*	13	690	0.43*	13	361	0.28*	7	118	0.44*	50	1513	0.36*
Vigilance and Selective Attention	8	152	0.17	9	512	0.47†	9	289	0.12	5	91	0.82†	31	1044	0.35†‡
Working Memory	8	160	0.25	8	406	0.24†	9	281	0.24†	2	27	0.41	27	874	0.25†
Learning	10	210	0.31†	10	625	0.61†‡	7	251	0.41†	6	108	0.24	33	1194	0.46†‡
Processing Speed	16	326	0.35†	12	648	0.43†	9	299	0.30†	6	107	0.35	43	1380	0.38†
Cognitive Flexibility and Abstraction	12	227	0.25	10	471	0.15	4	189	0.10	3	50	0.33	29	937	0.17†
Verbal Fluency	15	319	0.44†	11	651	0.25†	5	207	0.06	6	107	0.63†	37	1284	0.30†
Visuospatial Processing	9	179	0.20	5	144	0.50†	3	65	0.39	1	11	0.56	18	399	0.35†
Motor Skills	4	68	0.64†	5	238	0.25	2	65	0.22	2	34	0.20	13	405	0.30†
Delayed Recall	13	280	0.25†	7	460	0.53†	5	211	0.46†	3	58	0.30‡	28	1009	0.43†‡

ORIGINAL ARTICLE

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

Richard S. E. Keefe, PhD; Robert M. Bilder, PhD; Sonia M. Davis, DrPH; Philip D. Harvey, PhD; Barton W. Palmer, PhD; James M. Gold, PhD; Herbert Y. Meltzer, MD; Michael F. Green, PhD; George Capuano, PhD; T. Scott Stroup, MD, MPH; Joseph P. McEvoy, MD; Marvin S. Swartz, MD; Robert A. Rosenheck, MD; Diana O. Perkins, MD, MPH; Clarence E. Davis, PhD; John K. Hsiao, MD; Jeffrey A. Lieberman, MD; for the CATIE Investigators and the Neurocognitive Working Group

Context: Neurocognitive impairment in schizophrenia is severe and is an important predictor of functional outcome. The relative effect of the second-generation (atypical) antipsychotic drugs and older agents on neurocognition has not been comprehensively determined.

Objective: To compare the neurocognitive effects of several second-generation antipsychotics and a first-generation antipsychotic, perphenazine.

Design: Randomized, double-blind study of patients with schizophrenia assigned to receive treatment with olanzapine, perphenazine, quetiapine fumarate, or risperidone for up to 18 months as reported previously by Lieberman et al. Ziprasidone hydrochloride was included after its approval by the Food and Drug Administration.

Setting: Fifty-seven sites participated, including academic sites and treatment mental health facilities representative of the community.

Patients: From a cohort of 1460 patients in the treatment study, 817 completed neurocognitive testing immediately prior to randomization and then after 2 months of treatment.

Main Outcome Measures: The primary outcome was change in a neurocognitive composite score after 2 months of treatment. Secondary outcomes included neurocognitive composite score change at 6 months and 18 months after continued treatment and changes in neurocognitive domains.

Results: At 2 months, treatment resulted in small neurocognitive improvements of $z=0.13$ for olanzapine ($P<.002$), 0.25 for perphenazine ($P<.001$), 0.18 for quetiapine ($P<.001$), 0.26 for risperidone ($P<.001$), and 0.12 for ziprasidone ($P<.06$), with no significant differences between groups. Results at 6 months were similar. After 18 months of treatment, neurocognitive improvement was greater in the perphenazine group than in the olanzapine and risperidone groups. Neurocognitive improvement predicted longer time to treatment discontinuation, independently from symptom improvement, in patients treated with quetiapine or ziprasidone.

Conclusions: After 2 months of antipsychotic treatment, all groups had a small but significant improvement in neurocognition. There were no differences between any pair of agents, including the typical drug perphenazine. These results differ from the majority of previous studies, and the possible reasons are discussed.

Arch Gen Psychiatry. 2007;64:633-647

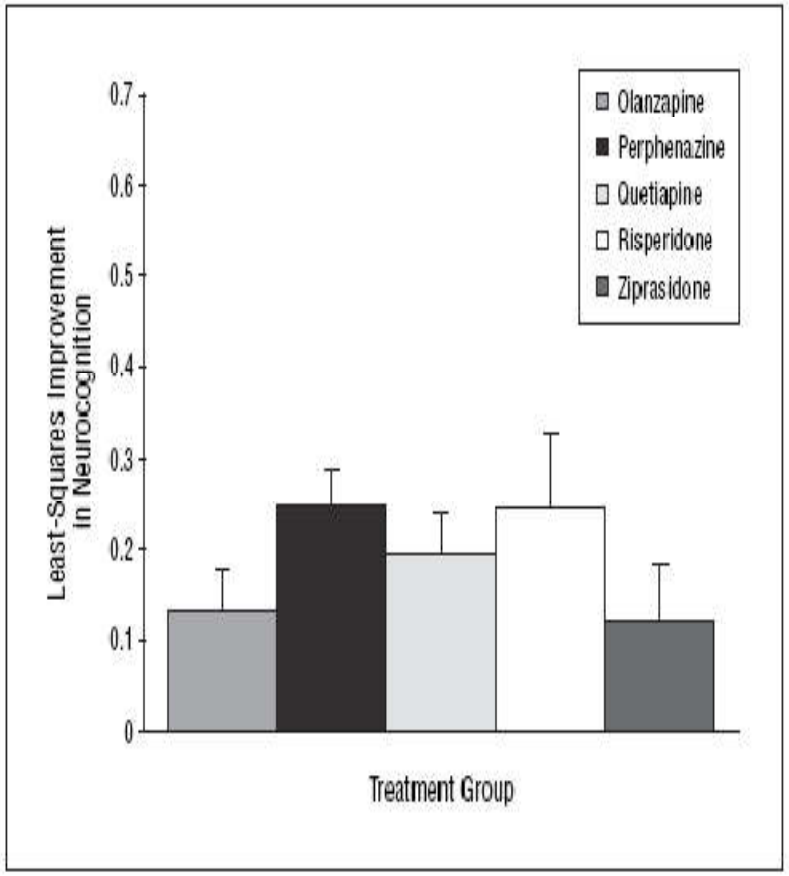


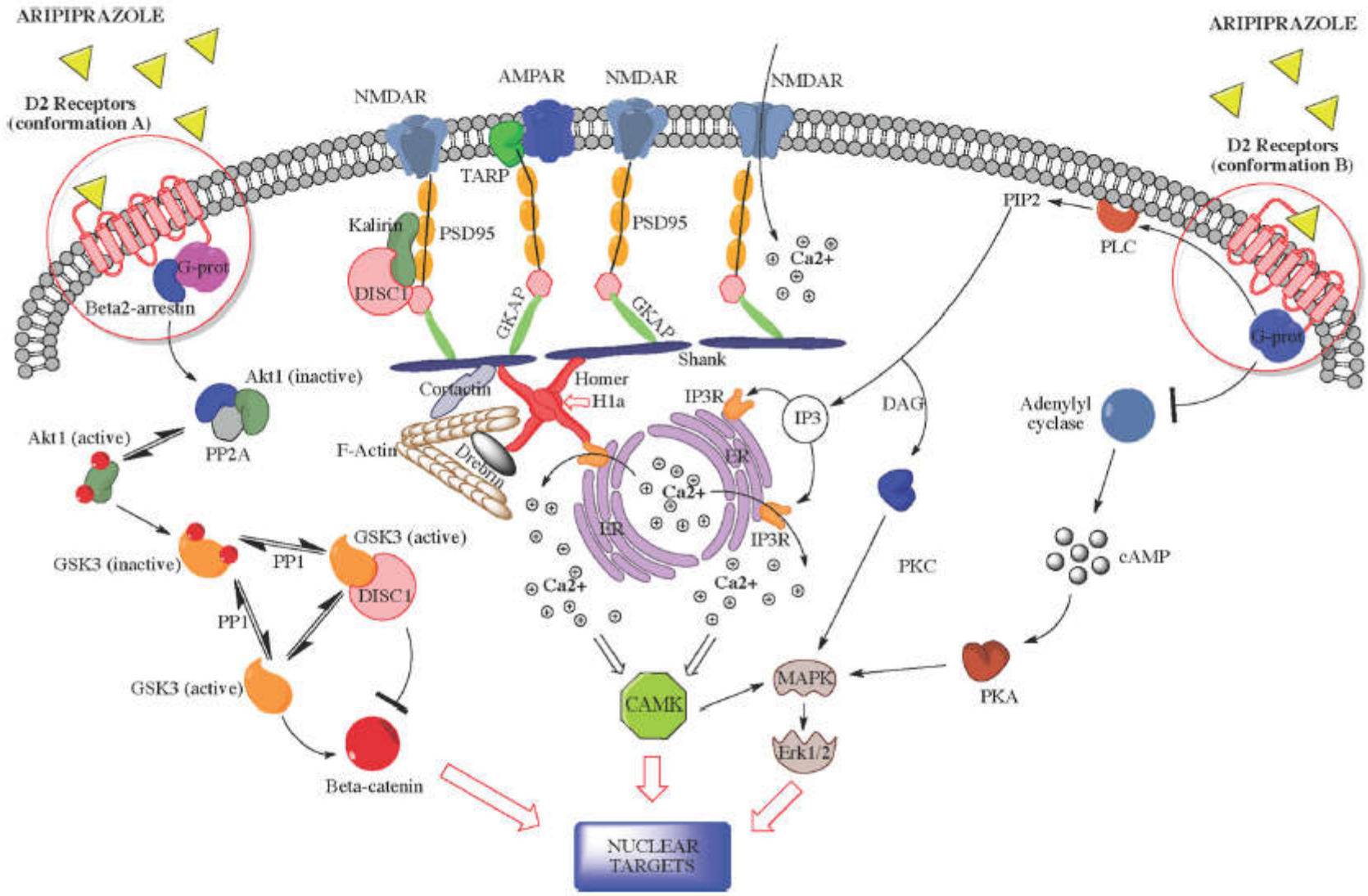
Figure 2. Least-squares mean improvement in neurocognitive composite score after 2 months of antipsychotic treatment, adjusted for baseline score and whether the patient required crisis stabilization in the 3 months prior to study entry. Patients with tardive dyskinesia were not included in the data 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.

CNS Drugs
DOI 10.1007/s40263-015-0278-3

REVIEW ARTICLE

Update on the Mechanism of Action of Aripiprazole: Translational Insights into Antipsychotic Strategies Beyond Dopamine Receptor Antagonism

Andrea de Bartolomeis[1] · Carmine Tomasetti[1] · Felice Iasevoli[1]



Psychiatry and Clinical Neurosciences 2014; 68: 425–431 doi:10.1111/pcn.12147

Regular Article

Effects of risperidone and aripiprazole on neurocognitive rehabilitation for schizophrenia

Yasuhiro Matsuda, MD,[1,2]* Sayaka Sato, PhD,[3] Kazuhiko Iwata, MD, MPH,[6] Shunichi Furukawa MD,[4] Norifumi Hatsuse, MD,[2] Yukako Watanabe, MD,[2] Nobuo Anzai MD, PhD,[5] Toshifumi Kishimoto, MD, PhD[1] and Emi Ikebuchi, MD, PhD[2]

Table 2 Synergistic effect of neurocognitive rehabilitation and antipsychotic medication

	Drug	Control		Rehabilitation		F		
		Mean	SD	Mean	SD	Rehabilitation	Drug	Drug×rehabilitation
PANSS								
Positive symptoms	RIS	−0.92	1.38	−1.67	1.58	4.30*	2.68	1.31
	APZ	1.30	2.00	−1.27	4.29			
Negative symptoms	RIS	−1.15	2.38	−1.56	1.33	0.55	0.37	0.08
	APZ	−0.40	2.80	−1.27	3.88			
General psychology	RIS	−0.54	4.35	−2.56	2.01	3.23	0.03	0.32
	APZ	0.70	5.48	−3.18	7.61			
Total score	RIS	−2.62	6.33	−5.78	3.70	3.90	0.65	0.61
	APZ	1.60	8.98	−5.73	12.59			
LASMI								
Interpersonal relations	RIS	−1.92	3.04	−4.22	6.83	1.97	1.22	0.02
	APZ	−0.50	5.02	−2.36	4.43			
Work	RIS	−0.85	1.14	−2.33	4.09	4.56*	0.32	0.58
	APZ	0.60	4.01	−2.55	4.37			
BACS (Z-score)								
Verbal memory	RIS	0.18	1.10	0.43	0.45	0.87	0.39	0.01
	APZ	0.35	0.46	0.57	0.90			
Working memory	RIS	0.19	0.94	0.35	0.74	3.85	6.07*	1.50
	APZ	−0.60	0.60	0.08	0.23			
Motor speed	RIS	0.56	0.67	0.40	0.43	1.43	1.47	4.38*
	APZ	−0.01	0.42	0.55	0.62			
Verbal fluency	RIS	0.04	0.88	0.39	0.77	0.28	0.72	0.82
	APZ	0.47	0.65	0.38	0.86			
Processing speed	RIS	−0.10	0.38	0.36	0.69	3.47	1.16	1.64
	APZ	0.25	0.42	0.33	0.42			
Executive functions	RIS	0.28	1.45	0.74	0.35	0.13	0.95	1.64
	APZ	0.37	0.45	0.11	0.62			
Composite score	RIS	0.16	0.41	0.40	0.31	2.95	0.02	0.22
	APZ	0.20	0.32	0.33	0.33			

Two-way factorial ANOVA.

*$P < 0.05$.

APZ, aripiprazole; BACS, Brief Assessment of Cognition in Schizophrenia; LASMI, Life Assessment Scale for the Mentally Ill; PANSS, Positive and Negative Syndrome Scale; RIS, risperidone.

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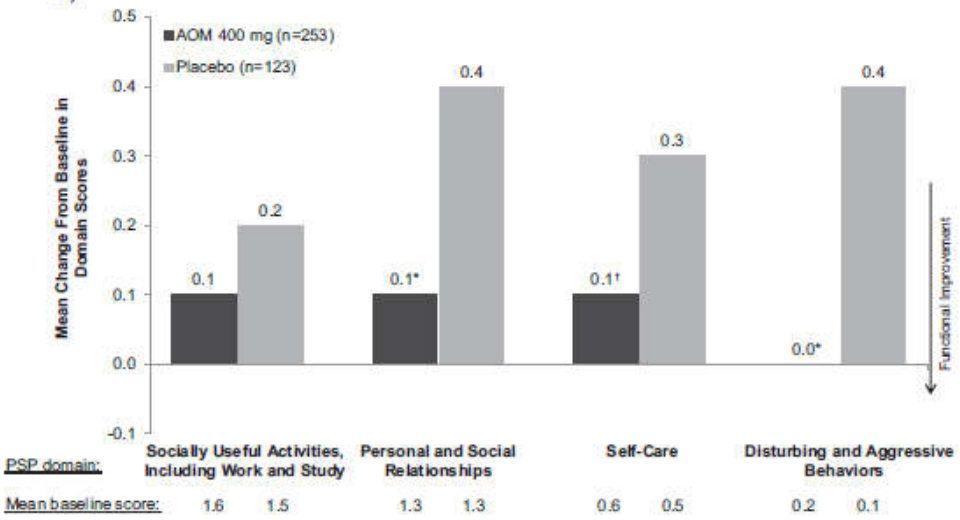
Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Effects of aripiprazole once-monthly on domains of personal and social performance: Results from 2 multicenter, randomized, double-blind studies

W. Wolfgang Fleischhacker [a,*], Ross A. Baker [b], Anna Eramo [c], Raymond Sanchez [b], Lan-Feng Tsai [b], Timothy Peters-Strickland [b], Pamela P. Perry [b], Robert D. McQuade [b], Brian R. Johnson [b], William H. Carson [b], John M. Kane [d,e]

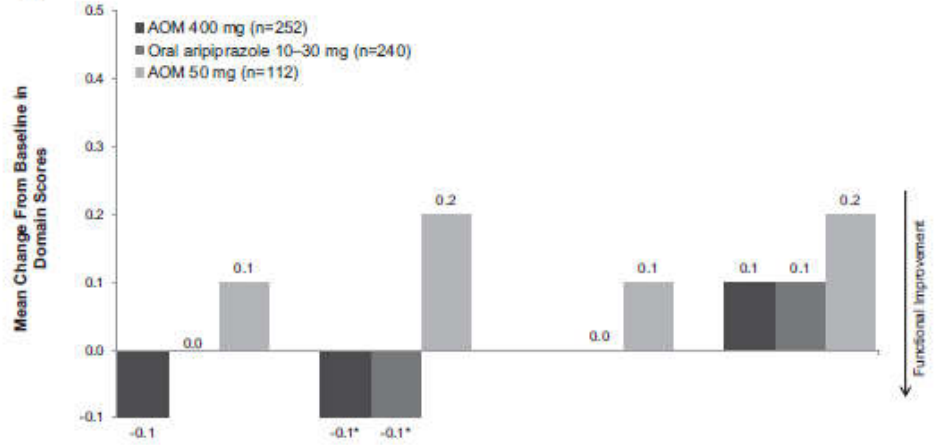
a)



PSP domain:	Socially Useful Activities, Including Work and Study		Personal and Social Relationships		Self-Care		Disturbing and Aggressive Behaviors	
Mean baseline score:	1.6	1.5	1.3	1.3	0.6	0.5	0.2	0.1

*$P<0.001$ vs placebo.
†$P<0.01$ vs placebo.

b)



PSP Domain:	Socially Useful Activities, Including Work and Study			Personal and Social Relationships			Self-Care			Disturbing and Aggressive Behaviors		
Mean baseline score:	1.8	1.7	1.7	1.6	1.6	1.5	0.7	0.6	0.6	0.2	0.1	0.1

*$P<0.05$ vs aripiprazole once-monthly 50 mg.

Schizophrenia Bulletin vol. 39 no. 3 pp. 564–574, 2013
doi:10.1093/schbul/sbr189
Advance Access publication January 30, 2012

Dopamine D_2 Receptor Occupancy and Cognition in Schizophrenia: Analysis of the CATIE Data

Hitoshi Sakurai[1], Robert R. Bies[2–4], Scott T. Stroup[5], Richard S. E. Keefe[6], Tarek K. Rajji[2,7], Takefumi Suzuki[1], David C. Mamo[2,7,8], Bruce G. Pollock[2,7], Koichiro Watanabe[1], Masaru Mimura[1], and Hiroyuki Uchida[1,2,*]

Table 4. Neurocognitive Scores Stratified by Dopamine D_2 Occupancy

		z Score (Mean ± SD)					
D_2 Occupancy Level	D_2 Occupancy Range (%)	Verbal Memory	Vigilance	Processing Speed	Reasoning	Working Memory	Summary Score
Low (n = 102)	15.5–62.7	0.084 ± 1.077	0.174 ± 0.964	0.159 ± 0.958	0.311 ± 0.866[a]	0.293 ± 0.787	0.275 ± 0.920
Slightly low (n = 102)	62.7–71.8	0.188 ± 1.015	0.306 ± 0.992[b]	0.223 ± 0.889	0.259 ± 0.899	0.229 ± 0.880	0.323 ± 0.937
Slightly high (n = 103)	71.9–77.2	0.180 ± 0.865	0.385 ± 0.951[c]	0.167 ± 0.913	0.285 ± 0.853	0.309 ± 0.736	0.354 ± 0.839[d]
High (n = 103)	77.2–85.8	0.025 ± 0.990	−0.110 ± 0.934	−0.085 ± 0.903	−0.013 ± 0.949	0.095 ± 1.017	−0.008 ± 0.951

Note: Significant differences were found in vigilance score, reasoning score, and summary score ($F_{3,406}$ = 5.21, P = .002; $F_{3,406}$ = 2.90, P = .04; $F_{3,406}$ = 3.36, P = .02, respectively) by the one-way ANOVA.
[a]P =.049 by the Turkey-Kramer HSD (honestly significant difference), vs high D_2 group.
[b]P = .012 by the Turkey-Kramer HSD, vs high D_2 group.
[c]P = .002 by the Turkey-Kramer HSD, vs high D_2 group.
[d]P = .025 by the Turkey-Kramer HSD, vs high D_2 group.

Schizophrenia Research 150 (2013) 51–57

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Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Predictors of cognitive and functional improvement and normalization after cognitive remediation in patients with schizophrenia

Antonio Vita [a,b,*], Giacomo Deste [b], Luca De Peri [a], Stefano Barlati [b], Roberto Poli [c], Bruno M. Cesana [d], Emilio Sacchetti [a,b]

Table 5
Predictors of functional improvement and normalization after cognitive remediation in patients with schizophrenia.

	Degrees of freedom	Exp(B) (outcome: HoNOS improvement)[a]	*P*
Predictors of functional improvement			
Age	1	0.890	0.006
Type of cognitive remediation (CACR > IPT-cog)	1	9.412	0.003
Model			<0.001
Predictors of functional normalization			
Antipsychotic dose (CPZ-eq)	1	0.996	0.032
Executive functions	1	2.496	0.069
Type of cognitive remediation (CACR > IPT-cog)	1	4.992	0.054
Model			0.001

[a] Exp(B) describes modification of the odds ratio of achieving the specific outcome with a 1-point change in the predictor variable.

Conclusion: Cognitive remediation could be more effective in younger, less disorganized, and cognitively less impaired patients, who take a smaller amount of antipsychotics. The predictive role of lower antipsychotic dosage on cognitive and functional outcome after remediation suggests either that patients with less severe illness could gain better advantage from cognitive remediation interventions or that high dose or complex antipsychotic therapy may limit the effectiveness of such interventions.

informa
healthcare

Influence of antipsychotic treatment type and regimen on the functionality of patients with schizophrenia

FRANCISCO J. ACOSTA, EUGENIO CHINEA, JOSÉ L. HERNÁNDEZ, FERNANDO RODRÍGUEZ, MIGUEL GARCÍA-BELLO, GEMA MEDINA, WILSON NIEVES

Table 3. Outcome variables with different antipsychotic drug types.

	First-generation ($n = 12$)	Second-generation ($n = 73$)	P
PSP	69.1 ± 19.5	68.9 ± 14.8	0.825
Self-care deficit	5 (41.7)	40 (54.8)	0.53
Activity-related deficit	9 (75.0)	58 (79.5)	0.72
Relationships-related deficit	10 (83.3)	53 (72.6)	0.72
Disturbing and aggressive behavior	4 (33.4)	12 (16.4)	0.23
CGI-SCH	8.8 ± 3.9	7.3 ± 4.9	0.157

Table 4. Outcome variables with different antipsychotic administration regimens.

Outcome	Depot ($n = 10$)	LAI risperidone ($n = 39$)	Depot plus oral first-generation ($n = 2$)	LAI risperidone plus oral second-generation ($n = 34$)	P
PSP	70.9 ± 21.0	71.4 ± 16.4	60 ± 1.41	66.0 ± 12.3	0.126
Self-care deficit	4 (40)	19 (48.7)	1 (50)	21 (61.8)	0.372
Activity-related deficit	7 (70)	26 (66.7)	2 (100)	32 (94.1)	0.007
Relationships-related deficit	8 (80)	23 (59)	2 (100)	30 (88.2)	0.012
Disturbing and aggressive behavior	4 (40)	6 (15.4)	0 (0)	6 (17.6)	0.242
CGI-SCH	8.6 ± 3.1	6.9 ± 4.7	10 ± 8.5	7.7 ± 5.2	0.291

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DOI 10.1007/s40263-013-0047-0

LEADING ARTICLE

Can Antipsychotics Improve Social Cognition in Patients with Schizophrenia?

Katarzyna Kucharska-Pietura · Ann Mortimer

Original Paper

Facial affect processing deficits in schizophrenia: A meta-analysis of antipsychotic treatment effects

Anthony S Gabay[1], Matthew J Kempton[1,2] and Mitul A Mehta[1]

Psychopharm

Journal of Psychopharmacology
2015, Vol. 29(2) 224–229

DOI: 10.1177/0269881114560184
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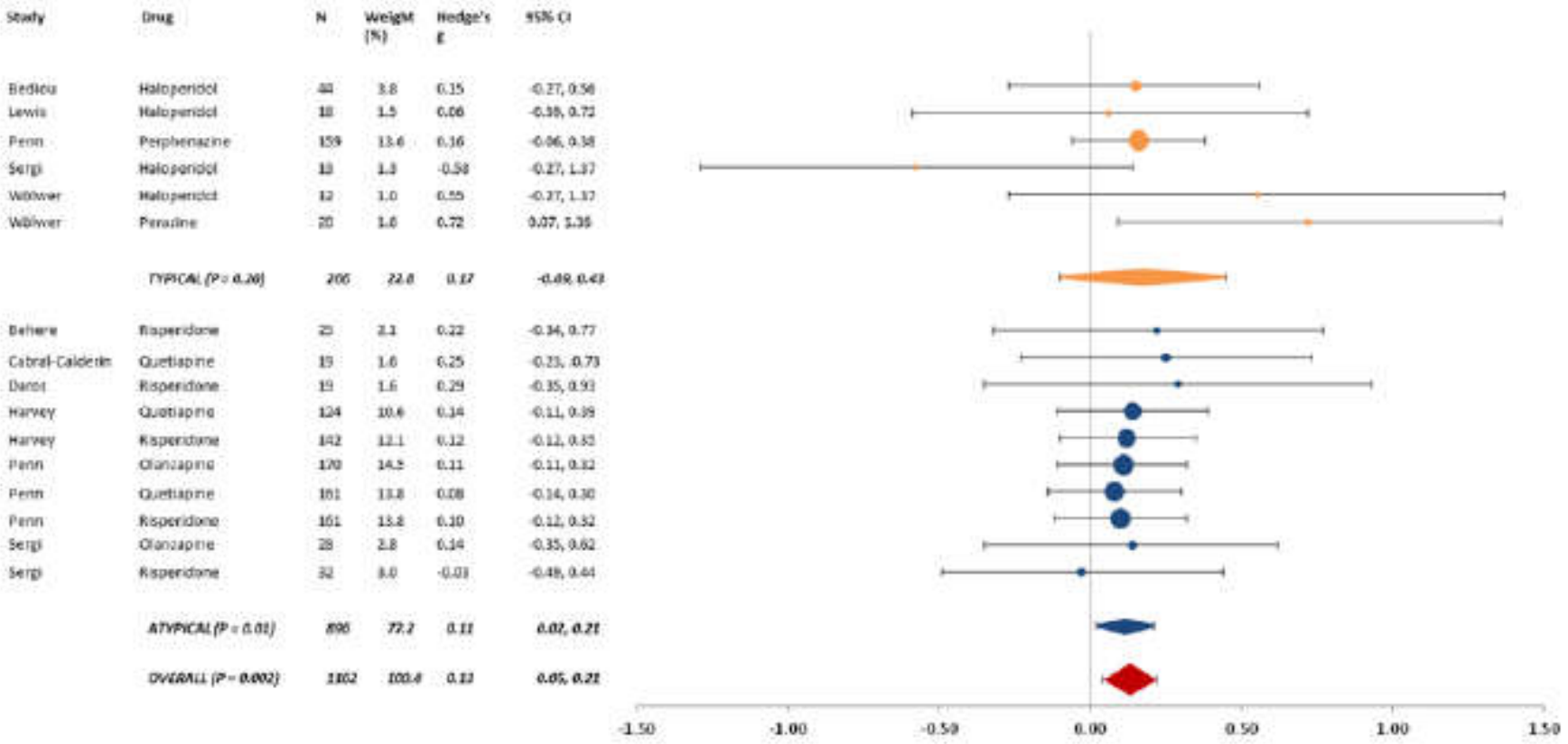
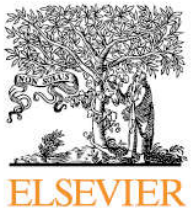


European Neuropsychopharmacology (2014) 24, 575-584



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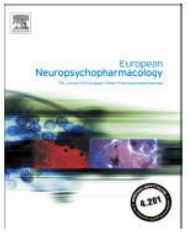

Open, randomized trial of the effects of aripiprazole versus risperidone on social cognition in schizophrenia

Arija Maat[a,*], Wiepke Cahn[a], Harm J. Gijsman[b], Johannes E. Hovens[c], René S. Kahn[a], André Aleman[d]

Table 4 Change from baseline to week 8 on test-score and reaction time for social cognition and neurocognition and change from baseline to week 8 on outcome measures by treatment [a]

Variable	Aripiprazole		Risperidone		*P*-value for comparing treatment groups[b]	
	Mean (SD)	*n*	Mean (SD)	*n*	*F*-statistic	*P*-value
Social cognition						
Facial affect recognition						
Baseline	49.28 (4.99)	18	47.04 (8.18)	24	$F_{1,39}$ =.01	.93
Change	1.11 (7.58)		2.63 (8.84)			
Emotional working memory						
Baseline	11.44 (1.93)	16	10.18 (2.95)	22	$F_{1,35}$ =.79	.38
Change	.94 (1.91)		1.32 (3.17)			
Baseline RT	141.09 (39.32)		140.80 (31.90)		$F_{1,35}$=8.41	.006
Change RT	−24.10 (31.57)		−1.62 (24.20)			
Emotional learning task						
Baseline	19.58 (8.12)	12	17.58 (9.95)	19	$F_{1,28}$ =.39	.54
Change	3.50 (7.10)		6.11 (8.86)			
Baseline RT	587.58 (99.13)		624.58 (243.87)		$F_{1,28}$=3.90	.06
Change RT	−134.81 (175.41)		−13.42 (220.34)			
Emotional memory						
Baseline	63.29 (8.97)	14	61.29 (8.22)	21	$F_{1,32}$=1.32	.26
Change	2.93 (7.36)		2.24 (9.23)			
Baseline RT	142.84 (36.62)		156.42 (43.00)		$F_{1,32}$=.02	.88
Change RT	−18.70 (28.52)		−26.89 (34.85)			
Neurocognition						
Digit symbol substitution						
Baseline	50.11 (14.97)	19	37.61 (9.99)	18	$F_{1,34}$=10.33	.003
Change	4.26 (5.93)		3.17 (4.53)			
Working memory						
Baseline	12.06 (1.82)	17	11.57 (2.64)	21	$F_{1,35}$ =.87	.36
Change	.82 (2.51)		.48 (1.91)			
Baseline RT	121.12 (32.60)		134.93 (36.89)		$F_{1,32}$=5.66	.023
Change RT	−17.20 (24.53)		−8.62 (30.09)			
Identity learning						

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Editorial

LONG-ACTING INJECTABLE (DEPOT) ANTIPSYCHOTICS AND CHANGING TREATMENT PHILOSOPHY: POSSIBLE CONTRIBUTION TO INTEGRATIVE CARE AND PERSONAL RECOVERY OF SCHIZOPHRENIA

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CAMBIAMENTO DELLA RELAZIONE TERAPEUTICA

PAZIENTE

- Luogo della cura
- Tempo della cura
- Appropriarsi della cura
- Libertà dalla cura

PSICHIATRA

- **Rinuncia allo schema di visita**
- **Perdita del rituale prescrittivo**
- **Parlare con una persona che sta bene**
- **Di cosa ?**

Possible medications to improve cognition in schizophrenia

Antipsychotics have modest effects if any

Newer options:

- COMT antagonists?
- GABA modulating agents
- Omega 3 Fatty acids
- Glutamate agonists
  - glycine and D-serine?
- Norepinephrine reuptake blockers
  - Atomoxetine?
- Dopamine partial agonists
  - Aripiprazole?
- Nicotinergic
  - Alpha-7 nicotinic receptor agonists?
- Muscarinic
  - Donepezil?

Needed: Safe and effective cognition enhancing agent