RESEARCH UPDATES: Improving Functioning In Schizophrenia?

Stephen R. Marder, MD
Professor and Director, Section on Psychosis
Semel Institute for Neuroscience and Human Behavior at UCLA
Director, Mental Illness Research, Education, and Clinical Center (MIRECC)
Los Angeles, California

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Stephen R. Marder, M.D.

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Recovery in Schizophrenia

• Controlling symptoms is too modest a goal.

• Patients and their advocates are interested in improving functioning and quality of life.
Improving functioning in people with psychotic illness: A new goal for treatment research

- Limitations of antipsychotic medications
- Combining pharmacological and non-pharmacological treatments
- Focus on functioning
- Pharmacology to facilitate training
Two-Year Outcome of Social Skills Training and Group Psychotherapy for Outpatients With Schizophrenia

Stephen R. Marder, M.D., William C. Wirshing, M.D., Jim Mintz, Ph.D., Joanne McKenzie, R.N., Kathleen Johnston, M.S., Thad A. Eckman, Ph.D., Malca Lebell, Ph.D., Karin Zimmerman, Ph.D., and Robert P. Liberman, M.D.

Am J Psychiatry 153:12, December 1996

- Drugs and Social Skills Training affect different outcomes
- Drugs treat psychosis
- Social Skills Training improves social adjustment
People receiving a newer antipsychotic were more likely to remain in treatment when they received enhanced skills training.
What does it take for someone with schizophrenia to function in the community?

Known Determinants
- Cognition
- Social Cognition
- Motivation

Domains of Community Functioning
- Family and Social Connections
- Work and Productive Activities
Neurocognitive Deficits and Functional Ability

Five Consensus Based Domains

- **Affective flattening**
  - Face, voice, gestures, spontaneous movement

- **Alogia**
  - Speech quantity, spontaneous elaboration

- **Anhedonia**
  - Anticipatory & consummatory

- **Avolition**
  - Productive self-care, work motivation

- **Asociality**
  - Family, friends, romantic

**Diminished expression**

**Diminished motivation & pleasure**
Social Cognition in Schizophrenia

What are the key social processing brain systems that are needed to navigate our social world?

- Social cue recognition
- Affect sharing
- Mentalizing
- Emotion regulation
From Perception to Functional Outcome in Schizophrenia

Modeling the Role of Ability and Motivation

Michael F. Green, PhD; Gerhard Hellemann, PhD; William P. Horan, PhD; Junghee Lee, PhD; Jonathan K. Wynn, PhD

Arch Gen Psychiatry. 2012;69(12):1216-1224.
Cognitive Impairment in Schizophrenia

- Patients tend to have deficits in multiple areas of cognitive functioning, suggesting generalized impairment.

- Cognitive impairment can be detected in preschizophrenic children as early as first grade.

- First-episode patients: Impairment consistent with those seen in more chronic patients.
Neuroplasticity-based training in Schizophrenia
(Fisher et al 2009)

FIGURE 2. Change in Cognitive Performance in Patients With Schizophrenia After 50 Hours of Computerized Auditory Training or 50 Hours of Computer Games

- Significant difference between groups (p<0.01, repeated-measures ANOVA).
- Significant difference between groups (p<0.05, repeated-measures ANOVA).
- Nonsignificant difference between groups (p>0.10, repeated-measures ANOVA).

Cognitive Training: Effects on Employment Rate

Innovative Strategies for Negative Symptoms

- Clinical Targets for Negative Symptom Treatments
- Adjunctive Medications
- Monotherapy Approaches
- Psychosocial Approaches
Recent Trials

- Bitopertin – GlyT1 – Negative Study
- Targacept -- α7 nicotinic – Negative Study
- Encenicline -- α7 nicotinic – Positive for Cognition and Negative Symptoms in Phase 2 and negative in Phase 3
- ABT-126 – α7 nicotinic -- Press Release – Positive for Cognition and Negative Symptoms
- DMXB-A -- α7 nicotinic – Positive for Cognitive and Negative Symptoms
Cariprazine versus risperidone monotherapy for treatment of predominant negative symptoms in patients with schizophrenia: a randomised, double-blind, controlled trial

György Nimeth, István Laszlovszky, Pál Czober, Erzsébet Szőkei, Balázs Szatmári, Judit Harsányi, Ágota Barabásy, Marc Debelle, Suresh Durgam, István Bitter, Stephen Marder, W. Wolfgang Fleischhacker
Nemeth et al:
Cariprazine and risperidone as monotherapy for negative symptoms
Psychosocial Treatments

• Social Skills training
• Cognitive Remediation
• CBTp
• Cognitive Behavioral SST
Randomized Trial to Evaluate the Efficacy of Cognitive Therapy for Low-Functioning Patients With Schizophrenia

Paul M. Grant, PhD; Gloria A. Huh, MSED; Dimitri Perivoliotis, PhD; Neal M. Solor, MD, PhD; Aaron T. Beck, MD

Context: Low-functioning patients with chronic schizophrenia have high direct treatment costs and indirect costs incurred due to lost employment and productivity and have a low quality of life; antipsychotic medications and psychosocial interventions have shown limited efficacy to promote improved functional outcomes.

Objective: To determine the efficacy of an 18-month recovery-oriented cognitive therapy program to improve psychosocial functioning and negative symptoms (avolition-apathy, anhedonia-asociality) in low-functioning patients with schizophrenia.

Design, Setting, and Participants: A single-center, 18-month, randomized, single-blind, parallel group trial enrolled 60 low-functioning, neurocognitively impaired patients with schizophrenia (mean age, 38.4 years; 33.3% female; 65.0% African American).

Interventions: Cognitive therapy plus standard treatment vs standard treatment alone.

Main Outcome Measures: The primary outcome measure was the Global Assessment Scale score at 18 months after randomization. The secondary outcomes were scores on the Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms at 18 months after randomization.

Results: Patients treated with cognitive therapy showed a clinically significant mean improvement in global functioning from baseline to 18 months that was greater than the improvement seen with standard treatment (within-group Cohen d, 1.36 vs 0.06, respectively; adjusted mean [SE], 58.3 [3.30] vs 47.0 [3.60], respectively; P < .03; between-group d = 0.56). Patients receiving cognitive therapy as compared with those receiving standard treatment also showed a greater mean reduction in avolition-apathy (adjusted mean [SE], 1.66 [0.31] vs 2.81 [0.34], respectively; P = .01; between-group d = 0.66) and positive symptoms (hallucinations, delusions, disorganization) (adjusted mean [SE], 9.4 [3.3] vs 18.2 [3.8], respectively; P = .04; between-group d = −0.46) at 18 months. Age was controlled in the analyses, and there were no meaningful group differences in baseline antipsychotic medications (class or dosage) or in medication changes during the course of the trial.

Conclusion: Cognitive therapy can be successful in promoting clinically meaningful improvements in functional outcome, motivation, and positive symptoms in low-functioning patients with significant cognitive impairment.

Trial Registration: clinicaltrials.gov Identifier: NCT00300883

Arch Gen Psychiatry.
Published online October 3, 2011.
doi:10.1001/archgenpsychiatry.2011.120
Global Functioning

Mean GAS Score vs Assessment Time

- ST alone (n=29)
- CT with ST (n=31)

Negative symptoms

avolution-apathy (A), anhedonia-asociality (B), affective flattening (C), and alogia (D)
CAN SOCIAL COGNITION BE IMPROVED?

Broad-based treatments


Unclear whether social cognitive interventions per se contribute to improvements

Targeted treatments

SCIT: Penn, Combs, Roberts et al; TAR: Wolwer et al., 2005; Ronconce et al., 2004; Russell et al., 2006; Silver et al., 2004;

Primarily inpatients, focus on facial affect perception
RCT Design

- 134 stabilized outpatients with psychotic disorders
- Randomly assigned to 1 of 3 12-week, group-based conditions

**SCST-Clinic**
- n = 47
- 24 SCST sessions (2/week)
- 6 extra practice sessions at clinic (1/week during final 6 weeks)
- Total 30 sessions

**SCST-In vivo**
- n = 41
- 24 SCST sessions (2/week)
- 6 extra practice sessions in community (1/week during final 6 weeks)
- Total 30 sessions

**Illness management**
- n = 45
- 24 sessions (2/week)
- 6 extra practice sessions at clinic (1/week during final 6 weeks)
- Total 30 sessions

**Assessments**
- Baseline, Mid-point (week 6), End-point (week 12), 3-month follow-up (week 24)
MODULE 1: Emotion processing

- Defining 6 basic emotions
  1. Happy
  2. Sad
  3. Anger
  4. Disgust
  5. Afraid
  6. Surprise

- Recognizing them on the face
- Identifying social situations that often elicit them
MODULE 2: Social perception

- Identifying basic emotions in the voice
- Identifying social cues: non-verbal gestures, proximity norms, social norms
MODULE 3: Attributional Style

• How our emotions impact our social interpretations

• Suspicious feelings in different contexts: helpful vs. harmful

• Avoiding jumping to conclusions in ambiguous social situations
  → gather further information
MODULE 4: Empathy

- Understanding how other people feel
- Using this information to Respond empathically
MODULE 5: Understanding intentions

• Perspective-taking skills

• Distinguishing among sincerity, sarcasm, and lying to be kind

• Detective work: are there mismatches among the social cues?

Your mother in law asks: “How do you like my new haircut?”

Your respond: Wow, it looks great!
## Social Cognitive Skills Training: Approach

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<th>Targeted treatment to four domains:</th>
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<td>• Affect perception, social perception, attributions, theory of mind</td>
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<th>Skills building approach</th>
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<td>• Gradually build from simple to complex – automate through practice</td>
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<th>Highly structured</th>
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<td>• Review, new material, practice</td>
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<th>Draws upon existing materials and exercises from Penn’s Social Cognition &amp; Interaction Training (SCIT; Penn et al., 2006)</th>
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| New training exercises & training materials |
In vivo community-based exercises (6-sessions)

- 2 individual, 4 small-group sessions
- Pre-specified locations (e.g., coffee shop, cafeteria, mall)
- Structured set of activities with corresponding worksheets

Sessions 1 and 2:
- attend to describing one’s own feelings
- identify social/emotional cues in others: face, body, voice

Sessions 3 and 4:
- identify type of relationships between interacting people
- practice empathy and perspective taking: others’ feelings, thoughts, intentions

Sessions 5 and 6:
- identify type of relationship between interacting people
- practice empathy and perspective taking: others’ feelings, thoughts, and intention
- members lead exercises and provide feedback to each other
Analyses

Generalized linear mixed models Group: between-subject factor
Time: within-subject

SCST-Clinic + SCST-In vivo] vs. CON from Baseline to End-point

SCST-Clinic vs. SCST-In vivo from Mid-point to End-point
Emotion processing

a. Facial Affect Identification

- SCST effect: $F = 13.71, p < .001$
- In vivo effect: $F = 2.73, p < .05$
Empathy

In vivo effect: $F = 4.50, p < .05$
Can drugs facilitate training?

- Oxytocin has been shown to increase the salience of social information.

- We evaluated whether administering oxytocin just before a session of social cognition training would improve learning.
Our research question

By increasing the salience of social information, can oxytocin – administered just prior to each training session -- facilitate learning for schizophrenia patients in social cognition training?

Supported by a NARSAD (BBRF) Distinguished Investigator Award
Oxytocin-Augmented Social Cognitive Skills Training in Schizophrenia

Screening and Consent

Baseline Evaluation Social Cog, MCCB, BPRS, CAINS

1 week

Randomize to Placebo or Oxytocin

1 week

Placebo or Oxytocin administered 30 min prior to each group

12 sessions of Social Cog Training over 6 weeks

7 weeks

Post Treatment Evaluation Social Cog, MCCB, BPRS, CAINS

1 month

One month Follow-up Social Cog, MCCB

1 month

7 weeks

Social Cog, MCCB
Oxytocin and Empathic Accuracy

* p=.03 treatment x time interaction
Improving functioning in schizophrenia

Antipsychotics can improve psychosis, but they can make people feel miserable.

Antipsychotics improve psychosis, but they do not improve functioning.

Targeted psychosocial treatments can improve functioning.

In the future, we may prescribe medications to facilitate psychosocial treatments.