ABSTRACT

Background: The NIMH-funded academic-FDA-industry partnership known as MATRICS delineated seven cognitive domains to assess cognitive impairment associated with schizophrenia (CIAS) and created a consensus test battery (MCCB), which represents one operationalization of the concept of CIAS. Fully computerized batteries now commercially available offer alternative ways to operationalize CIAS.

Methods: As part of a noninterventional, cross-sectional study all subjects were tested on the MCCB (WHS) while half were randomized to do one of two fully computerized tests, CNS Vital Signs (N = 103) or Cogstate (N = 99). Subjects were stable, outpatient schizophrenia patients aged 18-55 years under treatment for CIAS; antipsychotics. Clinical (PANSS, CGI) and functioning (UPPSA-2, Sc2rs) measures were administered. Two global clinician-rated functioning measures were also included.

The correlations of the computerized batteries and MCCB were examined using linear regression and factor analytic methods. The influence of symptom measures on functional endpoints was explored.

Results: Correlations between computerized tests and the MCCB were fairly high (r=.75); at the domain level they were in the moderate range (r=.30-.50). Fit for a one-factor model was good for MCCB, marginal for CNS Vital Signs, and poor for Cogstate. Across all three, the domains of working memory and attention domains were among the highest loadings. The comparability of these different operationalizations of CIAS is analyzed in terms of domain structure and associations with the clinical severity and functioning measures.

INTRODUCTION

- Cognitive impairment associated with schizophrenia (CIAS) is a target for future pharmacotherapy with the potential to provide meaningful functional improvements in outcomes for patients with schizophrenia.
- The NIMH-funded initiative the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) brought together the FDA, academic and pharmaceutical partners to develop a cognitive test battery to assess the 7 domains most relevant to CIAS.
- The result was the MATRICS Consensus Cognitive Battery (MCCB) which is now widely accepted as satisfying one of the two FDA requirements to show improvement on a neurocognitive battery and a functional endpoint.
- The MCCB has drawbacks including the requirement for highly skilled administrators, the need for extensive training to learn how to administer it, lengthy administration time, and few available translators for use outside the U.S.
- Alternatives to the MCCB exist, including fully computerized batteries that are now commercially available. Many of these purport to assess the 7 MATRICS domains while overcoming many of the limitations of the traditional battery.
- This objective of this post hoc analyses was to extend previous work comparing 2 fully computerized neurocognitive batteries (CNS Vital Signs & Cogstate) to the MCCB to inform the selection of instruments for future clinical trials.
- These analyses explore whether the two alternative batteries offer comparable ways to operationalize the CIAS domains.

METHODS

Study Design: Post hoc analyses of data from a cross-sectional, unblinded study with medication adherence as the end point. All participants completed the MCCB, half completed the Cogstate Battery while the other half completed the CNS Vital Signs (CVS) battery. Battery administrations were in counter-balanced order.

Subjects: Participants were 204 adult outpatients (ages 18-65) with schizophrenia or schizoaffective disorder (DSMIV-TR). Inclusion Criteria:

- Clinically stable – no medication changes for past month & none anticipated for next month
- CGI Severity 4.4
- Currently taking a FDA-approved antipsychotic
- Willing to provide an informant

Exclusion criteria included active substance abuse/dependence, neurological disease or head injury, and other medical conditions that might interfere with participation. Thirteen states in the U.S. participated.

Statistical Analyses:

- Neuropsychological tests were scored two ways: (1) corrected for norms per test administration and (2) based on practice effects (standardized on sample). Norms were based on age and gender (MCCB) or age (CNS Vital Signs & Cogstate). Analyses reported here were done on the un-normed data.
- Correlations (Pearson’s r) among the domains of the 3 batteries were calculated, as well as correlations of the tests with other selected measures. Confidence intervals for correlations were calculated using the bootstrap method. Group data were plotted using the “vcd” package.
- Regression models were fit using linear-leasts with each domain regressed on the other 5 domains.

RESULTS

- Tests of the equivalence of correlation matrices comparing each of the computerized batteries to the MCCB showed that they are not equivalent.
- Regressing each domain onto the other 6 domains showed that for the MCCB the R-squared values for the 7 domains ranged from .20-.52; for CNS Vital Signs from .23-.52; and for Cogstate from .15-.36
- The correlations between the computerized batteries at the domain level and the corresponding MCCB domains varied from .30-.51 for CNS Vital Signs and .23- .81 for Cogstate. Most correlations were in the .30-.50 range. All were statistically significant from zero but the correlations were not significantly different for the 2 fully computerized batteries.

CONCLUSIONS

- The correlations between the computerized batteries and the MCCB at the composite level were fairly high and the correlations observed at the domain level were more modest. The correlations among the 7 domains on the 3 batteries varied greatly. Formal testing of the equivalence of the matrices demonstrated they are not strictly equal.
- The domains from each of the batteries varied in how well they correlated with measures of functioning related to cognition. Most of these correlations were in the modest range and there was variability in the magnitude of the correlations across the 3 batteries. Finally, the severity of clinical symptomatology did not appear to strongly influence the clinician’s global rating of functioning related to cognition.
- A single underlying construct appears to explain most of the variance observed on the MCCB domains whereas it does not appear to for the fully computerized batteries. Further analyses are needed to fully explore these differences.

REFERENCES


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