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Impairment in Executive Function in First Degree Relatives of Bipolar Affective Disorder- A Cross Sectional Study

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Abstract | **Original Research Article**

Introduction*:** Impairment in different neuropsychological domains especially executive functions are reported in few studies earlier in unaffected first degree relatives of bipolar affective disorder but the results are not consistent in nature. Studies have indicated that executive functions may have endophenotypic significance considering the amount of genetic similarity with probands. In this study, first degree relatives of bipolar disorder are compared to matched normal controls for executive functioning. ***Materials and Methods: 20 unaffected FDRs of patients of bipolar affective disorder and matched 20 normal controls were involved in the study for assessment of executive functioning by WCST. Sampling was done by purposive method. After collection of data, analysis was done using statistical methods. ***Results:*** Executive function deficits were present in many domains of WCST in FDRs of bipolar affective disorder compared to healthy controls. It was more significant in number of trials administered, total number of errors and percentage of error. ***Conclusion:*** Deficits of executive functions may be attributed to degree of genetic similarity and may have endophenotypic significance.

Keywords: WCST- Wisconsin Card Sorting Test (WCST), Executive function (EF), first degree relatives (FDRs).

INTRODUCTION

Bipolar disorder is a mental disorder with relapsing and remitting pattern causing significant disability in a person and requires long term prophylactic therapy. Bipolar disorders have high genetic contribution as disorders are more common in higher genetic similarity populations as established by family, adoption and twin studies. For such a disorder, having a biological marker would be of great help in early intervention and preventing disability. Now a days the term endophenotype is used to denote biomarkers as vulnerability markers having genetic relation and so more common in first degree relative (FDRs) as they have about 50% similarity to the index case and are about 10-20 times more vulnerable to develop bipolar disorders than normal population. Studies for different endophenotypes which adjust to multivariate genetic models of BPAD are an important step in said disoredrs [1-4].

Deficits in neurocognitive functions can serve as an endophenotype as it fulfils most of criteria as a biomarker- associated with illness, presence in patients in remission phase, heritable and presence in FDRs. Neurocognitive deficits are finding in prior studies in different phases of illness i.e.- acute phase, patients in partial remission and remitted patients. However type of neurocognitive functioning involved are diverse e.g.- language, attention and concentration, verbal memory, working memory and executive functions and the results are equivalent. In one of the most recent meta-analysis involving FDRs of BPAD and normal controls, the results were positive for executive functions but strength was low. It was more specifically associated with speed based executive functions [5]. Data on executive function deficits in FDRs of schizophrenia is low and there is a need to have more studies on given topic.

MATERIALS AND METHODS

This study was conducted at a tertiary level mental health institute- Institute of Mental Health and hospital. Study was done involving 20 persons of unaffected FDRs of patients with established diagnosis of bipolar disorders. Age and gender matched 20 healthy normal controls were included for comparison.

All the subjects were included using purposive sampling method. In both the groups, age of the subjects was 20-50 years and at least 8th pass. General Health questionnaire (GHQ 12) was applied in both the groups for screening of overall psychological health or wellness [6]. A cut off score of GHQ <15 were taken for the study as is indicated in the literature. Wisconsin Card Sorting Test (WCST) was used for assessment of executive functions [7]. WCST is one of most used test for assessing the executive function both in Indian setting and outside. WCST tests set shifting based on stimulus parameters- c, f, n (color, form, number) and 4 types of stimulus card are used. Total number of response card used in WCST is 128. Participants were informed about the study in writing or reading out for illiterate persons. Consent was taken prior to participation in the study. Institute ethical committee was informed and their permission was taken.

RESULTS

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

WCST Domains	BPAD FDRs	Control	Comparison of EF between BPAD FDRs and Normal Controls (Post hoc)	
			Mean difference	P
NTA	118.55±15.59	100.10±16.14	18.45*	0.000
TNC	71.00±15.09	76.40±9.28	-5.40	0.300
TNE	47.40±22.25	24.20±8.86	23.20*	0.000
PE	39.85±16.34	23.55±6.49	16.30*	0.000
PR	27.20±20.56	12.05±6.50	15.15*	0.004
PPR	32.55±24.26	14.10±11.09	18.45*	0.002
PeE	23.75±17.38	11.15±5.41	12.60*	0.004
PPE	29.45±23.62	13.30±10.88	16.15*	0.005
NPE	23.60±12.12	12.50±4.52	11.10*	0.001
PNPE	19.40±8.64	11.75±3.32	7.65*	0.002
CLR	57.95±19.38	69.55±7.53	-11.60*	0.033
PCLR	50.55±19.74	70.45±8.24	-19.90*	0.000
NCC	3.80±1.99	6.15±1.22	-2.35*	0.000
TCFC	25.55±24.88	15.20±7.73	10.35	0.212
FMS	5.55±18.04	0.50±0.69	5.05	0.286
LTL	-9.93±16.63	-0.57±16.13	-9.36	0.407

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 16 WCST domains were compared by statistical methods- ANOVA and Post hoc Tukey. In nearly all the domains, FDRs had higher mean value than normal control. The mean value was higher in bipolar disorder FDRs in number of trials administered, total number of errors, percentage of error, perseverative responses, percentage of perseverative responses, perseverative error, percentage of perseverative error, non-perseverative error, percentage of non-perseverative error, trial to complete first category, failure to maintain sets and learning to learn score. Normal controls were having higher mean value in total number of correct responses, conceptual level responses, percentage of conceptual responses and number of categories completed. In post hoc tukey analysis, mean difference was significant in number of trials administered, total number of errors, percentage of error, perseverative responses, percentage of perseverative responses, perseverative error, percentage of perseverative error, non-perseverative error, percentage of non-perseverative error, conceptual level responses, percentage of conceptual responses and number of categories completed.

DISCUSSION

In the said study, both the groups were comparable in age and sex as they were matched prior to the study. Prior many studies have demonstrated the efficacy of WCST in measuring executive functions and have been used in many studies in India too [8]. The diversity of assessment indicators in WCST is one of its advantages compared to other instruments. It has been shown that tasks like WCST activate a neural network that includes important areas of brain such as dorsolateral region of prefrontal cortex [9]. Poor WCST performance is thought to reflect prefrontal cortical dysfunction [10].

The findings in the present study indicate presence of executive dysfunction in the unaffected first degree relatives of BPAD. Executive deficits were present in many of the domains of WCST but not

generalized in nature. The domains in which executive deficits were present could serve as trait or vulnerability marker. FDRs performed poorly on number of trials administered, total number of errors, percentage of error, perseverative responses, percentage of perseverative responses, perseverative error, percentage of perseverative error, non-perseverative error, percentage of non-perseverative error, conceptual level responses, percentage of conceptual responses, number of categories completed. Thus impairment in executive function may lie in continuum from normal population to high risk of BPAD to overt bipolarity.

Set Shifting indicates cognitive flexibility and is assessed by percent perseverative error, number of categories completed and total number of trials administered. Through set shifting, a person modulates his cognitive processes to meet the demands of changes in the environment. In this study, FDRs of BPAD are found to have significantly higher perseverative errors and total number of trial administered compared to normal controls indicating deficits in cognitive flexibility in these groups. Non- perseverative errors on the WCST are indicators of deficits in generalized reasoning [11]. In present study, all the said domains are significantly high in FDRs.

FDRs made more number of errors which implies that they had more difficulty in understanding the concept of the test. More number of non-perseverative errors and perseverative errors implies that either they were not interpreting the feedback properly or they were matching the cards without any concept in mind and also that they had difficulty in shifting between categories, although they were receiving the feedback to do so.

The FDR 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.

In two of the prior meta-analysis which included cognitive functions assessment by different methods; effect size was small but significant across cognitive domains in FDRs of BPAD [12].

A recent review of different types of FDRs of mania (which is included in BPAD in DSM-V) also indicated that executive function is predictor of bipolarity [13]. Our study is in line of the findings and indicates that executive function and can be used as an endophenotype in bipolar disorders.

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