Cognitive dysfunction and associated factors in patients with chronic schizophrenia

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ABSTRACT
Background: Deficits in neurocognitive function are a hallmark of schizophrenia. They are associated with clinical manifestations and the course of the illness. A study of cognitive dysfunction in Indian patients with schizophrenia is of significance in view of a more benign course and outcome of the illness in this region.

Aim: To study cognitive deficits and associated factors in patients with chronic schizophrenia and compare them with those in the normal population.

Methods: We compared 100 patients with chronic schizophrenia with 100 matched normal controls on multiple measures of attention, executive function and memory.

Results: Compared to normal individuals, patients with schizophrenia performed poorly in all cognitive tests. Cognitive deficits in patients were related to gender, education, age, duration of illness, and presence of positive and negative symptoms.

Conclusion: The neurocognitive profile of Indian patients with chronic schizophrenia resembles those of patients in developed countries.

Key words: Cognitive dysfunction, schizophrenia

INTRODUCTION
Schizophrenia is accompanied by impairments in several domains of cognitive function.1 Patients with schizophrenia have been found to perform more poorly than normal controls on tasks of attention, memory, executive function, language, learning and motor control.2–4 In recent times, cognitive impairment has gained importance in terms of emerging theories on the aetiology and treatment of schizophrenia.5

Cognitive impairment in schizophrenia has been found to be related to measures of psychopathology6–7 and outcome.8,9 Much research on cognition in schizophrenia has been done in developed countries where the outcome was found to be poorer than that in developing countries such as India. It is of interest to know the degree and nature of cognitive dysfunction in Indian patients with schizophrenia. Studies in India have described cognitive deficits in schizophrenia.10,11 However, a comprehensive evaluation of deficits in all major cognitive domains, and their relation with demographic and clinical variables, has not been done. We compared cognitive deficits and associated factors in patients with chronic schizophrenia with those of a matched normal population.

METHODS
The case group was a consecutive sample selected from outpatients attending the treatment and rehabilitation centre of the Schizophrenia Research Foundation (India) in Chennai and comprised 100 subjects (men: 60; women: 40) fulfilling the DSM-IV criteria for chronic schizophrenia. A clinical interview and chart review established the diagnosis. All of them were on antipsychotic drug treatment at the time of evaluation. Subjects between the ages of 18 and 45 years, with at least 10 years of school education, were selected. The control group comprised 100 healthy subjects (men: 60; women: 40) with no current, past or family history of any psychiatric disorder. They were selected from among volunteers by the stratified sampling method and matched with subjects from the study group for age, sex and education. All participants gave a written informed consent after being explained the nature of the study. The cases and controls did not differ significantly in their mean age (33.6 years, SD±8.2 vs 33.9 years, SD±8.1; t=0.251) and years of formal education (14.3 years, SD±3.1 vs 13.9 years, SD±2.8; t=0.893). The patients were ill for a mean duration of 10.4 years (SD±6.8). The neuropsychological tests done are listed in Table 1.12–16
psychological tests that differentiated normals from patients. Mahalanobi distant statistic method to identify neuro-

analysis were entered into classification analysis using the continuous variables. The variables significant at univariate
analyses were done to measure the relationship between univariate analysis. Simple correlation and partial correlation
for data analysis. The chi-square and

for executive function, and immediate recall on the Visual
attention, executive function, memory—except the number
of perseverative responses on the Ruff Figural Fluency test
in the neuropsychological tests.

The patients performed significantly poorer than normal subjects on all tests of cognitive functions evaluated—
attention, executive function, memory—except the number
of perseverative responses on the Ruff Figural Fluency test
for executive function, and immediate recall on the Visual Reproduction task of memory (Table 2).

The step-wise, discriminant function analysis identified 10 tests measuring tasks of attention, executive function and
memory which differentiated most between patients and normal controls. The minimum D squared statistic and
standardized canonical discriminant function coefficients (SCDFC) of the tests are listed in Table 3. A classification
analysis based on the SCDFC of these 10 variables classified
92% of the study population appropriately into their original
groups as patients and normal subjects.

Social and clinical factors and cognition

Women performed better than men on only one task: the Visual Paired Associate learning test (mean scores: immediate
recall=12.7, SD±3.8 vs 10.7, SD±5.5, t=2.06, p<0.05; delayed
recall=5.4, SD±1.0 vs 4.7, SD±1.3, t=3.03, p<0.01). The years of education did not correlate with age or clinical factors. The age and duration of illness correlated with each other (r=0.723,
p<0.001) but not with PANSS subscale scores. The three
PANSS subscale scores correlated positively with each other at a significance level of 0.01 or less (correlation coefficients:
PS with NS=0.280; PS with GS=0.499 and NS with GS=0.461).

Table 4 presents the significant correlations (p<0.05)
among scores on cognitive tests with education, age
(controlling for duration of illness), duration of illness
(controlling for age) and scores on each of the subscales of
PANSS (controlling for scores on the other two subscales of
PANSS). Increasing age correlated with scores on the Digit
Span and Digit Symbol Substitution Tests of attention, Ruff
Figural Fluency Test of executive function, and verbal
working memory tested by the Letter–Number Span test. More
years of education correlated with better performance on tasks
of attention, executive function, verbal and visual memory. A longer duration of illness correlated with indicators of
executive dysfunction on the Wisconsin Card Sorting Test
(WCST) and verbal memory. The positive symptom score
was related to deficit on a single test of verbal memory, and
negative symptoms with performance on measures of
attention, executive function and visual memory. The GS
score did not correlate with any cognitive deficit.

RESULTS

The mean scores on the Positive and Negative Syndrome Scale
(PANSS) were 10.2 (SD±3.9) for the positive subscale (PS),
9.6 (SD±3.2) for the negative subscale (NS) and 23.6
(SD±5.7) for the general psychopathology subscale (GS).

Cognitive deficits

The patients performed significantly poorer than normal subjects on all tests of cognitive functions evaluated—
attention, executive function, memory—except the number
of perseverative responses on the Ruff Figural Fluency test
for executive function, and immediate recall on the Visual Reproduction task of memory (Table 2).

DISCUSSION

Cognitive deficits in chronic schizophrenia

We did not have any difficulty in using the neuropsychological tests developed in other cultures. The significant level
of schooling of patients during which English was one of main
languages taught seemed to facilitate their ability to
understand and perform on tests that had numerate or verbal
tasks. We feel cultural factors had little impact on performance in the neuropsychological tests.

Patients with schizophrenia performed poorly on all tests of cognitive function compared with the normal population
matched with respect to gender, age and education. The classification analysis showed that patients with schizophrenia

Table 1. Neuropsychological tests done on the study sample

| Test done (subtests) | Function measured |
|---------------------|------------------|
| Digit Span Test (forward and backward) | Span of attention (verbal task) |
| Visual Memory Span (forward and backward) | Span of attention (non-verbal task) |
| Digit Symbol Substitution Test | Sustained attention and speed |
| Visual Number Scanning Ability Test (time taken, number/minute) | Visual scanning and attention |
| Ideational Fluency Test* | Executive function—verbal fluency |
| Ruff Figural Fluency Test (unique and perseverative responses) | Executive function—non-verbal fluency |
| Wisconsin Card Sorting Test | Executive functions and cognitive flexibility |
| Letter–Number Span test (correct and longest) | Working memory |
| Delayed Response Learning Test* | Working memory |
| Verbal Learning and Memory* (immediate, delayed recall) | Logical memory and learning |
| Visual Learning and Memory* (immediate, delayed recall) | Immediate visual memory |
| Verbal Paired Associate Learning Test* (immediate, delayed recall) | Associate learning (verbal) |
| Visual Paired Associate Learning Test* (immediate, delayed recall) | Associate learning (visual) |
| Visual Reproduction Test* (immediate, delayed recall) | Immediate and delayed visual memory |

*NIMHANS Battery (unpublished)
can often be clearly differentiated from the normal population based on their performance on some of the tests of attention, executive function and memory.

Factors associated with cognitive deficits

Gender differences in cognitive dysfunction have been reported. Males have been found to have more cognitive deficits than females, a trend attributed to the interplay of sex hormones, neurodevelopmental and psychosocial sex differences.\(^19\) We did not find any major gender difference except for a poorer performance of males on a memory task. Age-related decline across most neuropsychological functions has been demonstrated in schizophrenia.\(^20\) We found that increasing age was related to poorer performance on tasks of attention, executive function and memory, which has been pointed out to be the result of an ageing brain in patients.

More years of education positively influenced performance on tasks that tested attention, executive function, memory and constructional ability. The duration of formal academic training reflected good pre-morbid functioning, intellectual level and a higher level of information-processing skills in the past. Patients with good education thus did well on cognitive tasks because of this inherent capability. A parallel can be drawn with the influence of education on cognitive changes reported in other neurological disorders.\(^21\)–\(^23\) Cognitive deficits have been found to remain relatively stable throughout the course of schizophrenia.\(^24\) We also found that all measures, except two measures of executive function on the WCST and one of verbal memory, were stable over a range of illness duration.

### Table 2. Comparison of the cognitive functions in patients with schizophrenia and normal controls

| Neuropsychological test                      | Normal subjects Mean±SD | Patients Mean±SD | t score |
|---------------------------------------------|-------------------------|-----------------|--------|
| **Attention**                               |                         |                 |        |
| Visual Scanning— time taken                 | 162.9±47.4              | 241.9±99.8      | 7.14*  |
| Visual Scanning— number/minute              | 23.5±3.4                | 17.0±4.6        | 11.37* |
| Digit Span— forward                        | 10.7±1.3                | 9.0±2.0         | 6.88*  |
| Digit Span— backward                       | 9.6±1.6                 | 7.3±1.9         | 9.29*  |
| Visual Memory Span— forward                | 10.9±1.5                | 9.0±2.0         | 7.08*  |
| Visual Memory Span— backward               | 9.5±1.18                | 7.5±2.4         | 7.26*  |
| Digit Symbol Substitution Test             | 57.0±10.5               | 41.0±11.6       | 10.18* |
| **Executive function**                     |                         |                 |        |
| Wisconsin Card Sorting Test                |                         |                 |        |
| Trials administered                        | 98.0±19.2               | 116.8±17.9      | 7.14*  |
| Total correct                              | 70.7±6.83               | 66.1±16.2       | 2.65*  |
| Total errors                               | 27.3±15.4               | 50.8±25.6       | 7.87*  |
| Categories completed                       | 5.8±0.6                 | 3.8±2.2         | 8.71*  |
| Trials to complete first category          | 13.2±5.1                | 35.7±40.7       | 5.49*  |
| Perseverative response— total              | 18.1±12.9               | 41.1±32.8       | 6.53*  |
| Perseverative errors— total                | 16.0±10.6               | 34.3±24.5       | 6.87*  |
| Non-perseverative errors— total            | 11.5±6.4                | 16.6±10.0       | 4.31*  |
| Conceptual level responses— total          | 63.9±6.6                | 51.6±22.0       | 5.36*  |
| Failure to maintain set                    | 0.21±0.43               | 0.84±1.2        | 4.99*  |
| **Other tests**                             |                         |                 |        |
| Ideational Fluency                         | 17.6±3.4                | 12.9±3.4        | 9.72*  |
| Ruff Figural Fluency— perseveration        | 6.5±6.4                 | 7.4±7.5         | 0.88 (NS) |
| Ruff Figural Fluency— unique responses     | 56.9±16.7               | 35.2±16.4       | 9.28*  |
| **Memory**                                 |                         |                 |        |
| Verbal Paired Association— immediate       | 21.6±1.7                | 19.0±3.6        | 6.43*  |
| Verbal Paired Association— delayed         | 7.9±0.3                 | 7.3±1.4         | 4.37*  |
| Visual Paired Association— immediate       | 15.6±1.9                | 11.5±5.0        | 7.75*  |
| Visual Paired Association— delayed         | 5.8±0.4                 | 4.9±1.2         | 6.60*  |
| Visual Reproduction— immediate             | 35.4±3.7                | 33.1±31.7       | 0.72 (NS) |
| Visual Reproduction— delayed               | 31.5±6.1                | 25.6±9.3        | 5.25*  |
| Verbal Learning and Memory— delayed        | 22.3±3.1                | 20.1±3.3        | 6.30*  |
| Visual Learning and Memory— delayed        | 16.6±3.2                | 13.5±4.9        | 5.20*  |
| Delayed Response Learning                  | 15.7±1.3                | 13.1±3.0        | 7.98*  |
| Letter–Number Span— correct responses      | 18.0±2.7                | 14.9±3.5        | 6.92*  |
| Letter–Number Span— longest item           | 5.9±0.7                 | 5.3±1.0         | 5.10*  |

*p<0.01, which is significant
NS: not significant
We observed that negative symptoms had a strong association with cognitive dysfunction in all the domains. This finding is in agreement with the results of studies which showed that both positive and negative symptoms were associated with distinct neuropsychological deficits. Heydebrand et al. observed that negative symptoms were related more frequently to cognitive dysfunction than positive symptoms.

CONCLUSION

In a group of patients with chronic schizophrenia in India, the nature and degree of cognitive deficits and their relationship to gender, age and clinical factors are comparable with observations made in developed countries. It would be of interest to explore the relationship between cognitive deficits in, and outcome of, schizophrenia among Indian patients, as they have a better outcome than patients with schizophrenia in developed countries.

Table 3. Function analysis of patients with schizophrenia and normal controls (standardized canonical discriminant function coefficient)

| Neuropsychological test | Patients with schizophrenia | Normal subjects |
|-------------------------|-----------------------------|-----------------|
| **Attention**           |                             |                 |
| Visual Scanning— time taken | 6.593                      | 0.319           |
| Visual Scanning— number/minute | 2.585                      | 0.509           |
| Digital Span— backward recall | 5.214                      | 0.220           |
| Digit Symbol Substitution Test | 6.333                      | 0.341           |
| **Executive function**  |                             |                 |
| Wisconsin Card Sorting Test |                           |                 |
| Failure to maintain set | 4.545                       | -0.359          |
| **Memory**              |                             |                 |
| Verbal Paired Association— delayed | 5.754                      | 0.248           |
| Verbal Learning and Memory— delayed | 6.876                      | 0.228           |
| Visual Learning and Memory— delayed | 6.007                      | -0.324          |

Table 4. Cognitive deficits and social and clinical factors (correlation coefficients)

| Neuropsychological test | Age | Education | DOI | PANSS |
|-------------------------|-----|-----------|-----|-------|
| **Attention**           |     |           |     | PS    |
| Visual Scanning— time taken |   | -0.257   | 0.255 |
| Visual Scanning— number/minute |   | 0.203   |       |
| Digit Span— forward      |   | -0.245   | 0.344 |
| Digit Span— backward     |   | -0.269   |       |
| Visual Memory Span— forward |   | 0.344   |       |
| Visual Memory Span— backward |   | 0.311   |       |
| Digit Symbol Substitution Test |   | -0.305   | 0.253 |
| **Executive function**  |     |           |     | NS    |
| Wisconsin Card Sorting Test |   |         |     | GS    |
| Trials administered      |   | -0.380   | 0.223 |
| Total errors             |   | -0.400   |       |
| Categories completed     |   | 0.373    |       |
| Trials to complete first category |   | -0.224   | 0.199 |
| Perseverative response   |   | -0.352   | 0.351 |
| Perseverative errors     |   | -0.356   | 0.338 |
| Non-perseverative errors |   | 0.255    |       |
| Conceptual level responses | |       |     |
| **Memory**               |     |           |     |       |
| Verbal Paired Association— immediate |   | 0.208    |       |
| Verbal Paired Association— delayed |   | 0.223    | -0.245 |
| Visual Paired Association— delayed |   | 0.392    | -0.213 |
| Visual Reproduction— immediate |   | 0.340    | -0.222 |
| Visual Reproduction— delayed |   | -0.197   | -0.333 |
| Verbal Learning and Memory— delayed |   | 0.286    |       |
| Visual Learning and Memory— delayed |   | 0.439    |       |
| Delayed Response Learning |   | -0.245   | 0.478 |
| Letter-Number Span— correct responses |   | -0.252   | 0.394 |
| Letter-Number Span— longest item |   |         |       |

DOI: duration of illness, PANSS: Positive and Negative Syndrome Scale, PS: Positive subscale, NS: Negative subscale, GS: General psychopathology subscale
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