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A case control study of association between cognition and functional capacity in schizophrenia

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Abstract

Background—Cognitive functions are important prognostic factors for schizophrenia (SZ), while ability to perform activities of daily living are important measures of functional capacity. The relationship between cognition and functional capacity has not been tested extensively in India.

Objective—To compare persons with SZ with controls on measures of cognition and functional capacity, and evaluate correlations between cognitive performance and functional capacity.

Method—Schizophrenia outpatients and controls without psychiatric illness (DSM IV) who completed the MATRICS Consensus Cognitive Battery and Functional Assessment Battery comprised of two tests from University of California San Diego (UCSD) Performance Based Skill Assessment (UPSA), one Test of Adaptive Behavior in Schizophrenia (TABS) and one test from University of California San Diego Performance Based Skill Assessment Brief edition (UPSA-B). Cognitive and functional domains were examined using regression analyses, with relevant covariates.

Results—Cases (N= 51) though younger, were more educated than controls (N= 41). Adjusting for education, controls performed better than cases in 3/7 cognitive and 4/5 domains of functional

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Contributors

Sreelatha S. Narayanan: data acquisition, review of literature, preparation of manuscript.

Triptish Bhatia: design for cognitive variables and data analysis.

Dawn I. Velligan: design of original study, manuscript review.

Vishwajit L. Nimgaonkar: concept, manuscript review.

Smita N. Deshpande: concept, design and manuscript review and editing.

Conflict of interest

There is no conflict of interest to be declared by any of the authors.

capacity but similarly in ‘household management’. Among both cases and controls, cognitive measures of verbal learning and speed of processing overlapped with functional capacity (3 domains). Working memory was associated with one functional domain.

Conclusions—Consistent with other studies, Indian patients with schizophrenia performed worse than controls on several domains of cognition and functional capacity; these domains were correlated. Speed of processing and verbal learning are most frequently associated with functional capacity indices and should be targeted to improve skills of daily living among persons with SZ.

Keywords

MATRICES; Cognitive functions; Functional capacity; Schizophrenia

1. Introduction

Schizophrenia (SZ) is associated with deficits in several cognitive domains as well as in functional capacity (Keefe and Fenton, 2007; Kraus and Keefe, 2007; Keefe and Harvey, 2012). Cognitive remediation can improve functional outcome in patients with schizophrenia. Since both cognition and functional capacity have several domains, there is a need to identify associations among different domains of cognition and functional capacity.

Functional capacity and real world functioning are different but interrelated domains (Miranda et al., 2015). For focused interventions, significant associations between specified domains of cognition and functional capacity (as reported by Holshausen et al., 2014) need to be targeted. Three domains of real world adaptive functions – interpersonal skills, work skills and community activities – can be assessed by neuropsychological tests (Bowie et al., 2010). The MATRICS consensus cognitive battery was developed and tested all over the world to determine its cultural acceptability and accuracy. A smaller modified version MFAB (MATRICS Functional Assessment Battery) is culturally acceptable and can be used in India (Velligan et al., 2014).

A previous, multicenter study of the ‘Cross-Cultural Reliability and Validity of Intermediate Measures’ (CIM II) of the ‘Measurement and Treatment Research to Improve Cognition in Schizophrenia’ (MATRICS) aimed at investigating the test retest reliability and concurrent validity of several intermediate measures of functional outcome in India and included the present site (Velligan et al., 2014). The present study included all participants from the previous report as well as additional control individuals.

2. Methods

2.1. Sites

The study was conducted at the Department of Psychiatry, Post Graduate Institute of Medical Education and Research (PGIMER), Dr. Ram Manohar Lohia Hospital (RMLH), a tertiary care government post graduate teaching hospital in New Delhi, India, from April 2012 to August 2014. RMLH offers services free of charge to all persons seeking treatment.

2.2. Participants

The inclusion and exclusion criteria for cases have been published (Velligan et al., 2014). Briefly, psychiatric outpatients with a clinical diagnosis of SZ (clinically stable), were referred by their treating psychiatrists to the research team. Consenting individuals were recruited. To reduce complex medication effects, persons who reported taking the following medications 12 h before assessment were excluded: clozapine, potentially pro-cognitive medications, antimentia medications, amphetamines, lithium, monoamine oxidase inhibitors, tricyclic anti-depressants, benzodiazepines, sedatives or anticholinergic medicines.

Control individuals were recruited from communities near RMLH and from psychiatrically healthy friends and non-blood relatives of out-patients at the RMLH Psychiatry outpatient clinic, and were evaluated in the same manner as the cases. All participants were able to read and understand Hindi. To enable better balance in educational status, individuals who were educated between fourth to eighth school grades were included as controls.

2.3. Informed consent

Before they were referred to the research team, treating psychiatrists discussed the study protocol and obtained oral consent. Potential research participants then contacted the study team, were explained all procedures and provided written informed consent (with the caregivers as witnesses for the patients), as approved by the Institutional Ethics Committee (IEC), RMLH.

2.4. Assessment instruments

- i. *Cognition*: Cognitive functions were assessed using the MATRICS Consensus Cognitive Battery MCCB (Nuechterlein et al., 2008), which has ten sub-tests. Instructions were provided in Hindi. Since test administration lasted approximately 1 h, participants were given a break after the sixth test, i.e. neuropsychological assessment battery. Information obtained from the tests was used to estimate cognitive domains as described in (Nuechterlein et al., 2008).
- ii. *Functional capacity*: Functional capacity was assessed using Functional Assessment Battery (FAB). Two tests were derived from University of California San Diego (UCSD) Performance Based Skill Assessment (UPSA) and a third test from Test of Adaptive Behavior in Schizophrenia (TABS). The first test about organization and planning, required participants to read about the Delhi zoo. Passage comprehension was assessed by questions related to the opening and closing time of the zoo and things they would take with them while visiting the zoo. The highest score in this test is 14. The second test, household management required participants to identify missing ingredients from a kitchen list to prepare the Indian simple dish of 'kheer' (dessert); highest score is two. The third test was a test of work and productivity. Each participant was required to

make stacks of colored cards as instructed. It is measured in percentage and highest score could be 100%.

- iii. *UPSA-B*: The *UPSA-B* assesses financial as well as communication skills of the participant. Financial skills are assessed from the participants' ability to count currency and convert it into change (Fin 1A). The participant was provided with an unpaid electricity bill. S/he was asked for details of mode of payment (Fin 1B). Communication skills were assessed by assessing the participant's ability to dial an emergency number and change doctor's appointment by looking up the doctor's details in a letter. Combined highest score is 10 in financial skills and 9 in communication skills.
- iv. *FAB* has been validated in India (Velligan et al., 2014) and *UPSA-B* is being used in India to assess functional capacity in MATRICS studies (as stated by Velligan et al., 2014).

2.5. Psychopathology

All participants were interviewed using the Hindi version of the Diagnostic Interview for Genetic Studies (DIGS, (Deshpande et al., 1998)) followed by consensus diagnosis with a board certified psychiatrist, using DSM IV criteria, as described by Thomas et al, (2011).

Apart from the Hindi DIGS used for diagnostic evaluation, the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) was used to assess the severity of psychopathology of cases.

2.6. Data analysis

Non-parametric tests (MannWhitney U Test) were used to compare cases and controls. Linear regression was carried out to evaluate association between cognitive and functional variables. Individual functional domains were used as outcome variables. Cognitive and demographic variables were included as independent variables. Separate linear regression was carried out for each cognitive domain. All data were analyzed using the Statistical Package for Social Sciences (SPSS), version 18.

3. Results

A total of 51 patients (34 men and 17 women, ages 18–60 years) and 40 controls (20 men and 20 women, ages 20–60 years) were included. The gender distribution was not statistically different (chi square = 1.88, $p = 0.199$; 1 df), but the cases were significantly younger than controls (average age — cases: 32.49 ± 9.68 ; controls: 40.03 ± 11.79 ; $Z = 3.05$, $p = 0.002$). Cases were more educated than controls as education level of controls was restricted to classes 4 to 8.

3.1. Group-wise differences

In spite of being significantly older, controls performed significantly better than cases on cognitive and functional domains. Significantly different cognitive domains included verbal

learning ($p = 0.000257$), reasoning and problem solving (0.000482) and composite cognition scores ($p = 0.021$). Controls also performed better in functional capacity domains: FAB organization and planning ($p = 0.011$), work and productivity ($p = 0.019$), UPSA financial skills ($p = 0.000157$) and UPSA communication skills ($p = 0.015$) (all analyses controlled for education). There was no significant difference between the two groups on 'speed of processing tasks', 'social cognition', attention and working memory; and 'household management' domain of functional capacity.

3.2. Association between cognitive domains and functional capacity

Linear regression analysis was carried out to evaluate associations between cognition and functional capacity domains. Demographic variables, namely age, gender and education were used as covariates. The functional domain 'organization and planning' was significantly associated with speed of processing ($p = 0.000063$) and verbal learning ($p = 0.00025$), controlling for group status, age, education or gender. Household management such as 'keeping track of things required at home for day to day activities' was associated with the working memory and verbal learning domains ($p = 0.00037$ and $p = 0.043$, respectively). The domain 'Work and productivity' was associated with speed of processing ($p = 0.000007$) and verbal learning ($p = 0.00047$). The UPSA Financial was associated with group status ($p = 0.0041$); social cognition (0.008); overall composite (0.001) and gender (0.005). Controls performed better than cases (Table 1) on communication skills domain ($p = 0.009$), which was significantly associated with speed of processing ($p = 0.00003$) and age ($p = 0.045$) (Table 2).

Stepwise linear regression (backward) analyses were performed using SPSS. All independent variables were added simultaneously in the beginning, non significant variables are removed automatically. Significant variables remained in the last step, which are shown in Table 2. Confidence intervals are given in the table to suggest variability.

4. Discussion

Consistent with prior reports, patients with SZ performed worse than controls on cognitive measures. We also found differences in domains of work and productivity between cases and controls similar to those reported by Nuechterlein et al. (2011). The ability to plan and execute a task (cognition) is critical for performance in day to day activities such as money planning or cooking (functional capacity). Thus, deficits in cognition would lead to impairment in functional capacity. As indicated in previous studies (McDowd et al., 2011), our study also showed evidence of association of both verbal learning and speed of processing with functional capacity.

In our entire sample (cases and controls taken together, and group taken as independent variable), verbal learning (language skill) and speed of processing were significantly associated with the domains of 'organization and planning', 'household management' and 'work and productivity'. Heinrichs has also reported that patients with SZ with exceptional verbal learning capacity can perform better on daily living skills (Heinrichs et al., 2008).

Cases were impaired in financial capacity irrespective of cognitive domains suggesting that they were not trusted with the responsibility and they were not able to manage money. Separately, performance on social cognition as well as composite scores (MCCB) were associated with financial capacity involving tasks such as paying electricity bills after identifying relevant details, paying a bill before last date, identifying and checking meter readings on the bill. Financial capacity was also associated with gender, males being more capable. This could be gender specific as Indian males are traditionally expected to carry out money management.

One of the most important domains associated with functional capacity is speed of processing. Speed of processing is a predictor of interpersonal behavior, work skills and community activities (Bowie et al., 2008). As reported previously (Ojeda et al., 2008), we found that three functional capacity domains, namely, organization and planning (visiting the zoo), work and productivity (stacking cards) and communication skills were significantly associated with speed of processing.

Cognitive domains like speed of processing, verbal learning and visual learning were important predictors of functional capacity not only in schizophrenia cases but also controls in our sample. These functional capacity domains require the individual to understand the incoming information, think about it, formulate a response and then react. Speed of processing is also dependent on a person's experience in the same or similar settings so that she can react with the most appropriate response at hand. If an individual has any difficulty in speed of processing, activities like solving puzzles (Oei and Patterson, 2013), jumbled words, play games with certain time limits help in improving the same.

Focusing on improving verbal learning could improve three domains of daily functioning. At a practical level, it would be of interest to see if increasing involvement in tasks such as reading newspapers or books, playing word games like scrabble, word puzzles, and tic tac toe could improve the verbal learning abilities of persons with SZ and thereby improve functional skills. In a similar vein, improving visual learning skills through activities like maps, video games, puzzles, matching activities, computers and word searches, could contribute to the financial skill improvement. Individuals who play video games show significant improvement in working memory, abstract reasoning, distractor inhibition and mental rotation performance (Basak et al., 2008).

A limitation of our study – apart from sample size and possible heterogeneity of cases – was the disparity of men versus women in the sample. The MCCB captures a wide range of cognitive functions with a series of tests, but its administration can be time consuming. This issue needs to be considered when designing future studies.

5. Conclusion

At a site in India, control individuals performed better than patients with SZ in 3/7 cognitive domains and 4/5 domains of functional capacity. Patients with schizophrenia performed worse than controls in cognitive domains of attention and problem solving. Functional capacity was also impaired. With regard to the household management domain, performance

of cases and controls was similar. The cognitive domains most likely to be associated with functional capacity were speed of processing and verbal learning. The findings could help us to focus on one or more cognitive domains to improve the targeted area of functional capacity known to be impaired in SZ through cognitive remediation programs.

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Table 1

Demographic, cognitive and functional capacity characteristics of cases and controls.

	Variables	Cases (n = 51) Mean $\pm$ SD	Controls (n = 40) Mean $\pm$ SD	Z*/χ^2	P value (2-tailed)*
Demographic variables	Age	32.49 $\pm$ 9.68	40.03 $\pm$ 11.79	3.05	0.002
	Education	10.04 $\pm$ 3.81	8.45 $\pm$ 4.051	-2.731	0.006
	Gender (M/F)	34/17	20/20	1.88	0.199
Cognitive domains	Speed of processing	12.12 $\pm$ 14.04	13.75 $\pm$ 14.13	-1.839	0.066
	Attention	23.14 $\pm$ 10.42	21.28 $\pm$ 9.71	-0.212	0.832
	Working memory	28.27 $\pm$ 13.38	26.43 $\pm$ 10.13	-0.464	0.643
	Verbal learning	32.84 $\pm$ 7.01	37.03 $\pm$ 7.10	-3.66	0.00026
	Visual learning	25.96 $\pm$ 13.99	29.70 $\pm$ 14.05	-1.883	0.060
	Reasoning and problem solving	30.24 $\pm$ 6.79	35 $\pm$ 6.83	-3.49	0.00048
	Social cognition	32.84 $\pm$ 9.80	36.00 $\pm$ 10.91	-1.291	0.197
	Overall composite	12.02 $\pm$ 11.97	14.68 $\pm$ 12.08	-2.30	0.021
Functional capacity	Org. and planning (maximum score: 14)	8.90 $\pm$ 2.63	10.18 $\pm$ 2.08	-2.53	0.011
	Household management (maximum score: 4)	2.92 $\pm$ 0.89	2.90 $\pm$ 0.87	-0.71	0.478
	Work and productivity (maximum score: 100%)	46.69 $\pm$ 20.76	52.05 $\pm$ 19.90	-2.34	0.019
	Financial skills (maximum score: 10)	9.098 $\pm$ 1.50	9.97 $\pm$ 1.32	-2.87	0.004
	Communication skills (maximum score: 9)	4.71 $\pm$ 2.03	5.23 $\pm$ 1.59	-2.42	0.015

FAB: Functional Assessment Battery; UPSA: UCSD Performance Based Skills Assessment.

Table 2

Association between MCCB domains, FAB and UPSA.

Dependent variables	Independent variables	Beta value	Level of sig.	95% confidence interval
FAB organization and Planning	Speed of processing	0.46	0.000063	0.043,0.120
	Verbal learning	0.36	0.00025	0.059,0.188
FAB household management	Working memory	0.38	0.00037	0.013,0.042
	Verbal learning	0.21	0.043	0.001, 0.049
FAB work and productivity	Speed of processing	0.43	0.000007	0.362,0.882
	Verbal learning	0.33	0.000467	0.411,1.403
UPSA financial	Group (case/control)	0.283	0.004	0.183, 0.946
	Social cognition	-0.285	0.008	-0.047, -0.007
	Overall composite	0.346	0.001	0.012, 0.045
	Gender	-0.298	0.005	-1.018, -0.189
UCSD communication skills	Group (case/control)	0.22	0.009	0.208,1.436
	Speed of processing	0.44	0.00003	0.032,0.085
	Age	-0.17	0.045	-0.055,-0.001

MCCB: MATRICS Consensus Cognitive Battery; FAB: Functional Assessment Battery; UPSA: UCSD Performance Based Skills Assessment.