Looking Beyond Mood & Psychosis: A Focus On Neurocognition

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**Position:** Dr. Harvey is the Leonard M. Miller Professor of Psychiatry and director of the Division of Psychology at the University of Miami Miller School of Medicine. He is also a VA Senior Health Scientist. He is the author of over 1,000 scientific papers and abstracts and he has written over 60 book chapters.

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Objectives

• Discuss the incidence and functional consequences of neurocognitive deficits in bipolar disorder and schizophrenia

• Explore the use of cognitive remediation for patients with schizophrenia

• Review and highlight the potential benefits of social cognitive interventions for those with schizophrenia
A Brief History of Neurocognition in BD

• **1898:** Kraepelinian’s Dichotomy

• **1978:** The first paper on BD and cognition

  Cognitive functions in manic-depressives: effects of lithium and physostigmine.
  
  R Telford and EP Worrall
  
  *The British Journal of Psychiatry*

• **1998:** Less than 10 papers published on BD and cognition
  – More than 200 published in SZ

• **2008:** Over 500 papers published on BD and cognition

• **2012:** Nearly 2000 published

BD, bipolar disorder; SZ, schizophrenia.

Categorical Diagnostic Overlap

• Bipolar disorder and schizophrenia have unique and overlapping clinical features\textsuperscript{1}

• The two disorders share more than half of their genetic determinants and progress in genetic studies suggests many shared risk variants\textsuperscript{1,2}

Within Disorder Heterogeneity

Cognitive Profiles in BD and SZ

* Values are related to the bipolar and healthy control comparison, not to the SZ group.

Att, attention; BD, bipolar disorder; Soc Cog, social cognition; Sp Proc, speed of processing; SZ, schizophrenia; Verb Learn, verbal learning; Vis Learn, Visual Learning; Work Mem, Working Memory.

Cognitive Heterogeneity in BD

BD, bipolar disorder; BP Psych, psychotic bipolar disorder; BP Nonpsych, nonpsychotic bipolar disorder; Schiz, schizophrenia; SD, standard deviation.

Cognition-Function Relationship

• Multivariate path models link neurocognitive ability with real world functional performance in patients with BD and SZ
  – Consistently shown in previous studies for patients with SZ
  – Fewer studies for patients with BD but evidence suggests similar pattern of prediction

• Pharmacological and nonpharmacological interventions are needed to target cognition in BD and SZ

BD, bipolar disorder; Schiz, schizophrenia; SD.

Meta-analysis of the association between cognitive abilities and everyday functioning in bipolar disorder

- A meta-analysis of 22 studies was conducted to examine the association between cognitive ability and everyday functioning in bipolar disorder*
- Primary findings include:
  - Significant mean correlation between neurocognitive ability and functioning (mean r=0.27, 95% CI=0.22–0.32, p<0.001)
    - Cognitive Domains:
      - Visual Learning and Memory (r=0.21)
      - Working Memory (r=0.29)
      - Composite Cognitive Functioning domain (r=0.33)
    - Functioning:
      - Self-reported (r=0.20)
      - Clinician-reported (r=0.23)
      - Performance-based (r=0.32)
      - Functional Milestone (r=0.33)
- The strength of association between cognitive ability and everyday functioning in bipolar disorder is similar to that seen in schizophrenia
  - While patients with bipolar disorder may have lesser impairment in cognitive ability and functioning when compared to patients with schizophrenia, the impact of cognitive impairment on everyday functioning appears quite similar
- Since cognitive impairments account for a significant degree of disability experienced by those with bipolar disorder, cognitive remediation, if effective, could potentially impact everyday functioning

* N=1,344
CI, confidence interval.
Mood State Effects on Cognition

Manic and Euthymic Patients

- In comparison to euthymic patients, manic patients exhibited impaired verbal learning
- Manic and euthymic patients exhibited impaired:
  - Attention
  - Verbal long-delay free recall
  - Phonemic and semantic fluency
  - Problem-solving
  - Speeded set-shifting

Depressed and Euthymic Patients

- In comparison to euthymic patients, depressed patients exhibited impaired CVLT performance and phonemic fluency
- Manic and depressed patients exhibited impaired:
  - Speeded visual scanning
  - Speeded set-shifting

CVLT, California Verbal Learning Test.

COGNITIVE IMPAIRMENT AND REMEDIATION IN SCHIZOPHRENIA
Overview

- Cognitive impairment has been described as an important feature that is commonly associated with schizophrenia\(^1-3\)
- Options to address cognition and functioning include psychosocial support programs and cognitive remediation interventions\(^3,4\)
- Cognitive remediation therapy (CRT) has a history of clinical research dating back to the 1960s, and may be delivered in computerized or traditional format\(^4,5\)
- A variety of computerized CRT interventions has been evaluated in patients diagnosed with schizophrenia, sometimes in combination with other interventions\(^6-8\)
- Social cognition in schizophrenia is a growing area of research\(^9,10\)

1. APA. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. American Psychiatric Association; 2013.
Cognitive Impairment Associated with Schizophrenia

- Cognitive impairment has been described as an important feature that is commonly associated with schizophrenia\textsuperscript{1-3}
  - Manifests early\textsuperscript{4} and is relatively stable throughout disease course\textsuperscript{5}
  - May affect patients across the IQ strata, including those with high IQs\textsuperscript{6}
  - Estimates of prevalence vary widely, from 65% to more than 90%, owing to the heterogeneity of studies\textsuperscript{7,8}

Cognitive deficits may help in explaining the functional impairment associated with schizophrenia\textsuperscript{3}

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IQ, intelligence quotient.

1. APA. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. American Psychiatric Association; 2013.
Cognitive Impairment Is an Important Intervention Target

- There is currently no FDA-approved treatment for cognitive impairment associated with schizophrenia¹
- Options to address cognition and functioning include psychosocial support programs and a variety of cognitive remediation interventions²,³

FDA, Food and Drug Administration.

What Is Cognitive Remediation?

“Cognitive remediation is an intervention targeting cognitive deficit (attention, memory, executive function, social cognition, or meta cognition) using scientific principles of learning with the ultimate goal of improving functional outcomes. Its effectiveness is enhanced when provided in a context (formal or informal) that provides support and opportunity for improving everyday functioning”
—Cognitive Remediation Experts Working Group, 2012

• Cognitive remediation therapy (CRT) is distinguished from other psychosocial programs (eg, work skills training or adaptive strategies) by its specific goals of improving cognitive functioning and self-management of cognitive difficulties

• CRT interventions may range from solo drill-and-practice exercises to facilitator-guided group sessions and strategy coaching
  – CRT may be linked to a larger psychosocial rehabilitation approach

Computerized CRT Has Been Evaluated in Combination With Functional Skills Training in a Short-Term Study

- In a short-term, randomized study of outpatients diagnosed with schizophrenia (N=107), computerized CRT was combined with functional skills training
  - Functional adaptation skills training addressed social skills, transportation skills (reading maps, using transit schedules), and medication management
- Patients were randomized to 1 of 3 conditions:
  - 12 weeks of CRT followed by 12 weeks of TAU
  - 12 weeks of functional adaptation skills training followed by 12 weeks of TAU
  - 12 weeks of CRT followed by 12 weeks of functional skills training

CRT, cognitive remediation therapy; TAU, treatment as usual.

Social Cognition Has Emerged as a Potential Intervention Target

Social cognition refers to making sense of the social world—the mental operations underlying social interactions, including the ability to perceive, interpret, and respond to the intentions and dispositions of others.\textsuperscript{1,2}

- Impairments in social cognition can have a detrimental impact on real-world functioning.\textsuperscript{3,4}
  - Social cognition may be more strongly associated with functional outcomes than neurocognition.\textsuperscript{3}

- A meta-analysis suggests that social cognitive impairments may be responsive to structured training interventions.\textsuperscript{5}

- Social cognition in schizophrenia is a growing area of research.\textsuperscript{3,6}
  - An expert panel has recently identified and validated measures of social cognition for use in clinical trials.\textsuperscript{7}

Summary

• Cognitive impairment is a core feature of bipolar disorder and schizophrenia\(^1-4\)
• Options to address cognition and functioning include psychosocial support programs and cognitive remediation interventions\(^3,5\)
• CRT has as its specific goals the improvement of cognitive functioning and self-management of cognitive difficulties\(^5\)
  – CRT interventions may be delivered in a computerized or traditional format\(^5,6\)
• Various computerized CRT programs have been evaluated in patients diagnosed with schizophrenia, including in combination with other interventions\(^7-9\)
• Social cognition has emerged as a potential intervention target\(^10,11\)

CRT, cognitive remediation therapy.

1. APA. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. American Psychiatric Association; 2013.
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