Executive functions and cognitive deficits in schizophrenia: Comparisons between probands, parents and controls in India

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Abstract

Background—Cognitive impairment is said to be a core feature of schizophrenia. Executive function is an important cognitive domain.

Aim—This study was undertaken to assess cognitive impairment among Indian patients with schizophrenia (Sz) or schizoaffective disorder (SzA), compared with their parents and unaffected individuals (controls).

Settings and Design—Executive functions as measured by Trail-making Test (TMT), of patients and their parents were compared with controls. The patients were recruited from the Outpatients' Department (OPD) of a government hospital.

Materials and Methods—Patients diagnosed as Sz or SzA (n=172) and their parents (n=196: families n=132, 119 fathers and 77 mothers) participated. We also included 120 persons with no history of psychiatric illness. Cognitive function was assessed with the TMT. The Information Score of the Post Graduate Institute Battery of Brain Dysfunction test, developed in India for Indian subjects was used as a proxy for general fixed knowledge.

Statistical Analysis—Logistic and linear regression was used to compare cognitive deficits of cases, parents and controls.

Results—Cases and their parents took significantly more time than controls on Part B of the TMT. There were no statistically significant differences between cases and parents on any of the TMT parameters. Using regression analysis, the most significant correlates of all TMT parameters among cases were with occurrence of auditory hallucinations and current age.

Conclusion—Cases, as well as their parents showed more cognitive impairment than controls on the TMT.

Keywords

Cognitive deterioration; executive functions; schizophrenia

Cognitive deficits are regarded as core aspects of the disease process in schizophrenia (Sz), independent of clinical symptomatology or anti-psychotic medications. Such deficits also strongly influence outcome.[1] While the degree of cognitive impairment can vary considerably among individuals, deficits are present in most cognitive domains in any given sufferer.[2–4] Although most authors claim that deficits seen in Sz are heterogeneous, neuropsychological studies place strong emphasis on impairments in executive functions.[5–9] Executive functions refer to cognitive processes that regulate capacity for attention, abstract reasoning, and integration of other cognitive skills. In general, Sz patients experience difficulty in formulating plans and combining information from various sources to perform new tasks.

The Trail-making Test (TMT) is a standard measure of perceptual-motor and set-shifting skills and tests both executive functions as well as attentional abilities. It is an easily administered paper and pencil test and is a standard component of the Halstead-Reitan Battery,[10–11] most often used for screening for cognitive impairment. There are two parts of this test: Part A (numbers) and Part B (numbers and alphabets alternating with each other). Sherer and Adams[11] interpret the TMT specifically Part B, as an executive task.

In general, performance was considered to be impaired if scores exceeded 40 sec for Part A and 91 sec for Part B of TMT when the test was administered to English-speaking American subjects. However, normal Indian subjects were found to score significantly differently on the TMT compared to these normative values.[12] Familiarity with English might be the reason for this difference. Lack of familiarity with cognitive tests in certain cultures may lead to scores that differ from American individuals.[13]

Compared with controls Sz/Schizoaffective disorder (SzA) sufferers and at risk subjects (such as relatives of Sz patients) perform abnormally on a wide variety of experimental information processing and neuropsychological paradigms.[14] Conflicting results on executive performance of siblings and other first-degree relatives of schizophrenic patients have been reported.[15–18] Some studies showed that relatives could perform variably depending on the cognitive tests used, poorly on the verbal fluency or the Trail-making Part B but normally on the wechsler wisconsin card sorting test (WCST) or the Trail-making Part A.[19–21] In contrast, Dolfus[22] did not find any difference on TMT between parents and cases. These relatives performed poorly on other tests of executive functioning. Persons with Sz/SzA and their siblings compared to controls were significantly impaired in executive functioning, measured by Part B of TMT.[23–24] So there are conflicting reports regarding executive functions of relatives of patients with Sz which need to be tested.

The present study compared Sz/SzA cases and their parents on TMT to determine factors affecting scores and to assess whether this test was an appropriate marker of vulnerability to Sz/SzA. There is scarcity of such studies in India. Very little research has been carried out on cognitive impairment in Sz in India and cultural factors can play a significant role in determining neurocognitive impairment in schizophrenia patients and their relatives. The TMT was selected because it is an easily administered paper and pencil test requiring only

knowledge of English alphabets and numbers. This would facilitate participation of maximum number of subjects, including those not fully literate in English.

Materials and Methods

Sample

A total of 172 cases (n=60 female and n=74 male) affected with Sz (n=134) or 38 cases (n=23 female and n=15 male) affected with SzA participated in the study. Cases were aged above 15 years and had a working knowledge of English numbers and letters. There were some cases whose parents did not participate in the study (n=23 cases). Dosages and types of antipsychotic medications varied from time to time. Hence it was not possible to calculate total exposure to antipsychotic medications.

The TMT initially was administered to 218 available parents conversant with English letters and alphabets. Parents with major psychiatric illness were excluded (n=18 with Sz/SzA n=4 with depression). A total of 196 parents (n=132 families, n=77 mothers, n=119 fathers) were finally included for analysis. There were fewer mothers than fathers, as many women were not literate in English.

The controls (n=120, n=86 males, n=34 females) were adults who sought treatment at the Department of Dermatology at Dr Ram Manohar Lohia Hospital, a publicly funded tertiary care hospital in New Delhi. To avoid bias every fifth patient reporting to the Dermatology OPD of the same hospital was recruited. If the fifth patient did not meet the inclusion criteria the next patient was approached for participation. All were screened for absence of psychiatric illness as described in Bhatia *et al.*[12]

Evaluation

Hindi version of Diagnostic Interview for Genetic Studies (DIGS)[25,26] (http://www-grb.nimh.nih.gov/gi.html) was used to ascertain cases. The TMT was administered on all cases, parents and controls to assess executive function. The information Subtest of Verbal Adult Intelligence Scale of Post Graduate Institute Battery of Brain Dysfunction (PGIBBD) [27] was administered to all three groups of participants and is marked Information Scores. This battery is based on the Wechsler Adult Information Scale (WAIS) and has been adapted to Indian conditions; PGIBBD is developed and tested in India and presently is extensively used to determine areas of brain damage. This subtest consists of 33 items of tests of general and fixed knowledge acquired by the subject. This test is included as proxy for measuring the intelligence of the participants.

Procedure

Cases were participants of our ongoing research, recruited after ethical clearance from the hospital Ethics Committee was received. They were recruited from private and public hospitals and clinics in New Delhi and surrounding areas to make the sample representative. Their treating psychiatrists were contacted initially and after preliminary information and verbal consent, they referred willing subjects to us. All referred subjects who met inclusion criteria were contacted irrespective of their gender, age or race. After written informed

consent DIGS was administered (cases alone) and consensus diagnosis was established according to DSM IV. All participants provided written informed consent before participation. DIGS was also administered on all parents suspected of suffering from mental illness.

The TMT was administered to the case as well as parents. Time taken to complete all parts of the test was recorded. Demographic details (age, education etc) were also recorded for parents.

The subject's responses were recorded verbatim for information test and the test discontinued if seven consecutive failures occurred. One point was scored for each correct response.

Statistical analysis

The distribution of the Part A and B of TMT scores was skewed among cases and parents. Hence logistic regression with groups as dependent variables was conducted separately for different pairs (parent / controls, parent / cases and case / controls). Age, sex and information scores were included as covariates. Regression analyses were performed to test for effects of different clinical and demographic variables on TMT among cases. Variables included were age, school years, age at onset, diagnosis, delusions (ever present), auditory hallucinations (ever present), visual hallucinations (ever present). Data was analyzed using SPSS 11.0.

Results

Demographic characteristics

The mean ages (± standard deviations, SD) of the cases, parents and controls were 30.34±9.78, 55.67±8.70 and 30.11±12.83 years respectively. Mean ages of cases and controls were not different statistically. Parents were expectedly older than cases (t=11.74, P=0.003). Gender-wise distribution of the sample was 48.2% females, 51.8% males among cases, 39.3% females, 60.7% males among parents and 28.3% females, 71.7% males among controls. There were significantly more number of males than females among controls and parents (χ^2=11.74, df=2, p=0.003). Information scores of cases, parents and controls were 18.51±6.71, 22.06±6.12, 20.89±5.38 respectively [Table 1]. There was no significant difference between parents and controls on information score. Parents and controls both had significantly higher information scores than cases (t=5.25, P<0.001; t=5.80, P=0.001)

The mean years of education (± standard deviations, SD) were comparable: for cases 12.25±3.14 years, parents 12.43±3.950 years and controls 12.13±3.13 years. There was no significant difference between cases, parents and controls on education.

Cases versus controls

There were no significant differences between cases and controls on Part A of the TMT. On Part B of the TMT, cases (216.51±173.48secs) took significantly more time than controls (150.69±49.84secs) (Wald χ^2 = 9.85, P=0.002). Similarly on Part (B-A), cases took

significantly more time (129.87±157.25secs) than controls (75.3±48.15secs). Number of females was significantly more in cases than in controls (Wald $\chi^2 = 9.42$, $P=0.002$).

Parents versus controls

Parents and controls were compared on Parts A, B and (B-A) of the TMT. There was no significant difference between these groups on Part A of the TMT. However, the parents took significantly more time to complete Part B (229.11±173.48 sec) than controls (150.69±49.84sec) (Wald $\chi^2 =4.86$, $P=0.027$). This could be attributed to significant age differences between the groups (Wald $\chi^2= 73.32$, $P<0.001$) [Table 2].

Parent versus cases

There was no significant difference between parents and cases on any of the TMT parameters. Significantly more fathers participated in the study than men in controls (Wald $\chi^2 = 6.23$, $P=0.01$) [Table 3].

Analyses among patients

Regression analyses were performed to test for effects of different clinical and demographic variables on TMT among cases. Variables selected for analysis included age, school years, age at onset, diagnosis, delusions (ever present), auditory hallucinations (ever present), visual hallucinations (ever present). Analysis suggested that higher scores on Part A of the TMT were positively predicted by age, diagnosis (Sz/ SzA), and ever presence of auditory hallucinations. On Part B, the main correlates were older age and presence of auditory hallucinations (ever present). Present age and information score influenced Part B-A.

Discussion

The key finding of this study is that both parents and cases performed worse than controls. There was no significant difference between parents and cases on TMT. To our knowledge, this is one of the first few reports of TMT function among Sz patients in India. We found that Indian subjects with Sz/SzA performed worse than controls on Part B of the TMT, as reported by others (in individuals of Caucasian ancestry).[28–30] Impaired performance on such tests can be the direct consequence of an isolated deficit in executive ability, or an indirect manifestation related to more widespread cognitive dysfunction such as impaired attention and global dementia.[25,26] Age seemed to adversely affect executive function, but the effect was accelerated among schizophrenic subjects more than controls.[31]

Our cases performed similar to their much older parents, contrary to previous studies.[32,33] Rybakowski and Borkowska[34] reported that time taken to complete Part B of TMT by parents was intermediate between cases and controls. Though there was no statistically significant difference between men and women on education in our sample, women had significantly lower scores on information scores than men, perhaps because Indian women are more likely to be confined to their houses and acquired less general knowledge and practice with executive tasks.

The parents took more time to complete Part B of TMT than normal subjects, in agreement with other studies.[32–,34] In our sample, parents and cases showed similar deficits, suggesting a vulnerability marker for Sz/SzA. There were significantly more fathers than mothers in the study. It appeared that mothers were not familiar with such tasks and hence were less adept at completing timed activities.

Age was an important predictor of TMT performance in our cases. Our results are consistent with those by Keefe.[20] In the Giovagnoli[35] study, only for Part A did females take longer than males where scores were affected by age, education and general intelligence.

Cognitive abilities were adversely affected by psychotic symptoms, even if present for some period during the course of their illness. Those with prominent affective symptoms (SzA) seemed to be less impaired than those with schizophrenia. The subjects with higher information scores took less time on all parts of the TMT, except Part A in case of parents. In a study by Giovagnoli[35] on Italian subjects, the TMT was affected by age, education and general intelligence. As TMT involves knowledge of English alphabets and numbers, literacy affects performance on these tests.

According to Bilder[36] and Liddle,[37,38] disorganized behavior and negative symptoms are related to several neurocognitive deficits, whereas positive symptomatology is not correlated with neurocognitive impairments. In contrast, auditory hallucinations were significantly correlated to impaired cognitive functioning in our case sample. This happened even if the subject was not suffering from hallucinations during the test. Positive symptoms have been correlated to deficits on tests such as verbal memory and distractibility.[39,40] While Davidson and McGlashan[41] found positive correlations between negative symptoms and cognitive deterioration, especially among older subjects, a meta-analysis by Nieuwenstein[42] reported few statistically significant correlations (measured on scales of positive and negative symptoms). Patterns of associations between cognitive functioning and negative and positive symptoms appear to depend on the sensory modality of the cognitive task being used.

In conclusion, we report a moderately large Indian sample of Sz/SzA individuals performed worse than controls on Part B and Part (B-A) of the TMT, but not Part A. An older parental group performed similar to cases on all four parts after adjusting for age. The parents performed worse than the controls, suggesting that executive function may be a vulnerability marker for Sz. There are some limitations of this study. The neurocognitive measure used in our study was cross-sectional. Parents were older than controls. The medication status of subjects was also not controlled for, but this may not account for the parent / control differences.

Acknowledgments

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Table 1

Demographic variables and trail-making test scores of parents, cases and controls

	Parents (N=196)	Cases (N=172)	Controls (N=120)
Age	55.67 (8.70)[*]	30.34 (9.78)	30.11 (12.83)
Education	12.43 (3.90)	12.25 (3.14)	12.13 (3.13)
Information score	22.06 (6.12)	18.51 (6.71)	20.89 (5.38)
Mean time Part A	91.78 (57.00)	86.64 (51.14)	75.38 (31.81)
Mean time Part B	229.11 (173.48)	216.51 (173.48)	150.69 (49.84)
Part B-A	136.49 (180.24)	129.87 (157.25)	75.3 (48.15)

[*] Values in parentheses are standard deviation scores

Table 2

Effect of group (case, parent, control) on trail-making test (logistic regression)

	Part A		Part B		Part B-A	
	Wald chi square	Odds ratio CI[*] 95%	Wald chi square	Odds ratio CI 95%	Wald chi square	Odds ratio CI 95%
Case / Control	1.061 (p=0.303)	0.997 (0.990–1.003)	9.857[†] (p=0.002)	0.996 (0.994–0.998)	9.320[‡] (p=0.002)	0.996 (0.993–0.999)
Parent / Case	0.102 (p=0.749)	0.999 (0.991–1.007)	0.068 (p=0.794)	1.000 (0.998–1.003)	0.133 (p=0.716)	1.001 (0.998–1.003)
Parent / Control	1.067 (p=0.302)	0.996 (0.988–1.004)	4.868[§] (p=0.027)	0.995 (0.991–0.999)	2.950 (p=0.086)	0.997 (0.994–1.000)

[*] Confidence interval;

[†] Cases performed worse than controls on Part B of TMT;

[‡] Cases performed worse than controls on Part B-A of TMT;

[§] Parents performed worse than controls on Part B of TMT

Table 3

Factors affecting TMT among cases (linear regression)

Part A	
Auditory hallucinations	β=0.187 (*P*=0.01)
Age	β=0.199 (*P*=0.02)
Diagnosis	−0.145 (*P*=0.04)
Part B	
Auditory hallucinations	β=0.182 (*P*=0.01)
Age	β=0.281 (*P*=0.002)
Part B-A	
Age	β=0.275 (*P*=0.003)
Age at onset	β=−0.219 (*P*=0.02)
Auditory hallucinations	β=0.144 (*P*=0.05)