EXECUTIVE FUNCTIONS IN PATIENTS WITH SINGLE AND MULTIPLE EPISODES OF MANIA ON CTMT

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ABSTRACT:

Background: Neuropsychological studies on Bipolar Disorders (BD) documented dysfunction in executive functioning and it has been reported that some dysfunction persists even after manic symptoms disappear. There is sufficient literature suggesting executive dysfunction in multiple episodes manic patients but there is lack of studies related to single episode manic patients. The present study was conceptualized to assess the neuropsychological deficits in the cases with Bipolar Affective Disorder (mania with the history of single and multiple episodes). Methods: Sample of the study consists of 60 subjects; thirty inpatients were with the history of multiple episodes of manic illness and 30 inpatients with single episode of manic illness. Each group received Comprehensive Trail Making Test (CTMT) and Executive Functioning Scale of Cognitive Symptoms Checklist, and the performances of both groups were compared on trail making Test and Executive functioning Scale. Results: At baseline, multiple episodes manic patients shown greater deficits relative to single episode manic patients on executive functioning measures. Deficits were in terms of psychomotor speed, visual search and sequencing, attention and impairment in set shifting. Though, the executive functioning deficits were found in single episode manic patients too in some extent. Conclusion: The results of the present study demonstrate that executive dysfunction remained in bipolar disorder cases even in remitted state but the degree of impairment differ in multiple episodes manic group and single episode manic group. The cognitive deficits are having detrimental effect on day to day functioning, such as daily routine work, taking care of personal hygiene and making decision in day to day life.

Key words: ***Bipolar Disorder; Multiple episodes manic; Single episode manic; Executive functions.***

The term *Executive functioning*, has encompassed number of meanings. Definitions have included those controls and regulatory processes that (i) Integrate information perceived in the external world and transform perception into higher order symbols, (ii) Compare incoming information with what knowledge stored in memory and (iii) Combine the incoming perceptions with information about the person's internal physiological state and biological drives. According to this terminology, executive functioning is arguably the most complex aspect of one's cognitive capacities, due to variety of functions required to select, plan, organize and implement a behavioural response appropriate to a constantly changing world. Bipolar disorder (BD) is a recurrent, cyclical disorder that is characterized by alternating episodes of depression and mania, interspersed with periods of apparent recovery, or eutymia (Goodwin, F. K., Jantison K. R., 1990). However, there is accumulating evidence that recovery in BD is incomplete (Ferrier, I. N, Thompson J. M., 2002). Patients with Bipolar disorder show persistent cognitive impairment during remission (Bearden C. E. et al, 2001; Clark L., Iversen S. D., Goodwin G. M., 2002; Thompson J. M., Gallagher P, 2005). Deficits have been observed on several tests of executive or frontal lobe function (Zubieta J. K. et al, 2001; Thompson J. M., Gray J. M., et al., 2003)

The CTMT is developed by Reynolds in 2002 (Reynolds C. R, 2002). The CTMT assess problems with psychomotor speed, visual search and sequencing, and attention and impairment in set shifting, also appear appropriate.

Some important studies have compared the performance of controls to remitted Bipolar Disorder patients on Trail Making Test (TMT).The results are consistent with that Bipolar Disorder patients' performance was worse in all studies; this difference did not always reach statistical significance (Jones B.P.et al, 1994; Tham A., Engelbrektson K et al, 1995; Hawkins K.A et al, 1997). Illness severity may be an important contributor to impaired TMT performance. Several studies have compared the

TMT performance of Bipolar Disorder patients to that of Unipolar disorder patients and schizophrenics. Remitted Bipolar Disorder patients performed worse than Unipolar Disorder (Paradiso S., 1997; Ferrier I.N. et al, 1999; Mojtabai R. et al , 2000). In some studies the performance of unipolar disorder was better than bipolar disorder cases (Jones, B.P., D et al, 1994). While two other studies found no differences between the two patient groups (Goldberg T.E.et al, 1993; Mojtabai R.et al, 2000). Chronic Bipolar Disorder and schizophrenic patients were compared twice, once when both groups were in acute relapse and then again after 4 weeks of treatment. BD patients performed better than schizophrenics during the acute phase. Despite significant symptomatic improvement, the performance of BD patients on the TMT was similar in the acute and recovery phases. So their advantage over schizophrenics disappeared after 4 weeks of treatment (McGrath J., Scheidt, S., Welham J. and Clair, A., 1997).

Material and Method

Sample:

The sample consists of 60 patients with Bipolar Affective Disorder (30 manic patients with the history of single episode and 30 manic patients with the history of multiple episodes) in the age range of 20-40 years. All participants were male and right handed. All the subjects were educated up to matric level. All were married, Hindus by religion and employed and most of them belongs to rural areas of Jharkhand and Bihar. Subjects with any other co-morbid neurological / psychological disorder or with major physical illness were excluded. All subjects participating in the study were co-operative. Informed consent was taken for the study.

The following tools were used in the present study:

Socio-demographic and Clinical Data Sheet: It is semi structured Proforma developed for the purpose of present study. It contains information about socio-demographic variables like age, sex, religion, education, marital status, domicile and occupation and clinical details like diagnosis, age of onset, total duration of illness, history of alcohol or substance abuse, family history of mental illness, any history of significant head injury, seizures, mental retardation and any other significant physical, organic or psychiatric illness.

Young Mania Rating Scale (YMRS): This scale has been developed and standardized by Young et al, 1978). It has been used for the assessment of severity of the manic symptoms in the patients. This scale included 11 symptoms constructs. Each item is rated on 5 point rating scale (0-4). Score '0' indicates "absence of symptoms" and '4' indicates "extremely severe symptoms".

Hand Preference Battery: This is a six item scale by Annett (1970) in which subjects is asked to show some everyday activities. Depending on the hand he uses for all six items he is assigned to that particular preference. Subjects were asked to "show me how you": Write letter legibly, Throw a ball to hit a target, Hold a tennis racket, Hammer a nail into wood, Hold a match while strike, Hold a toothbrush while cleaning your teeth.

Comprehensive Trail Making Test (CTMT): The CTMT is developed by Reynolds. The CTMT comprises a standardized set of five visual search and sequencing tasks that are heavily influenced by attention, concentration, resistance to distraction and cognitive flexibility (or set shifting), in addition to more obvious visual search and sequencing demands of the task. The basic task of trail making, and thus of CTMT, is to connect a series of stimuli (numbers, expressed as numerals or in word form, and letters) in a specified order as rapidly as possible.

Executive Functioning Scale of Cognitive Symptoms Checklist:

The original Cognitive Symptoms Checklist was developed by O'Hara et al (1993) which was translated into Hindi to facilitate local Indian population for the identification and treatment of problems in five basic cognitive areas: attention and concentration, memory, visual processes, language and executive functions. Executive functioning was divided into following sub divisions-processing speed/ reaction time, initiation/follow- through, self correction, mental flexibility, planning, organization and reasoning It can be either self-administered or administered by clinicians, with further inquiry or interpretation performed by appropriately trained clinicians.

Procedure:

Patients were selected as per ICD-10 DCR criteria. All the subjects who were included in the present study were assessed with the help of semi structured clinical data sheet. Detail about history of co-morbidity, substance abuse, family history of mental illness, history of any neurological problem, mental retardation, etc. were noted. Each subject was assessed through clinical history. After applying Young Mania Rating Scale clinical population was selected. Each subject was assessed with Hand Preference Battery and only right handed patient were included in the sample. After initial screening of the patients, Comprehensive Trail Making Test was administered and subsequently Executive Functioning Scale of Cognitive Symptoms Checklist was also administered on all patients.

Results and Discussion:

Table 1: Showing Socio-Demographic Profile of Sample

Variables	Educational Level	Single Episode Mania M ± SD/N	Multiple Episode Mania M ± SD/N	X^2
Age		29.07 ± 5.93	30.16 ± 5.48	741
Education	Up to Matric	24 (80.0%)	16 (53.3%)	7.20
	Up to Intermediate	6 (20.0%)	9 (30.0%)	
	Up to Graduation	-	2 (6.7%)	
	Up to PG	-	3 (10.0%)	
Religion	Hindu	25 (83.3%)	21 (70.0%)	2.35
	Muslim	2 (6.7%)	6 (20.0%)	
	Christian	-	-	
	Sama	3 (10.0%)	3 (10.0%)	
Marital Status	Single	18 (60.0%)	11 (36.7%)	3.27
	Married	12 (40.0%)	19 (63.7%)	
Domicile	Rural	16 (53.3%)	16 (53.3%)	7.64
	Urban	14 (46.7%)	8 (26.7%)	
	Semi-urban	-	6 (20.0%)	
Occupation	Employed	11 (36.7%)	11 (36.7%)	7.33
	Unemployed	2 (6.7%)	7 (23.3%)	
	Student	7 (23.3%)	1 (3.3%)	
	Others	10 (33.3%)	11 (36.7%)	
Family type	Nuclear	20(66.7%)	24 (80.0%)	1.36
	Joint	10 (33.3%)	6 (20.0%)	

The data have been analyzed and presented in table 2 and table 3.Table 2 shows the performance of the (Single Episode Manic) SEM and (Multiple Episode Manic) MEM groups on the Comprehensive Trail Making Test. The groups differed significantly in their performance, in term of time taken on all five trails of the Test. Considering performances in terms of errors made, the groups differed significantly in Trail 1, Trail 2, Trail 3, Trail 5 and not significantly in Trail 4 of the test in terms of error. The analysis further reveals that the MEM group took greater time than SEM groups and also committed more number of errors on all five trails of the test.

Table 2: Showing the performances of both groups on Comprehensive Trail-Making Test.

Variables	Groups	Mean Rank	Sum of Ranks	Z- Score
TRAIL 1 (Time)	SEM	22.67	680.00	3.48**
	MEM	38.33	1150.00	
TRAIL 1 (Error)	SEM	26.23	787.00	2.45*
	MEM	34.77	1043.00	
TRAIL 2 (Time)	SEM	23.70	711.00	3.02**
	MEM	37.30	1119.00	
TRAIL 2 (Error)	SEM	25.00	750.00	2.67**
	MEM	36.00	1080.00	
TRAIL 3 (Time)	SEM	23.22	696.50	3.23**
	MEM	37.87	1133.50	
TRAIL 3 (Error)	SEM	27.40	822.00	1.97*
	MEM	33.60	1008.00	
TRAIL 4 (Time)	SEM	25.33	760.00	2.29*
	MEM	35.67	1070.00	
TRAIL 4 (Error)	SEM	27.32	819.50	1.72
	MEM	33.68	1010.50	
TRAIL 5 (Time)	SEM	21.27	638.00	4.10**
	MEM	39.43	1182.00	
TRAIL 5 (Error)	SEM	22.03	661.00	3.99**
	MEM	38.73	1169.00	

**p< 0.01 level of confidence
*p < 0.05 level of confidence

In the area of time taken in Trail1, Trail 2, Trail3 and Trail 5 both the group differs significantly at 0.01 level whereas on Trail4, Trail 2 the difference was found at 0.05 level. Similarly, in the area of error on Trail 2 and Trail 5 the difference was found significant at 0.01 level and Trail 1 and Trail 3 both the groups differ significantly at 0.05 level, where as in the area of error on Trail 4 the difference was apparently existing as mean value (33.68) for multiple episode manic group is higher in comparison to mean value (27.32) of single episode manic group but the difference is not significant. Findings of the study further suggest that poor performance in Comprehensive Trail Making Test is indicator of impairment in maintaining; shifting mental set is significantly higher in multiple episodes manic group than single episode manic group. Though,

the performance of any neuropsychological test implies sum degree of attention engagement but the Trails making test have large attentional component although we cannot eliminate the possibility that some medication effect might have caused greater impairment and probably that would have only hindered more the cognitive performance of multiple episodes manic group as they are on pharmacotherapy since longer time.

In most of the previous studies sample the subjects included who were much older and who had long term exposure to psychotropic medication. Present study has tried to find out the difference in Neurocognitive functions during the medication between their repeated episodes and the short term exposure to medication having only the first episode. The cognitive deficits in multiple episodes group could be the endophenotype of mood disorder (Nehra R., Chakrabarti, S, Pradhan, B.K. Khera, N, 2006). It has been shown that neuropsychological deficit in Bipolar Disorders correlate with both the number of affective episode and overall duration of illness. The result of present study evidenced for the indication of greater impairment with larger time spent in affective episodes. It is possible that the progression of illness and greater correlation between neuropsychological deficits and severity of illness are often considered to be indicator of progressive disease process.

Illness severity could be an important contribution to impaired TMT (Trail Making Test) performance, has been reported by some previous studies. Poor performance on CTMT by multiple episodes manic group can be attributed to psychomotor slowness and deficits in visual scanning as the comparison of single episode manic group. This could be due to impairment in the ability to focus, sustained attention, and execution of the task (Mirsky A. F. et al, 1995). The difference was most evident for the "time-taken" criteria in all Five Trails, wherein multiple episode patients performed poorly than single episode patients. The multiple episode patients did not differ from single episode patients in terms of errors made, on Trail 4. Patients with multiple episodes were more impaired on TMT when compared the groups only on "Time Taken" and "Errors Made" were not considered.

Table 3 shows the problems that reported by SEM and MEM groups on the Cognitive Symptoms Checklist: Executive Functioning Area. The groups differed significantly in Processing Speed/Reaction Time, Initiation/ Follow-Through, Self Correction, Mental flexibility, Planning and Problem Solving. The groups did not differ significantly in Sequencing, Organization and Reasoning. The analysis reveals that the MEM group experiencing problem more than SEM group.

Table 3: Showing the Executive Functions Score on Cognitive Symptom Checklist on Both Groups.

Variables	Groups Rank	Mean Ranks	Sum of	Z- Score
Processing speed / Reaction Time	SEM	20.92	627.50	4.48**
	MEM	40.08	1202.50	
Initiation/Follow-Through	SEM	25.03	751.00	2.78**
	MEM	35.97	1079.00	
Self-Correction	SEM	24.35	730.50	3.04**
	MEM	36.65	1099.50	
Mental Flexibility	SEM	27.80	834.00	1.37*
	MEM	33.20	996.00	
Planning	SEM	24.27	728.00	3.04**
	MEM	36.73	1102.00	
Sequencing	SEM	29.70	891.00	0.497
	MEM	31.30	939.00	
Problem Solving	SEM	23.42	702.50	3.36**
	MEM	37.58	1127.50	
Organization	SEM	27.33	820.00	1.79
	MEM	33.67	1010.00	
Reasoning	SEM	26.72	801.50	1.78

** $p < 0.01$ level of confidence
* $p < 0.05$ level of confidence

In the sub area of executive functioning, processing of speed/reaction time, initiation/follow through, self correction, planning and in problem solving sub area both the group differ significantly on at 0.01 level, whereas on mental flexibility sub area the difference was found significant at 0.05 level. The difference on mean value of sequencing, organization and reasoning sub area was apparently existing as mean value (31.30), (33.67) and (34.28) for multiple episodes group was higher in comparison to mean value (29.70), (27.33) and (26.72) of single episode group respectively. Though it was not significant but the findings suggest that multiple episode patients report more impairment than single episode patients. This indicates that multiple episode patients have more problems in Executive Functioning Area. Particular significance has been attached to these deficits because they have been linked to the intensity of the disease process and are persistent despite the psychiatric symptoms

reduction and have been linked to psychosocial and competitive employment[1]. The result of the present study clearly indicates that multiple episode group has executive deficits in the form of slower information processing than the single episode group.

Cognitive impairment in bipolar illness may be a stable characteristic of the illness, although discrepancies have emerged with regard to what dysfunctions remain during remission periods (Martinez-Aran. A et al, 2004). Although the traditional view of bipolar affective disorder is that the majority of patients have full remission between episodes. Recent evidence suggests that residual cognitive deficits are still present (Kessing L V, 1998; Cavanagh J.T.et al, 2002; Tham A., 1995). The nature of the cognitive deficits in bipolar illness in general is shown by impaired performance in tests of executive function, attention and memory (Bearden C. E.et.al, 2006; Quraishi, S. Frangou, S, 2002; Martinez-Aran 2000). Findings are consistent with the findings of the Mishra et. al, 2009). However, the groups differ significantly in Sequencing, Organization and Reasoning. Neuropsychological deficits are possibly trait-related. The deficits in the long run can cause considerable impairment in psychosocial and occupational functioning (Martinez-Aran et al, 2004b & a, Thompson J. M.et al, 2005. Cognitive deficits have detrimental effect on day to day functioning related to cognitive areas which have been found significantly more in multiple episode patients as compared to single episode patients in present study.

Conclusion:

The findings of the study suggest that subject suffering with mania having multiple episodes shown more impairment than single episode manic group in the area of executive functioning. It has been found that neuropsychological deficit in bipolar disorders positively correlated with both the number of affective episodes and overall duration of illness. In present study manic patients group with multiple episodes have been found poor in Attention, Concentration, Abstract Reasoning, Set Shifting, Mental Flexibility, Abstract Thinking, Processing Speed/ Reaction Time, Initiation/Follow-Through, Self Correction, Mental Flexibility, Planning And Problem Solving task. This cognitive impairment in bipolar illness may be stable characteristics of the illness and in the long run can cause considerable impairment in psychosocial and occupational functioning. The cognitive deficits of this nature have detrimental effect on day to day functioning such as daily routine work, taking care of personal hygiene and making decision in day to day life, delivering / bearing occupational and professional responsibilities.

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