

## Assessment of Executive Function in First Degree Relatives of Schizophrenia and Healthy Controls- A Comparative Study

Shivendra Kumar DPM, DNB<sup>1</sup>, Rohit Kothari<sup>2</sup>, Anil Sisodia<sup>3</sup>, DMS Rathor<sup>4</sup>, Sudhir Kumar<sup>5\*</sup>

<sup>1</sup>Senior Resident, Psychiatry, AIIMS, Patna, Bihar, India

<sup>2</sup>Consultant Psychiatrist, Sarvam Neuropsychiatric Clinic, Panchkula, Haryana, India

<sup>3</sup>Associate Professor and HOD Psychiatry, IMHH, Agra, UP, India

<sup>4</sup>Associate Professor, Psychiatry, IMHH, Agra, UP, India

<sup>5</sup>Professor of Psychiatry and Director, IMHH, Agra, UP, India

\*Corresponding author: Sudhir Kumar

Email: [psychiatrist1000@gmail.com](mailto:psychiatrist1000@gmail.com)

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### Abstract

### Original Research Article

**Introduction:** The lifetime risk of developing schizophrenia in first degree relatives (FDRs) of schizophrenia is very high compared to general population. Executive functions are proposed as an important endophenotype in schizophrenia when it is compared in patients and first degree relatives. So, assessment and comparison of executive function among first degree relatives and healthy controls could provide important information regarding executive function as a marker for schizophrenia. **Materials and Methods:** 20 unaffected FDRs of Schizophrenia patients and 20 normal controls were included in the study by purposive sampling. Cross sectional executive function (EF) assessment was done by Wisconsin Card Sorting Test (WCST). Statistical analysis was done to identify various factors. **Results:** Results show deficit in executive function in FDRs of schizophrenia compared to healthy controls. FDRs of Schizophrenia performed poorly on near half of the WCST domains out of 16 domains of WCST. Percentage preservative error and percentage non preservative error was most significant among all domains. **Conclusion:** WCST domains (which are commonly used for assessment of executive function) deficits are having heritable risk with endophenotypic significance.

**Keywords:** Wisconsin Card Sorting Test (WCST), First Degree Relatives (FDRs), Executive Function (EF).

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## INTRODUCTION

Schizophrenia is often a chronic and disabling disorder with prevalence of about 1% and is having complex inheritance pattern with most important predictor for developing schizophrenia is having a first degree relative (FDR) of schizophrenia. However in many cases, no such clear family history is present. Studies have been done to focus on different groups to identify factors which may indicate towards more susceptibility of developing schizophrenia. Due to said reason, many studies were done on unaffected relatives; mainly first degree relatives of schizophrenia to identify factors as the first degree relatives harbor most genetic similarity to patients of schizophrenia compared to others. Studies done in this field have indicated that FDR of schizophrenia have sub threshold positive and negative symptoms of schizophrenia along with subtle neuro cognitive deficits. It may be postulated that if the genetic susceptibility of schizophrenia do not develop to full blown syndromal schizophrenia, they may still affect the brain and develop certain behavioral and

neuropsychological deficits. These related constructs were proposed initially by Paul E. Meehl and he coined the term "Schizotaxia" for the different deficits [1].

Assessment of the endophenotypes have several clinical implications- how can milder forms of schizophrenia be diagnosed specially when now a days concept of spectrum is taking over unitary concept of syndrome, does these milder forms have implications for family intervention in schizophrenia, what may be the treatment options and can schizophrenia be prevented by early intervention when these endophenotypes are present.

Different neuropsychological domains assessed in first degree relatives of schizophrenia are- motor ability, perceptual motor speed, short term memory, sustained attention, language and verbal ability, memory, visuo-spatial ability and executive functions. Executive functions comprise different functions of mind consequently causing voluntary

control of behavioral responses. Executive functions mainly involve- planning, organization, sequencing and abstraction. Deficit in executive functions may be central to schizophrenia and is present in adolescents at risk of developing the disease (ultra-high risk), in patients with a first outbreak of schizophrenia, and apparently in their first-degree relatives [2-4].

Previously many studies have been done India assessing neuropsychological functioning in schizophrenia [5-7], but there are few studies done on FDRs. Also studies done previously have used different tools for assessment. So, more studies taking FDRs and using comprehensive tools are needed to focus on specific domains of neuropsychological evaluation with comparison to healthy controls.

## MATERIALS AND METHODS

The present study is a cross sectional; hospital based study and conducted at the Institute of Mental Health and Hospital, Agra (IMHH). 20 unaffected FDR of patients of Schizophrenia and 20 healthy normal controls age and sex matched to FDRs were included in

the study using purposive sampling. Subjects were 20-50 years old and minimum 8th grade pass. To assess overall psychological health or wellness, General Health Questionnaire 12 (GHQ 12) was used [5]. FDRs and healthy controls having GHQ 12 score <15 were included in the study. To measure executive functions, Wisconsin Card Sorting Test (WCST) was used [6]. WCST tests the ability to develop and maintain an appropriate problem solving strategy across changing stimulus conditions in order to achieve a future goal. WCST is thought to measure specific abilities of planning, organization, abstract reasoning, concept formation, cognitive set maintenance, set shifting ability and inhibition [7]. WCST consists of 128 response cards. There are four stimulus cards, each having three variations. These stimulus cards reflect three stimulus parameters - COLOUR, FORM and NUMBER, which are displayed in four different ways. Written informed consent was taken from the participants in the study. Before starting the study, clearance from institute ethical body was taken.

## RESULTS

**Table-1: Comparisons of means among groups and comparison of EF in FDRs and controls**

WCST Domains	Schizophrenia FDR	Control	Comparison of EF between Schizophrenia FDR and Normal Controls (Post hoc)	
			Mean difference	P
NTA	122.20±10.2	100.10±16.14	22.10*	0.000
TNC	75.60±8.75	76.40±9.28	-00.80	0.973
TNE	46.65±14.88	24.20±8.86	22.45*	0.000
PE	37.55±9.98	23.55±6.49	14.00*	0.001
PR	25.00±12.54	12.05±6.50	12.95*	0.017
PPR	20.15±9.33	14.10±11.09	6.05	0.474
PeE	21.80±10.04	11.15±5.41	10.65*	0.019
PPE	17.50±7.42	13.30±10.88	4.20	0.673
NPE	24.90±10.26	12.50±4.52	12.40*	0.000
PNPE	19.45±7.14	11.75±3.32	7.70*	0.002
CLR	60.25±13.30	69.55±7.53	-9.30	0.107
PCLR	50.30±14.29	70.45±8.24	-20.15*	0.000
NCC	3.90±1.86	6.15±1.22	-2.25*	0.000
TCFC	23.55±20.67	15.20±7.73	8.35	0.361
FMS	1.65±1.26	0.50±0.69	1.15	0.936
LTL	-2.21±29.70	-0.57±16.13	-1.63	0.972

\* Significant at  $P < .01$

NTA- number of trials administered, TNC- total number of correct responses, TNE- total number of errors, PE- percentage of error, PR- perseverative responses, PPR- percentage of perseverative responses, PeE- perseverative error, PPE- percentage of perseverative error, NPE- non perseverative error, PNPE- percentage of non-perseverative error, CLR- conceptual level responses, PCLR- percentage of conceptual responses, NCC- number of categories completed, TCFC- trial to complete first category, FMS- failure to maintain sets, LTL- learning to learn score.

Total number of trials administered was higher in unaffected FDR of Schizophrenia patients compared to the control group. On post hoc analysis it was significant ( $p < 0.001$ ). Total number of errors and percentage of errors in unaffected FDR of schizophrenia had higher mean score compared to the control group and post hoc analysis was significant ( $p = 0.001$ ) indicating markedly poor performance.

Preservative responses were higher in FDRs compared to the control group with marginally significant result on post hoc analysis, ( $p = 0.017$ ) indicating markedly poor performance. Percent of non-perseverative error was higher in unaffected FDRs compared to control group and post hoc analysis was significant ( $p = 0.002$ ). Percentage of conceptual level responses was lower in unaffected FDRs compared to the control group with

significant post hoc analysis ( $p < 0.001$ ). Number of categories completed was lower compared to the control group and post hoc analysis was significant ( $p < 0.001$ ).

Although difference was also present in other domains of WCST between the two groups, e.g.- in total number of correct responses, percentage of perseverative responses, percentage of perseverative error, conceptual level responses, trials to complete first category, failure to maintain set and learning to learn score ; difference was not significant with no significant post hoc analysis present.

## DISCUSSION

In this study, WCST tapping was used to assess EF among unaffected FDRs of schizophrenia and normal controls. Each group included 20 subjects with a total of 40 subjects. Both groups were matched on gender, suggesting that the differences in the neuropsychological domains seen in the present study cannot be attributed to gender. There was no statistically significant difference in any of the socio-demographic profile.

We already know that patients in remitted symptoms of schizophrenia show impairments of EF, verbal memory, psychomotor speed, and sustained attention. This study was primarily intended to explore the executive function in FDRs of schizophrenia. Several studies have demonstrated the validity of the WCST as a comprehensive tool in assessing EF [8]. However most of the authors often report only 2 scores [9]. In this study, detailed analysis of WCST was done on 16 different scores related to several parameters.

On WCST; FDRs performed significantly low on almost half of the domains when compared with healthy controls. They made more number of errors which implies that they had more difficulty in understanding the concept of the test ( $p < 0.001$ ). Among the errors the FDR made significantly more number of non- perseverative errors ( $p < 0.001$ ), as well as, perseverative errors ( $p = 0.019$ ), which implies that they were not interpreting the feedback properly or they were matching the cards without any concept in mind or they had difficulty in shifting between categories, despite of receiving the feedback.

The FDRs made significantly less number of conceptual responses and more trials to complete the first category further supporting the notion that their understanding of the test was poorer than the controls. Though both number of conceptual response and trial to complete first category didn't turn out to be significant.

Significant deficits were found in many domains which suggest that such FDRs have difficulty in set shifting, planning, and understanding of the problem, concept formation, problem solving and trial

and error learning. These may be represented clinically in the form of poor psychosocial functioning. Other studies of WCST in relatives are consistent with our study of increased perseveration scores in unaffected siblings compared to controls. Meta analytic review comparing WCST performance in relatives of schizophrenia and controls reported that FDRs performed poorly than controls. In number of categories completed, controls performed better than FDRs of schizophrenia [10]. Our study is having identical results overall but also indicated deficits in other domains also. In one recent study done in India, there was significant difference in neuropsychological assessments in FDRs of schizophrenia and healthy controls but found non-significant difference in domains of WCST [11]. Our study used randomization to eliminate effect of age and gender and found significant difference in many WCST domains. It indicates that other domains of WCST may also contribute to further understanding of endophenotype of schizophrenia.

## CONCLUSIONS

First degree relatives of schizophrenia lie between overt psychotic symptoms of schizophrenia and normal controls. The deficits in executive function was persist even without having schizophrenia and is significant in nature. So this study suggests that executive functioning deficits can be used as an endophenotype to differentiate more firmly between persons with higher susceptibility for developing schizophrenia to normal controls and early intervention(s) could be carried out to prevent chronicity and disability.

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