

How do key co-primary measures of functional capacity predict real world function in schizophrenia?

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INTRODUCTION

METHODOLOGICAL TOPIC ADDRESSED: Determining the relative ability of measures of functional capacity that are used as co-primary measures in schizophrenia cognition clinical trials to predict real world functioning.

- Research suggests that cognitive impairment in schizophrenia accounts for more disability in real world functioning than any other aspect of the illness, including psychosis (e.g. August, 2012).
- FDA has required that clinical trials for cognitive impairment in schizophrenia demonstrate improvement on a standard performance-based cognitive assessment, as well a co-primary measure of 'functional capacity' that can serve as an intermediary between cognitive and functional improvement and may signal increased potential for improved outcomes.
- Although the relationship between cognitive performance and standard measures of functional capacity have been well-described, less attention has been devoted to the relationship between functional capacity and measures of real world function.
- We examined the relationship between real world function and performance on three measures of functional capacity, including the University of California San Diego Performance-Based Skills Assessment (UPSA-VIM), the Schizophrenia Cognition Rating Scale (SCoRS) and Virtual Reality Functional Capacity Assessment Tool (VRFCAT).

METHODS

PARTICIPANTS

- 158 patients who met DSM-IV TR criteria for schizophrenia.
- Participants were recruited as part of a non-treatment psychometric validation study conducted across three research sites, including the University of South Carolina, the University of Miami - Miller School of Medicine, and the University of California, San Diego.

Table 1. SAMPLE CHARACTERISTICS

| | |
|------------------------|--------------|
| Age, Mean (SD) | 43.6 (11.84) |
| Male, N (%) | 87 (55%) |
| Caucasian, N (%) | 75 (47%) |
| PANSS Total, Mean (SD) | 71.6 (21.93) |

PROCEDURE

- Real world function was evaluated using the Specific Levels of Functioning (SLOF; Schneider & Struening, 1983).
- All subjects completed measures of real-world function, cognition and functional capacity at the same study visit.
- Correlations between the SLOF, MCCB composite score and each measure of functional capacity were assessed using Pearson correlation coefficients.

Table 2. MEASURES ASSESSED

| Construct | Instrument | Description |
|--------------------------------|--|---|
| Real-World Functional Outcomes | Specific Levels of Functioning (SLOF) | 43-item informant-rated scale of behavior and functioning. The primary dependent variable assessed was the SLOF sum of three domain means associated with Interpersonal Functioning, Everyday Activities, and Vocational Functioning. |
| Cognition | MATRICES Consensus Cognitive Battery (MCCB) | The MCCB measures seven separable cognitive domains, including speed of processing; attention/vigilance; working memory (verbal and nonverbal); verbal learning; visual learning; reasoning and problem solving; and social cognition. The dependent variable is a standardized composite T score. |
| Functional Capacity | Schizophrenia Cognition Rating Scale (SCoRS) | Patient and informant interview-based measure of cognitive impairment with questions aimed at the degree to which this impairment affects day-to-day functioning. Dependent variable is the Total of interviewer ratings across all items. |
| Functional Capacity | UCSD Performance-Based Skills Assessment- Validation of Intermediate Measures (UPSA-VIM) | The UPSA-VIM is a performance-based measure designed to assess the ability to perform everyday tasks needed for independent community functioning (Sabbag et al., 2011). |
| Functional Capacity | Virtual Reality Functional Capacity Assessment Tool (VRFCAT) | The VRFCAT is a computerized performance-based assessment of functional capacity designed to assess the ability to complete instrumental activities of daily living (IADLs). Dependent variables include total time to complete a series of IADL scenarios, as well as number of errors committed. Raw scores are converted to standardized T scores, with higher scores indicating better performance. |

RESULTS

Table 3. DESCRIPTIVE STATISTICS

| Measure | Mean | Std. Deviation |
|---------------------------|--------|----------------|
| MCCB Composite T score | 28.13 | 12.91 |
| SLOF (3 domain)* | 11.07 | 1.64 |
| SLOF Total | 117.66 | 15.17 |
| SCoRS Total | 38.24 | 9.88 |
| UPSA-2-VIM Total | 71.03 | 11.85 |
| VRFCAT Total Time T score | 32.49 | 16.59 |
| VRFCAT Errors T Score | 37.65 | 22.40 |

* SLOF sum of three domain means associated with Interpersonal Functioning, Everyday Activities, and Vocational Functioning. Range: 0-15.

Figure 1. Distribution of SLOF Scores

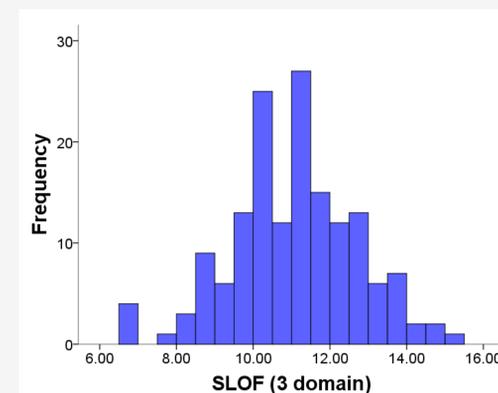


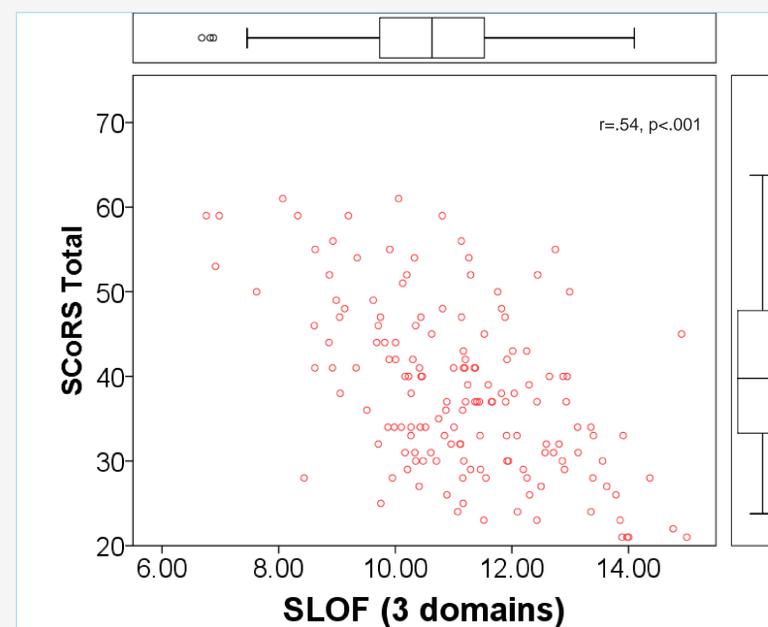
Table 4. CORRELATION BETWEEN REAL WORLD FUNCTION, FUNCTIONAL CAPACITY AND COGNITION

| | SLOF | MCCB | SCoRS | UPSA | VFCAT Time | VRFCAT Errors |
|---------------------|---------|---------|---------|--------|------------|---------------|
| SLOF (3 domain) | 1 | | | | | |
| MCCB Composite T | .350** | 1 | | | | |
| SCoRS Total | -.543** | -.416** | 1 | | | |
| UPSA-2-VIM | .250** | .698** | -.243* | 1 | | |
| VRFCAT Total Time T | .220* | .570** | -.291** | .594** | 1 | |
| VRFCAT Errors T | .287** | .389** | -.276** | .409** | .690** | 1 |

Note: For all T scores, higher scores indicate better performance.

* Correlation is significant at the 0.01 level (2-tailed) ** Correlation is significant at the 0.001 level (2-tailed)

Figure 2. Scatterplot of SCoRS and SLOF



SUMMARY OF FINDINGS

- All three measures of functional capacity demonstrated significant correlations with real world function as assessed by the SLOF (Table 4).
- Of the three functional capacity measures, the SCoRS demonstrated the strongest correlations with the SLOF ($r = -.54$, $p < .001$; Figure 2).
- Correlations between the SLOF and performance-based measures of functional capacity were more modest:
UPSA-VIM: $r = .25$, $p < .001$
VRFCAT Errors: $r = .29$, $p < .001$
VRFCAT Time: $r = .22$, $p < .01$
- Consistent with prior findings, the correlation between cognition (MCCB) and real world function as measured by the SLOF was modest but significant ($r = .35$, $p < .001$, Table 4).

CONCLUSIONS

- Current measures of functional capacity in schizophrenia demonstrate medium to large correlations with assessment of real world function.
- Performance-based functional capacity measures have stronger correlations with performance based measures of cognition, while the interview-based measure of functional capacity had a stronger correlation with a real-world functional scale.
- Results are consistent with the conception of functional capacity as a potential mediator of the relationship between cognition and real world function.

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DISCLOSURES

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