

Assessment of Cognition in Depression Treatment Studies

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Disclosures

- In the past 12 months Dr. Harvey has served as a consultant for:

Abbvie, Boehringer-Ingelheim, Forest Labs, Forum Pharma, Genentech, Otsuka-America, Roche Pharma, Sunovion Pharma, and Takeda

How Do You Assess Cognitive Functioning?

- Performance-based tests
- Self-report
- Informant report

Strategies for Cognitive Assessment

- Battery length and comprehensiveness varies considerably in previous research
 - Extensive Batteries
 - Expanded Halstead Reitan, maybe 8 hours
 - Shorter Batteries
 - MATRICS Consensus Cognitive Battery
 - Abbreviated Batteries
 - BAC;BCATS, etc.

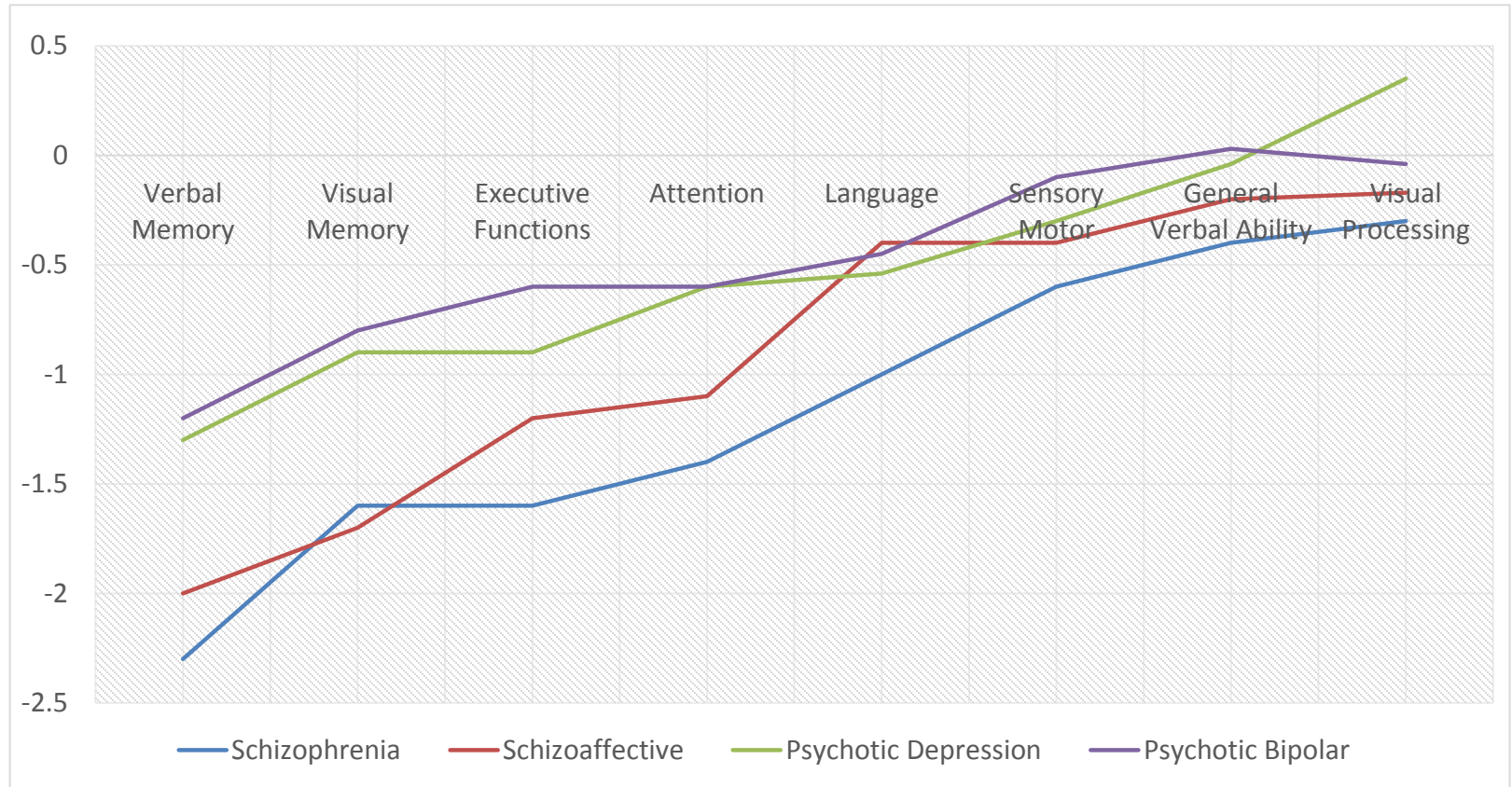
Advantages for Each Strategy

- Longer
 - Higher Reliability
 - Greater coverage (especially if you are not sure what's impaired)
- Shorter
 - Practicality
 - Tolerability

Tailoring the Assessment for Mood Disorders

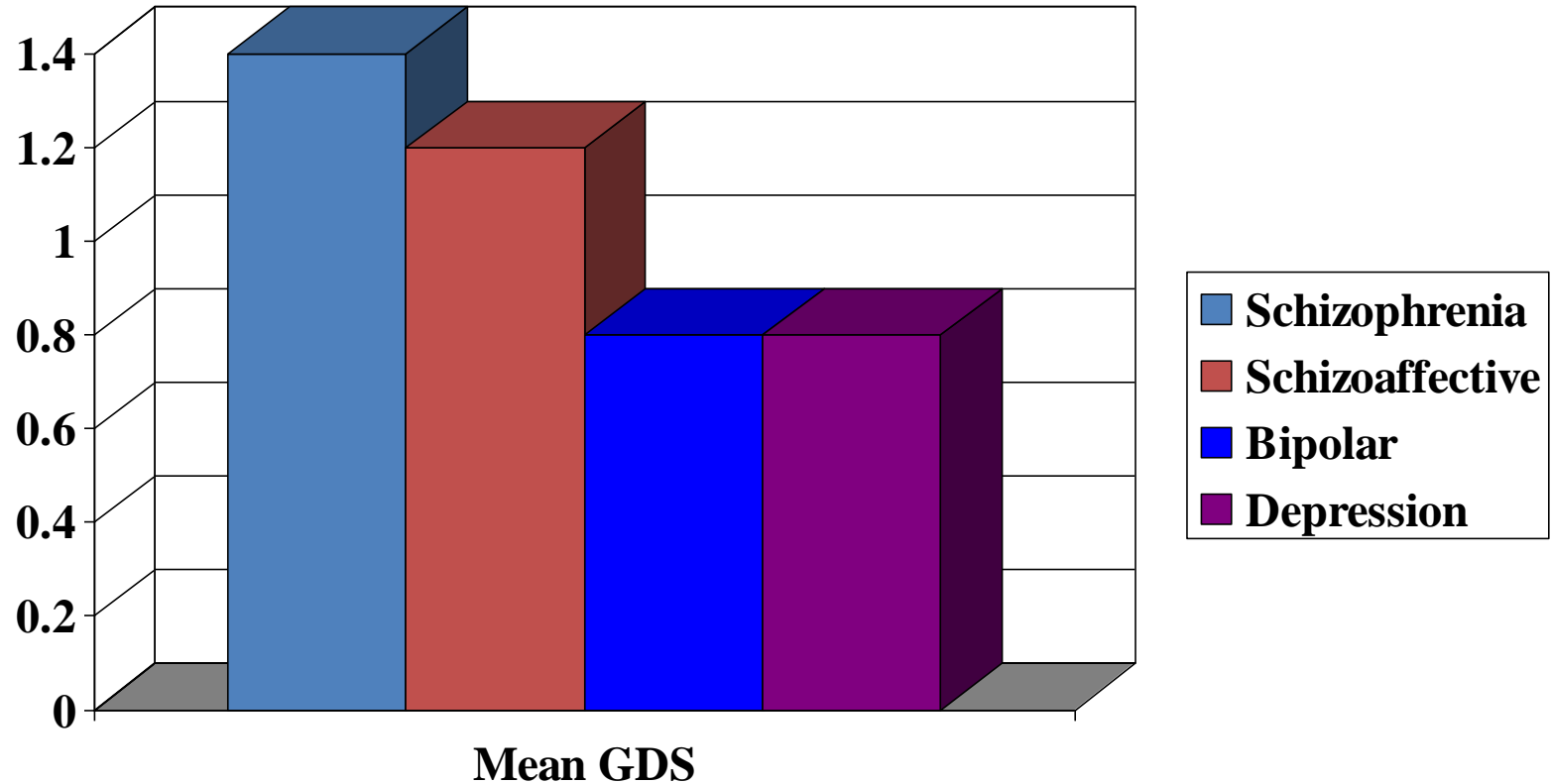
- As noted in the last talk, there are several highly salient domains in mood disorders
- These include attention, executive functioning, and, importantly, processing bias
- Processing bias as a “hot” cognition domain is not covered by many NP assessment strategies
- Setting aside the issue of hot cognition, are there truly different domains of cognitive impairment in mood disorders and other areas with well validated cognitive assessments?

Performance of First Episode Patients Compared to Normative Standards



From Reichenberg et al., 2009

Mean GDS Scores Across groups



Note. GDS+ Global Deficit Score

Schizophrenia= schizoaffective>mania=depression

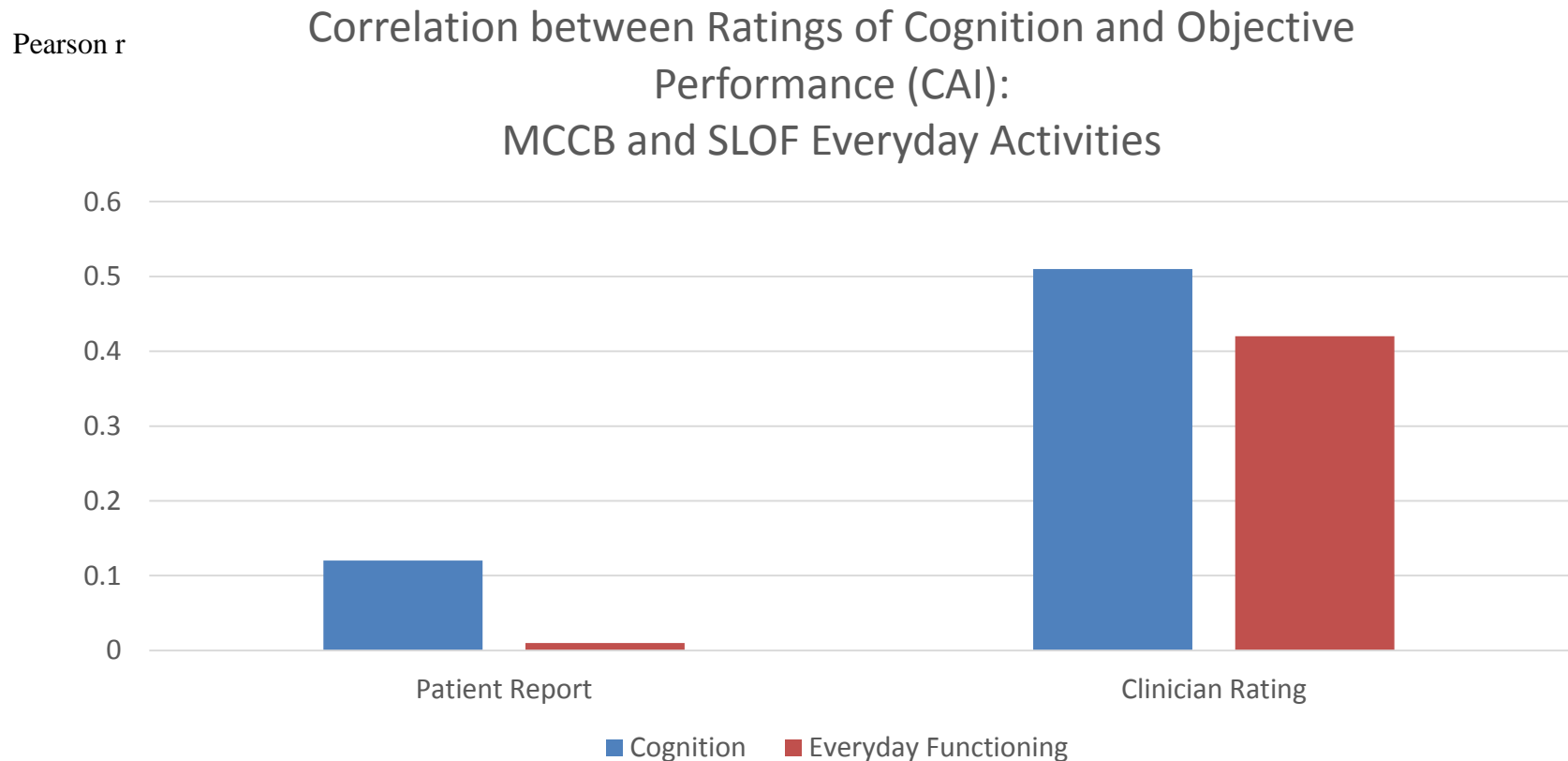
Interview-Based Strategies

- Several structured inventories are developed
- Some are aimed at mood disorders in specific
- Others are aimed at schizophrenia and have been partially validated in mood disordered populations

Very Consistent finding

- Self-reported mood symptoms, particularly in the residual state when augmentation therapy would be considered, are poorly correlated with performance-based measures
- Sometimes the correlation is 0
- The open question, however, is whether informant/observer ratings would be better

High Contact Clinicians as Cognition Raters



Bipolar depression patients; n=30

Self reports of Functioning and Cognition in Bipolar Disorder are Driven by Depression

Pearson Correlations Between Self-reported vs Clinician Rated Functioning

Clinician Rated	Patient Reported
SLOF Interpersonal Functions	.17
SLOF Activities Subscale	.01
SLOF Vocational Subscale	.30 ^a
Cognitive Assessment Inventory	.07

Correlations Between Self-reported vs Clinician Rated Functioning and Performance and Symptom Measures

	MCCB Total Score	UPSA-B	WCST Performance	BDI Total
Clinician Rated				
SLOF Interpersonal Functions	.16	.07	.10	-.20
SLOF Activities Subscale	.31*	.39*	.29 ^a	.21
SLOF Vocational Subscale	.23	.37*	.28	-.20
Cognitive Assessment Inventory	.41*	-.30 ^a	.54*	.20
Self-Reported				
SLOF Interpersonal Functions	.24	-.13	-.06	-.58*
SLOF Activities Subscale	.11	.14	-.06	-.40*
SLOF Vocational Subscale	.08	.00	.22	-.59*
Cognitive Assessment Inventory	.22	-.29	.06	.60*

What about Co-Primary Measures

- Regulatory agencies have asked for co-primary measures in AD and SCZ trials
- Both Performance-based and Interview based measures have been used
- The Performance-Based measures are typically functional capacity measures
- The FDA has allowed the use of interview-based measures aimed at functional cognition in previous studies
- These measures were reviewed in the previous section

UCSD Performance-Based Skills Assessment (UPSA)

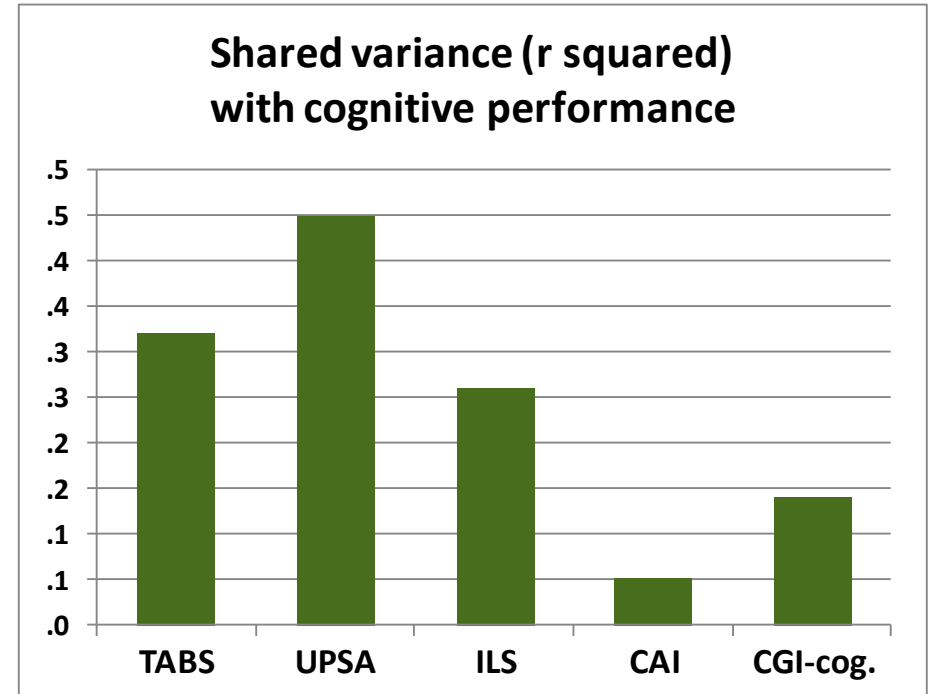
- Developed as a performance-based measure of everyday living skills
- Five domains
 - Comprehension/Planning
 - Finance
 - Communication
 - Mobility
 - Household Chores
- Scaled to 100-point score

Modifications of the UPSA

- UPSA-II
 - Medication Management added
- UPSA-VIM
 - Difficulty altered
- UPSA-B
 - Two Subtests empirically selected
 - Communication
 - Finances

VIM Study Results

	Pearson r	r ²
TABS	.57	.32
UPSA	.67	.45
ILS	.51	.26
CAI	.23	.05
CGI-cog.	.38	.14



UPSA > ILS > CGI-cog. CAI

TABS > CGI-cog, CAI

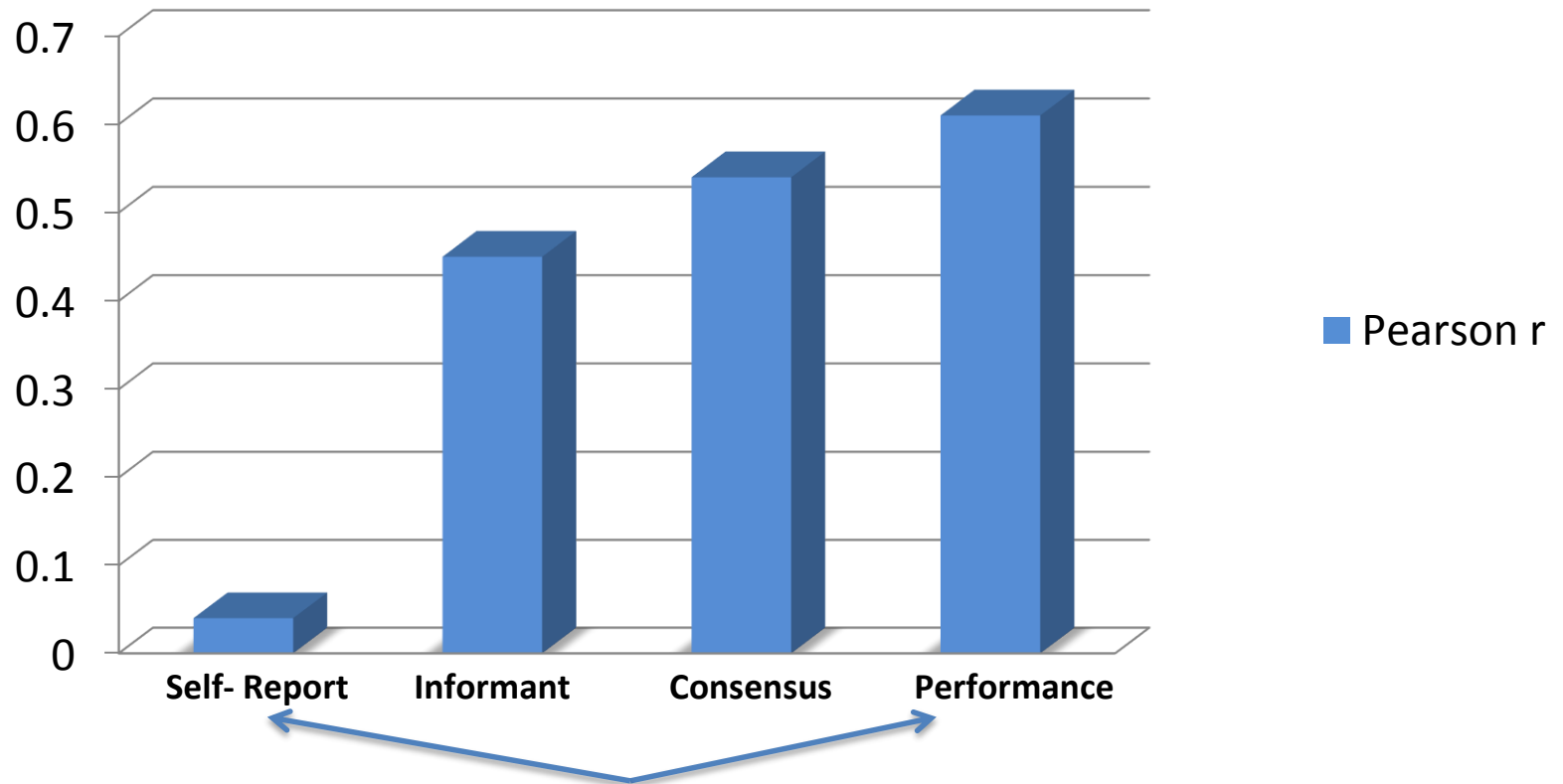
Note. VIM: Validation of Intermediate Measures

Interviews vs. Performance based Co-Primaries

- Most studies use either performance-based or interview based co-primary measure
- In this study a performance-based cognitive assessment was correlated with
 - Self report
 - Informant Report
 - Interviewer impression based on two reports
 - UPSA

Correlation Between Cognition Scores, Functional Capacity, and Ratings of Impaired Cognition in Schizophrenia

Pearson r



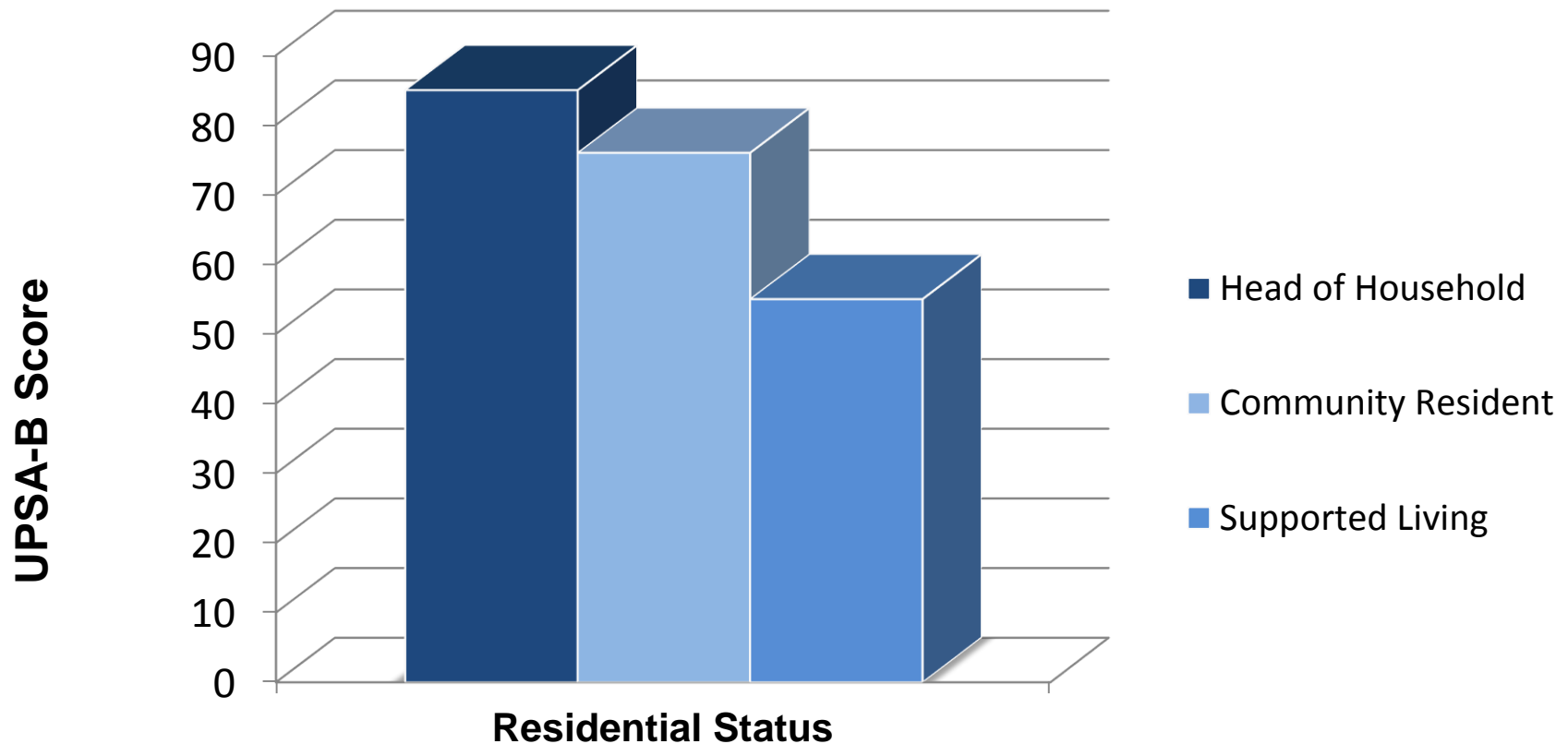
Performance More Closely Related to Cognitive Functioning than Self-Report

Keefe et al., 2006

Validity in Other conditions

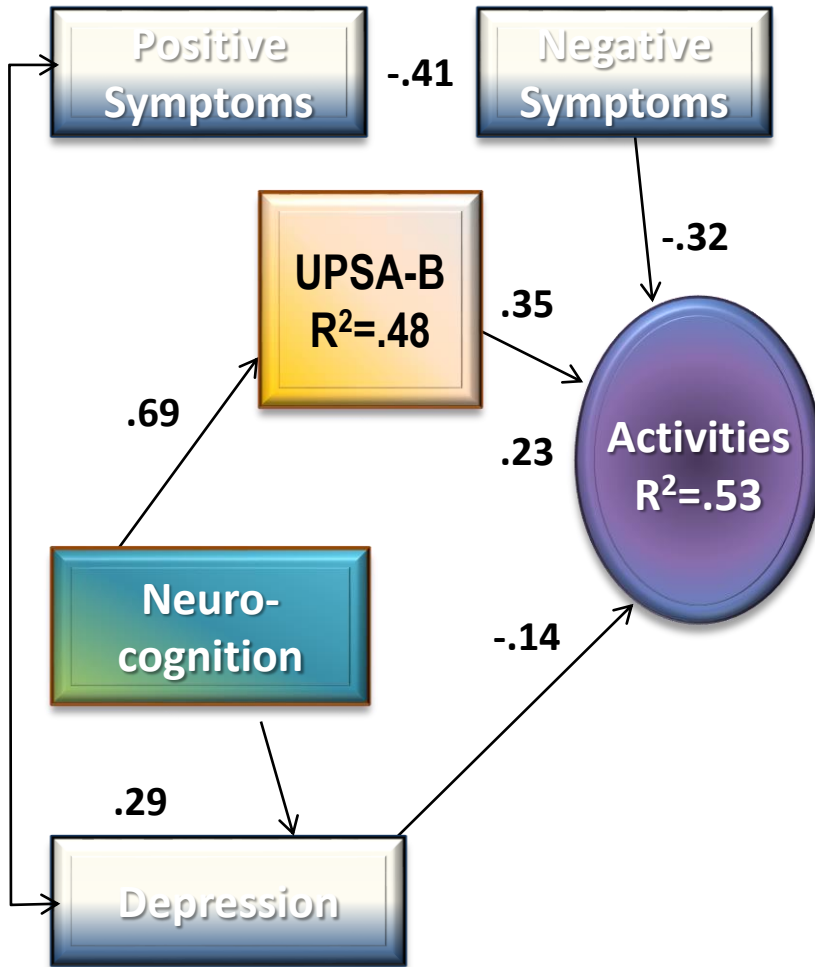
- The UPSA has been widely used in other conditions, including bipolar disorder and bipolar depression
- There is considerable evidence of evidence of validity in Bipolar disorder

UPSA B Scores as a Function of Residential Status



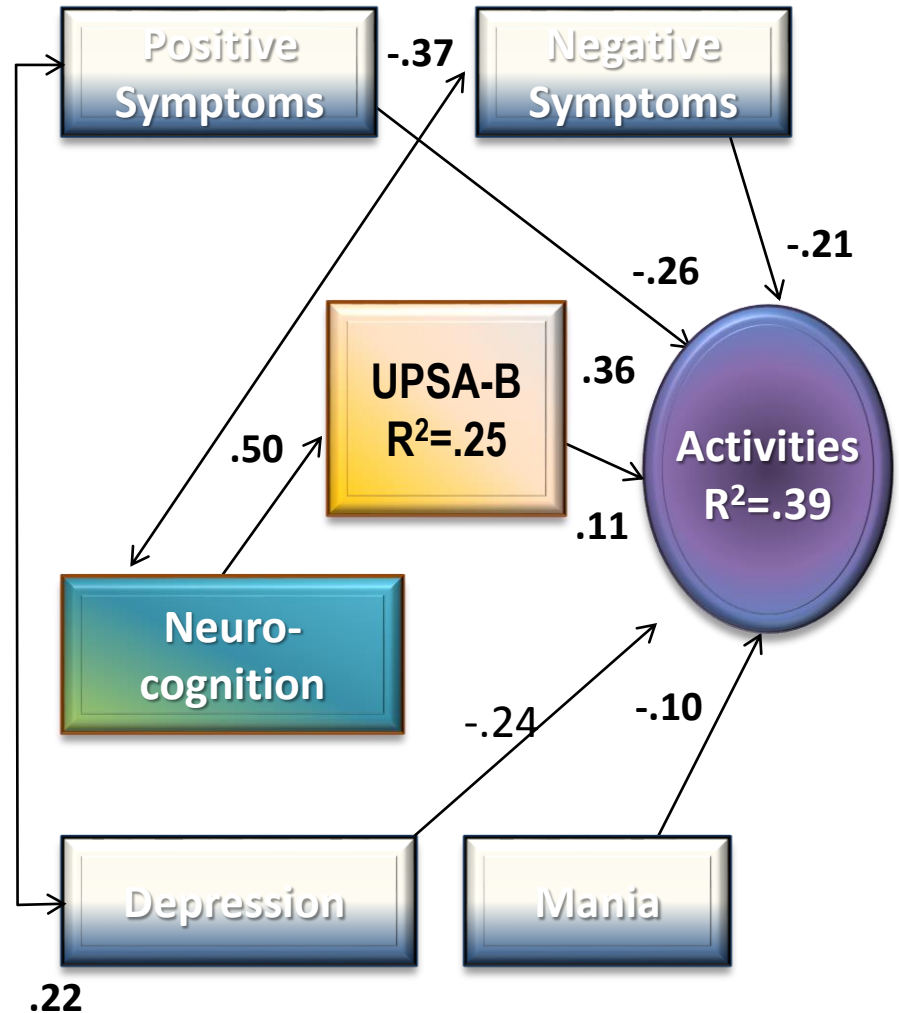
Note: Diagnostic effect: $F = 0.66$, $p = .417$;
Mausbach et al., in 2010

Schizophrenia



Bowie et al., 2010

Bipolar



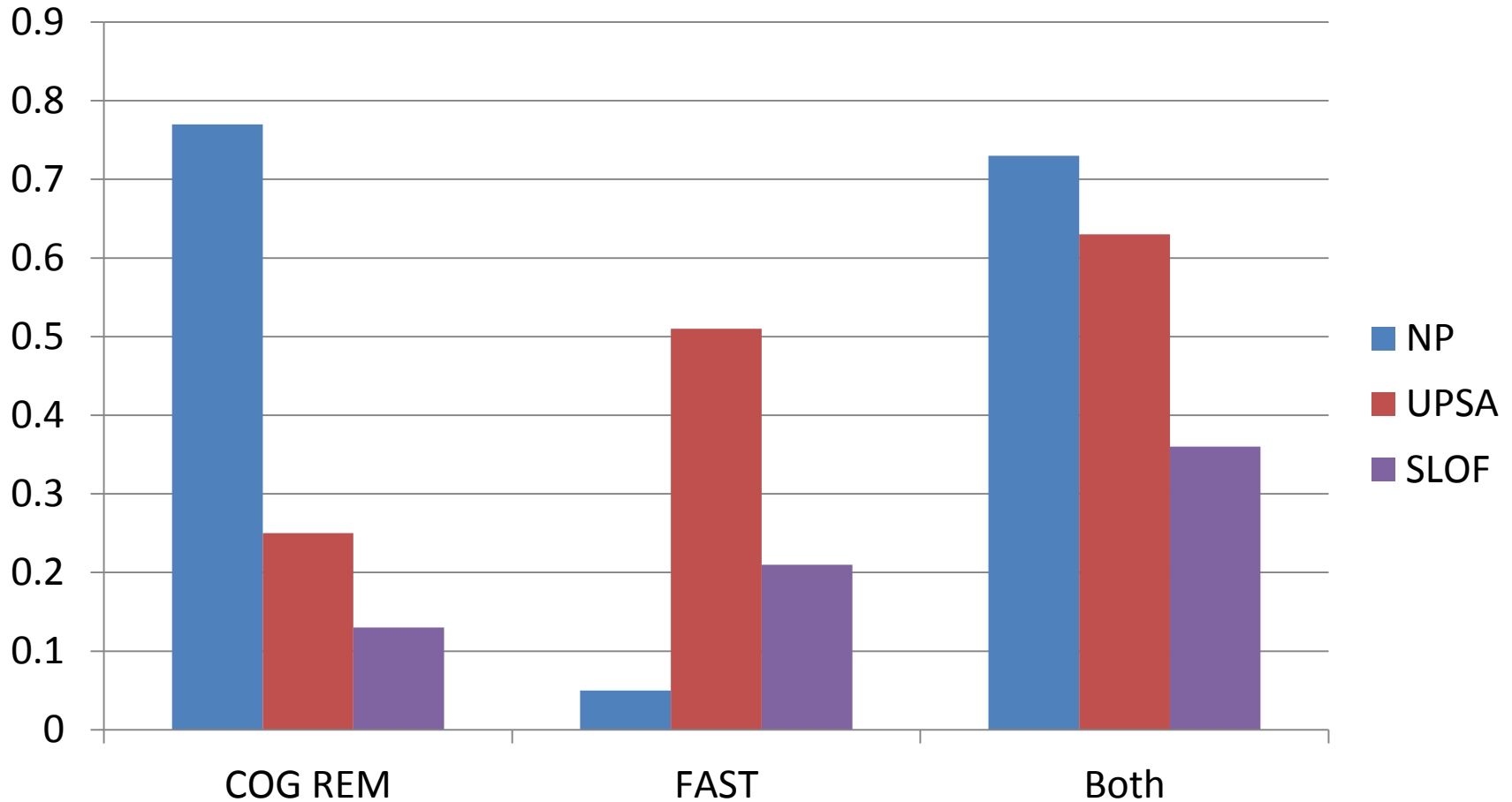
Sensitivity to Treatment for co-primary measures

- Several studies have found the UPSA to be sensitive to treatment in pharmacological studies of schizophrenia
 - Davunitide
 - Pregnenolone
- Similarly, interview based measures have shown sensitivity as well

Outcomes of the Study:

End of Treatment

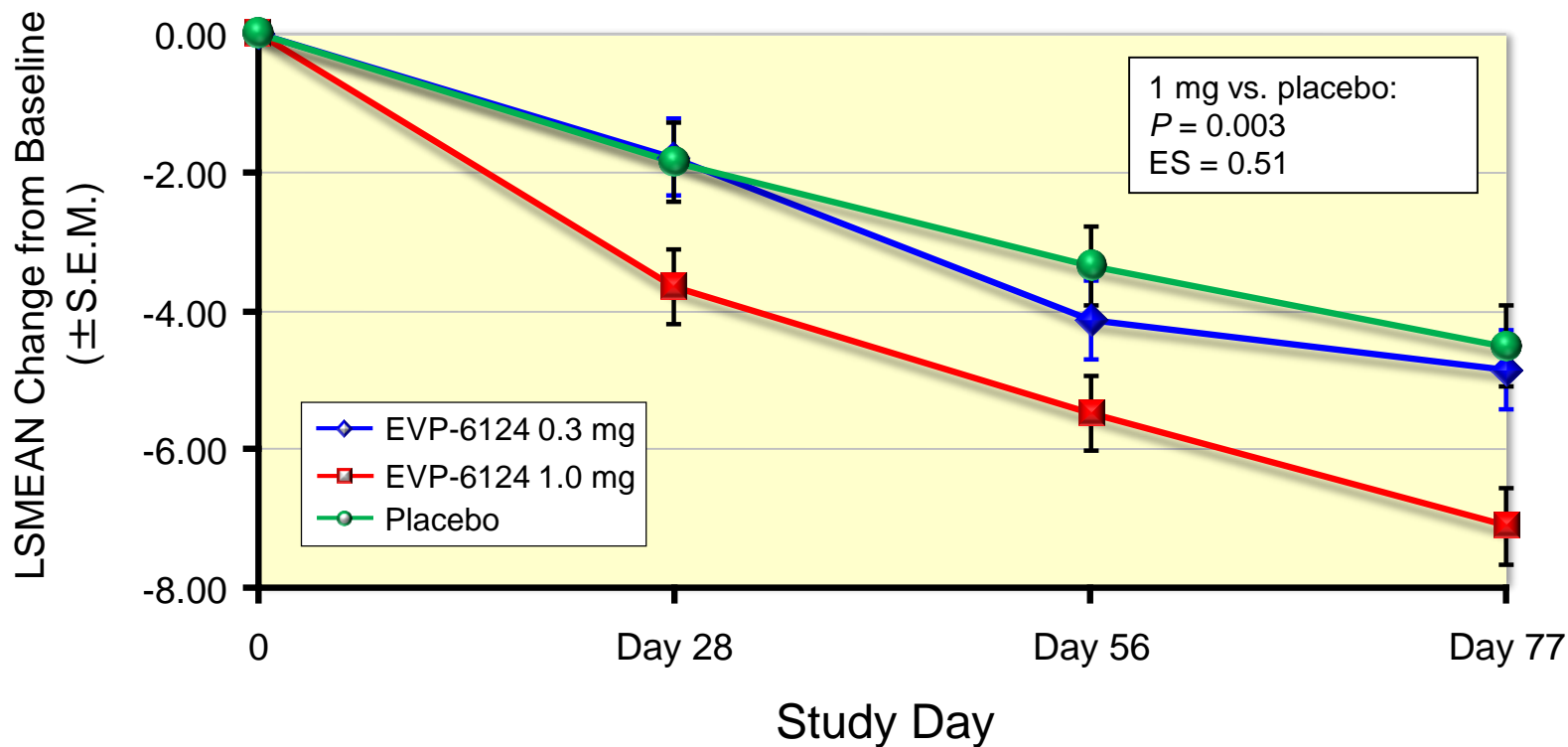
Effect Size (Cohen's d)



FAST: Functional Adaptation Skills Training

SCoRS (Visits with Informant Present)

SCoRS Interviewer Total (Subjects with Informants)
(Adjusted Mean Change from Baseline)

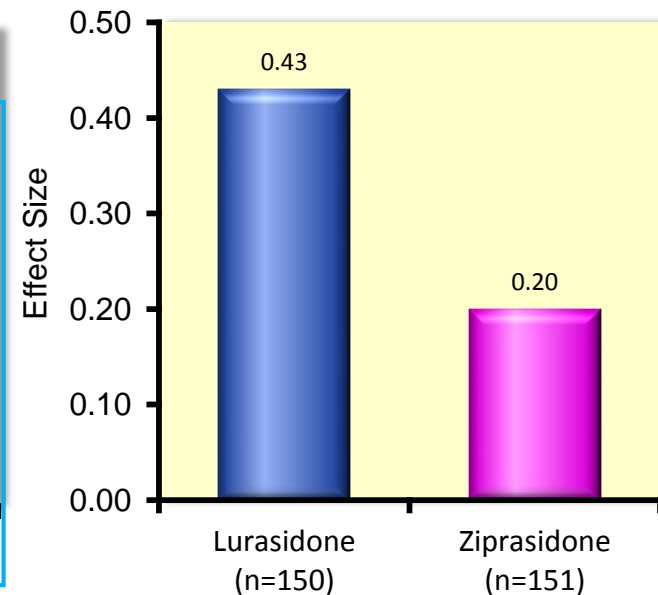
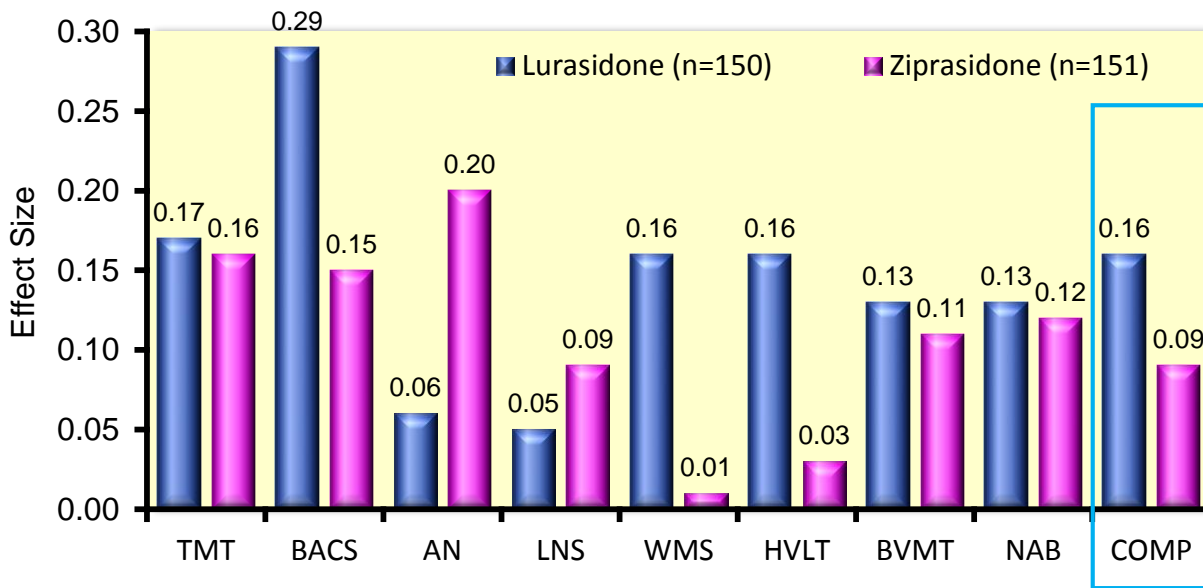


SCORS: Schizophrenia Cognition Rating Scale

Effect Sizes for Pre-Post Improvement in Cognitive Measures

MCCB Effect Sizes

SCoRS Effect Sizes



AN, animal naming; BACS, BACS Symbol Coding; BVMT, Brief Visual Memory Test total learning; COMP, Cognitive Performance Composite Score; HVLT: Hopkins Verbal Learning Test total learning; LNS, Letter-Number Sequencing; LOCF, last observation carried forward. MCCB, MATRICS Consensus Cognitive Battery; NAB, NAB Mazes Subtest; SCoRS, Schizophrenia Cognition Rating Scale; TMT, Trail Making Test Part A; WMS, Wechsler Memory Scale Spatial Span. Based on LOCF endpoint data.

Uses of the UPSA Outside SCZ and BD

1. UPSA scores correlate with NP performance in healthy older controls
2. UPSA scores separate MCI from AD and HC
3. UPSA scores correlate with MCCB scores and lifetime functional outcomes in PTSD
4. UPSA scores correlate with NP test scores and current residential and vocational outcomes in schizotypal PD
5. UPSA scores correlate with WCST performance in abstinent methamphetamine abusers
6. Lower UPSA Scores predict poorer response to diabetes management programs in non psychiatric patients