

## **A Study of Pattern of Cognitive Inflexibility and it's Relationship with Suicidal Behaviour in Patients with Major Depressive Disorder (MDD)**

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### **Abstract**

**Background:** Impairment in cognitive inhibition and flexibility is responsible for negative cognitive bias in depression. There is inconsistency in research findings regarding cognitive deficits underlying suicidal behaviour and its relationship with severity of depression and scarce Indian studies.

**Aim:** This study aimed to study pattern of cognitive inhibition and mental flexibility in major Depressive Disorder (MDD) subjects along with association between suicidal ideation and cognitive deficits.

**Method:** This was a cross-sectional observational study conducted in the outpatient department of a tertiary care centre. Eighty men with major depressive disorder diagnosed as per DSM5 were recruited and assessed using the Montgomery and Asberg Depression Rating Scale (MADRS) for severity of depression, WCST (Wisconsin card sorting test) and Trail making test A and B (TMT A, TMT B) were applied to assess the cognitive function of subjects. Beck's

scale for suicidal ideation (BSSI) was used for assessment of suicidal ideation. Other variables were assessed using a semi-structured pro forma. Comparative analysis was done using student t-test/Mann-Whitney U Test and Chi square test and one-way ANOVA. Correlation was done using Pearson's correlation test.

**Result:** The WCST performance in ideator group was poorer than non ideators in Total Trials, Total Errors and Categories Completed. The Total trials taken during card sorting in WCST significantly correlated with severity of depression. There was significant positive correlation between total trials and BSSI and negative correlation with categories completed.

**Conclusion:** The cognitive rigidity is a core characteristic of suicidality in MDD. The EF is considered to be mostly widely used and validated tool. The current study studies the different domains of executive function and comparatively analyses ideators, attempters and non-ideators.

**Keyword:** Cognitive Inflexibility, Executive Function(EF), Major depressive disorder, Suicide

## Introduction

Suicidal ideation is a common, core symptom of major depressive disorder (MDD). India accounts for 18% of the global population and 26.6% of global suicide deaths. For every death by suicide in India, there were more than 200 people with suicidality and more than 15 suicide attempts. [1] Depressed patients with suicidal thoughts tend to see their coping options in terms of all or none of a miserable life and perceived lack of alternate solutions to their distress which may then lead individuals to feelings of hopelessness and an eventual focus on suicide as a solution. [2]. The prediction and prevention of Suicide remains a major challenge for the clinician to recognise and treat as suicide is a major cause of mortality in major depressive disorder. Beck's cognitive triad, a part of cognitive theory of depression involves automatic, spontaneous and seemingly uncontrollable negative thoughts about the self, the environment and the future. Cognitive inflexibility is defined as the inability to change decision-making behaviour in response to external feedback and changing environmental circumstances [3]. It can cause incorrect appraisal of one's life situation and inability to find effective solutions to problems leading to stressful situations and hopelessness. Indeed, impaired neurocognitive functioning has been found in patients with a history of suicide attempts [4-7] and in those with current suicidal ideation [8,9]. Individuals with depression have been found to selectively attend more to negative information than to positive information. Various theories have been developed which propose that negative bias plays the central role in the onset and maintenance of depression [10]. Patients with MDD show cognitive deficits in various neuropsychological domains, such as visual and verbal memory, working memory, attention, executive function, and processing speed, [11] with impairments in executive function (EF) [12,13] being the most prominent. However, the existence and nature of impairment in EF associated with MDD remain strongly debated, with some arguing that patients with MDD have no appreciable impairments in cognition [14] and others claiming that they have pronounced neuropsychological impairments.[15] EFs refer to cognitive competencies that allow individuals to determine objectives in changing environments and to find ways of meeting them by constantly adapting themselves to their circumstances [16]

Only recently studies have started to examine the processes responsible for negative cognitive bias in depression because of which the mechanisms related to these biases is not well understood. The proposed mechanism is hypothesized to be a deficit in cognitive inhibition and flexibility in persons with depression. The pattern of cognitive inhibition and flexibility and its relationship with the severity of depression in relation to suicidal risk has not been

studied extensively. Improved understanding of the neurocognitive impairments that may exist during suicidal behaviour will be critical to the development of effective neurocognitive treatments that are specifically designed to reduce suicidal behaviour.

As there are still inconsistency in researches published worldwide regarding Neurocognitive deficits in suicide, and there are scarce Indian studies related to this aspect, the present study aimed to explore the relationship between suicidal ideation and cognitive deficits in MDD patients and compare the level of cognitive deficits in MDD patients with suicidal ideation and without suicidal ideation in order to better predict and prevent the Suicide in a person with major depressive disorder.

### **Materials and Methods:**

It was a cross-sectional, observational study design. Institute ethic committee approval was taken before inclusion of the subjects in the study. 80 cases with current major depressive episode diagnosed as per DSM-5 between 18 years and 60 years with at least 7 years of formal schooling were recruited from the psychiatry department of a tertiary health care centre in eastern India. Subjects were recruited through Convenient sampling method. Verbal and written informed consent were taken from all participants and confidentiality of patients was ensured at all stages of the data collection.

Patients with any comorbid Axis I disorder, organic brain disorder or neurological disorder, intellectual disability, substance abuse or dependence other than nicotine, having any auditory or visual impairment and history of treatment with electro-convulsive therapy in past 6 months were excluded from the study.

Semi structured proforma was used to collect the data for socio-demographic, clinical details variables. Montgomery and Asberg Depression Rating Scale (MADRS) was used to assess severity of depression. WCST(Wisconsin card sorting test) and Trail making test A and B (TMT A, TMT B) were applied to assess the cognitive function of study subjects. Beck's scale for suicidal ideation (BSSI) was used for assessment of suicidal ideation in the study subjects. The patient's socio-demographic details along with clinical variables such as duration of episode, total duration of illness, age of onset, their relevant history of psychiatric illness, and family history was recorded with semi-structured proforma.

The patients were divided into two groups on the basis of presence or absence of current suicidal ideation and relevant sociodemographic and clinical variables as well as neuropsychological profile(WCST and TMT) was compared. A comparison was also made between ideators and attempters.

### **Results:**

The mean age of patients was ( $35.6 \pm 13$ ) years. Most of the participants of our study were married males, belonged to the Hindu religion, nuclear family, and urban background and belonged to Hindu nuclear family of low SES. The majority of the patients had studied upto 10th standard and were employed (37%). With an age of onset of  $32.3 \pm 12.8$

**Table 1: Socio demographic and clinical profile of Suicidal ideator vs Non-ideator in MDD subjects**

Characteristics	Non-ideator (n=39)	Ideator (n=41)	$\chi^2$ /t	df	P value
Age in years (Mean $\pm$ SD)	34.1 $\pm$ 12.5	37.0 $\pm$ 13.5	1.004	78	0.310
Age of onset(Mean $\pm$ SD)	31.4 $\pm$ 12.1	33.8 $\pm$ 13.6	.810	78	0.420
Gender			$\chi^2$ -	1	
Male	31 (79.4)	27 (65.8)	.1863		0.172
Female	8 (20.5)	14 (34.2)			
Education			$\chi^2$ -	2	
Primary	04 (10.2)	06 (14.6)	1.799		0.407
Secondary	13 (33.3)	18 (47.4)			
Higher	22 (56.4)	17 (39.4)			
Marital status			$\chi^2$ -	2	
Single	14 (35.9)	11(26.8)	1.619		0.655
Married	24 (61.5)	28 (68.3)			
Widow/divorced/ separated	1(2.5)	02 (4.8)			
Family type			$\chi^2$ -	1	
Nuclear	19 (48.7)	23 (56.0)	0.436		0.509
Joint	20 (51.2)	18(43.9)			
SES			$\chi^2$ -	3	
Low	08 (20.5)	10 (24.3)	2.522		0.471
Low-middle	11 (28.2)	17 (41.4)			
Middle	17 (43.5)	12 (29.2)			
Upper	03 (7.7)	02 (4.8)			
Religion			$\chi^2$ -.400	1	
Hindu	37 (94.9)	40 (97.5)			0.527
Muslim	02 (05.1)	01 (02.4)			
Occupation			$\chi^2$ -	3	
Unemployed	01 (2.5)	04 (9.7)	6.834		0.077
Housewife	05 (12.8)	13 (31.7)			
Student	11 (28.2)	09 (21.9)			
Employed	22 (56.4)	15 (36.6)			
Duration of episode			$\chi^2$ -	2	
>2 weeks $\leq$ 2 month	12(22.7)	06 (15.8)	2.985		0.225
>2months $\leq$ 6months	13 (45.5)	17 (39.5)			
>6months	14(31.8)	18 (44.7)			
Mean duration of episode in weeks	18.9 $\pm$ 14	21.7 $\pm$ 11.1	1.005	78	0.318
Duration of illness			$\chi^2$ -	2	
<5 years	28 (81.8)	33 (86.8)	3.686		0.158
5-10 years	10 (13.6)	05 (05.3)			
>10 years	01 (04.5)	04 (07.9)			
Mean duration of illness in years	3.0 $\pm$ 2.9	3.2 $\pm$ 4.3	0.234	78	0.815
Number of episode (Mean $\pm$ SD)	1.4 $\pm$ 0.8	1.5 $\pm$ 0.9	0.555	78	0.580

Suicide attempts in past			$\chi^2$ -	1	
No	37(90.9)	34 (84.2)	2.856		0.091
Yes	02 (09.1)	07(15.8)			
Current suicide attempt			$\chi^2$ -	1	
No	38(95.5)	23 (55.3)	18.861		0.000
Yes	01 (04.5)	18 (44.7)			
Family history			$\chi^2$ -	1	
Yes	10(25.6)	13(31.7)	0.359		0.549
no	29(74.3)	28(68.2)			

A comparison of sociodemographic and clinical variables between depressed patients with and without suicidal ideation is in Table 1, which revealed no significant statistical difference between the two groups.

**Table 2: Cognitive profile of Ideator vs non Ideator**

characteristics	Non ideator (N=39)	Ideator (N=41)	Mann-Whitney U-test	Z	P
MADRAS (Mean $\pm$ SD)	28.0 $\pm$ 8.3	33.0 $\pm$ 7.5	529.5	2.605	0.009
TMT A (Mean $\pm$ SD)	62.7 $\pm$ 39.2	62.8 $\pm$ 32.8	738.5	0.587	0.557
TMT B (Mean $\pm$ SD)	153.0 $\pm$ 113.3	158.6 $\pm$ 71.2	646.5	1.474	0.141
WCST-TT (Mean $\pm$ SD)	121.0 $\pm$ 14.3	128 $\pm$ 0.0	594.5	3.434	0.001
WCST-TC (Mean $\pm$ SD)	54.1 $\pm$ 23.6	62.9 $\pm$ 15.7	725.0	0.718	0.473
WCST-TE (Mean $\pm$ SD)	54.1 $\pm$ 23.6	65.0 $\pm$ 15.6	563.5	2.273	0.023
WCST-PR (Mean $\pm$ SD)	43.8 $\pm$ 27.4	43.2 $\pm$ 15.0	718.5	0.780	0.435
WCST-PE (Mean $\pm$ SD)	36.0 $\pm$ 21.6	40.5 $\pm$ 14.0	645.0	1.489	0.137
WCST-CC (Mean $\pm$ SD)	3.4 $\pm$ 2.0	2.4 $\pm$ 1.3	597.5	1.981	0.048

**SD: Standard deviation, TT: Total Trials, TC: Total Completed, TE: Total Errors, PR: Perseverative responses, PE: Perseverative errors, CC: Categories completed**

The neuropsychological profile between the two groups has been compared in Table 2. The WCST performance in Ideator group was poorer than non ideators in Total trials (TT, 128 vs 121, p=0.001), Total errors (TE, 65.0 vs 54.1, p=0.023) and Categories completed (CC, 3.4 vs 2.4, p=0.048) and it was statistically significant. The depression severity score (MADRS) was also significantly higher in depressed patients with suicidal ideation compared to those without suicidal ideation. (33.0 vs 28.0, p value=0.009).

**Table 3 : Comparison of Neurocognitive functioning scores between active and passive suicidal ideation**

characteristics	Passive (n=17)	Active (n=24)	P value
MADRS	31.4 $\pm$ 6.5	34.1 $\pm$ 8.1	0.434
TMT A	58.9 $\pm$ 36.6	65.6 $\pm$ 30.4	0.289
TMT B	158.2 $\pm$ 80.4	159 $\pm$ 65.7	0.691
BSSI	6.7 $\pm$ 6.2	13.5 $\pm$ 6.0	0.000
WCST-TE (Mean $\pm$ SD)	63.5 $\pm$ 14.4	66.1 $\pm$ 16.7	0.508
WCST-TC(Mean $\pm$ SD)	64.5 $\pm$ 14.5	61.8 $\pm$ 16.9	0.516
WCST-PR (Mean $\pm$ SD)	41.3 $\pm$ 12.7	44.3 $\pm$ 16.5	0.781
WCST-PE (Mean $\pm$ SD)	41.5 $\pm$ 12.3	44.5 $\pm$ 16.8	0.979
WCST-CC(Mean $\pm$ SD)	2.5 $\pm$ 1.1	2.3 $\pm$ 1.2	0.529

A comparison between depressed patients with active vs passive suicidal ideation showed that both groups (patients with passive or active SI) were comparable in terms of cognitive measurement scores (WCST and TMT scores). The active SI group was associated with a higher BSSI score(13.5 vs 6.7, p value-0.000)compared to the passive SI group.

**Table 4: Comparison of Neurocognitive profile between Attempters and ideators**

characteristics	Attemptor (n=21)	Ideator (n=20)	Mann-Whitney U-test	Z	P
MADRAS (Mean $\pm$ SD)	33.5 $\pm$ 7.6	32.5 $\pm$ 7.6	186.5	0.615	0.539
BSSI (Mean $\pm$ SD)	11.5 $\pm$ 7	9.8 $\pm$ 7	177.5	0.850	0.395
TMT A (Mean $\pm$ SD)	63.8 $\pm$ 38.0	61.8 $\pm$ 28	203	0.183	0.855
TMT B (Mean $\pm$ SD)	150.7 $\pm$ 76.9	166.1 $\pm$ 66.4	168	1.096	0.273
WCST-TT (Mean $\pm$ SD)	128.0 $\pm$ 0.0	128 $\pm$ 0.0	210.0	0.000	1.000
WCST-TC (Mean $\pm$ SD)	65.7 $\pm$ 16.7	60.2 $\pm$ 14.7	171	1.019	0.308
WCST-TE (Mean $\pm$ SD)	62.2 $\pm$ 16.7	67.6 $\pm$ 14.5	172	0.993	0.321
WCST-PR (Mean $\pm$ SD)	43.2 $\pm$ 17.0	43.3 $\pm$ 13.2	200	0.261	0.794
WCST-PE (Mean $\pm$ SD)	40.5 $\pm$ 15.5	40.4 $\pm$ 13.6	203.5	0.170	0.865
WCST-CC (Mean $\pm$ SD)	2.5 $\pm$ 1.3	2.2 $\pm$ 1.	177.0	0.889	0.374

A comparison between depressed patients with suicidal attempts and suicidal ideation showed that both groups were comparable in terms of cognitive measurement scores (WCST and TMT scores). There were no statistically significant difference between the two groups

**Table 5: Correlation of depression severity scores and Suicidal Ideation score with TMT scores, WCST scores**

Variable	Correlation type	TMT A	TMT B	TT	TC	TE	PR	PE	CC
MADRS	Pearson correlation	.057	.169	.278	-.101	.294	.163	.218	-.355
	Significance two tailed	.615	.134	.013	.371	.008	.148	.152	.001
BSSI	Pearson correlation	-.022	.012	.245	-0.030	.189	.005	.084	-.286
	Significance two tailed	.988	.919	.029	.792	.092	.968	.461	.010

Correlation analysis between severity score of depression(MADRS) andTMT A and TMT B and various WCST parameters showed that total trials (TT) taken during card sorting in WCST significantly correlated with severity of depression. (r-0.278,p-0.013) Total errors(TE) during card sorting significantly correlated with depression severity(r-.294, p-0.008) whereas there was significant negative correlation between depression severity and categories completed (CC) during WCST(r-0.355,p-0.001). Correlation analysis was also done between scores of suicidal ideation (BSSI) and TMT A, TMT B as well as WCST scores. There was significant positive correlation between total trials and BSSI(r-.245,p-0.029) and negative correlation with categories completed(CC)(r—.286,p-0.010).

#### **Discussion:**

The current study found significant difference in the domains of executive function deficit between depressed patients with and without suicidal ideation.( TT score, TE score, CC score). The present findings concur with those of previous studies suggesting that executive function deficit is associated with suicidal ideation in patients with MDD (17,8,9). Study by Marzuk et al.comparing 25 depressed patients with current suicidal ideation and 28 depressed patients without suicidal ideation found that the patients with current suicidal ideation performed more poorly on tests of executive functioning, including those measuring cognitive flexibility, compared to the patients without suicidal ideation (8) In the study by westheide et al patients with current suicidal ideation demonstrated more severe executive deficits, i.e., an impaired decision-making compared with the suicide attempters without current suicidal ideation and healthy controls.

Total error (TE) score in WCST is a measure of reasoning, problem solving, self monitoring and switching .Total error score in the present study was higher in depressed individuals with suicidal ideation than in those who did not have suicidal ideation.The findings are consistent with the studies that suggest social problem solving deficits interact with depression to increase risk for suicidal behaviour (21). Negative emotions have been shown to exacerbate problem-solving deficits, including avoidant style (22,23).

CC in WCST is a measure of the participants' ability to solve problems through the use of feedback each time he or she is presented with cognitive challenge.Depressed patients with suicidal ideation in the study had higher scores of mean categories completed in WCST than those without suicidal ideation indicating lesser cognitive flexibilities . Studies on executive functioning in suicidality have found that the deficits in inhibition which have been linked with

impaired impulse control may be associated with suicide attempts (24), whereas shifting deficits which have been linked with ruminative thinking may be associated with ideation (25).

Our study did not find any significant difference in the executive function domain of suicide ideators and attempters. The support to our finding comes from similar studies which have yielded no significant relationships between neuropsychological performance and measures of suicidality in patients with depression and psychotic disorders, some also hypothesise that suicidality is a separate domain that is distinct from psychiatric symptomatology and neurocognitive performance (26,27). This finding is in contrast with the study comparing ideators with attempters with different psychiatric diagnoses where disinhibition (stroop interference total T score) was found to be significantly associated with the suicide Attempter group. Better problem-solving ability was also associated with the suicide Attempter group. (28) Mann and colleagues asserted that prominent impulsivity and aggression are characteristics of people at risk for suicide, independent of psychiatric diagnosis (29) Nangle and colleagues claimed that better executive functioning (e.g., better problem solving) is associated with better planning and initiation of behaviour, which may lead to increased risk of attempting suicide. (30). Interestingly a study by [Miranda et al. \(2012\)](#) found that cognitive inflexibility prospectively predicted suicidal ideation at 6-month follow up among a non-clinical sample of suicide attempters.

The executive function was also compared between depressed patients with passive or active SI. The present study did not find any difference in the WCST and TMT scores between two groups. This is in contrast with the study that found that patients with active SI are associated with greater cognitive inflexibility than those with passive SI. (31).

The severity of depression MADRS score correlated with executive functioning (WCST Score-TT, TE, CC) in our study which is consistent some previous findings like by Taylor et al. (2002), in which depression severity, as measured by the HAM-D was found to be an independent predictor of total errors, perseverative responses, and failure to maintain set on the WCST. Other studies have found that EF deficits are greater in patients with more severe depressive symptoms (McClintock et al. 2010, McDermott & Ebmeier, 2009). Contrary to this finding, Harvey and colleagues (2004) found no relationship between depression severity and the WCST in 22 depressed patients.

However, in our study trail making test scores were not affected by severity of depression which matches the result of metanalysis by Synder HR et al. (32) Depressive symptom severity has been associated with deficits in executive functioning (33), which is believed to underlie the implementation of emotion regulation strategies, such as social problem-solving, in the face of stressors (34).

Our study found positive correlation between suicidal ideation scores and total trials (TT) in WCST and negative correlation with categories completed (CC). The present study found a significant negative relationship between executive function and suicidal ideation in men with MDD.

The major strengths of our study were the use of reliable and cross-validated clinical diagnostic assessments, and the significant results it produced. Majority of the studies have been cross sectional based on history of suicidal behaviour but in our studies we have taken subjects who currently have suicidal ideation or had recent suicide attempts. There is significant lack of



studies in Indian population in this regard. To our knowledge, there are negligible studies in Indian population, where such extensive domains of EF have been evaluated in MDD. Our studies have been done in 80 subjects with MDD which is adequate as compared to earlier studies and hence gives adequate power to generalise the findings. However, there are several limitations to this study. First, because it is cross-sectional, no causality can be assumed between the executive functions and suicidality. Second, because the study population was limited to the tertiary hospital setting, which might have induced some selection bias, and limits generalisability to the broader Indian population. Third, the less sample size might have reduced the power of the study and increased the margin of error. However, the results of this study are in keeping with the scientific literature on this subject, and provide ample data to enhance the understanding of the cognitive inflexibility and their relationship with suicidal behaviour in the subjects with MDD.

### **Conclusion:**

The cognitive inflexibility is proposed and hypothesized to be a core characteristic of suicidality irrespective of the nature and type of Psychiatric disorder. The EF is considered to be mostly widely used and validated tool and is also proposed as candidate “Endophenotype” in suicide research. EF as an abstract is known to be multidimensional and there are association with suicidal behaviour. The relationship between EF and suicidal behaviour in MDD is also found to be complex and inconsistent across various domain of EF. The systematic review and metaanalysis have not yet found robust association between different aspects of suicidal behaviours with various domains of EF framework proposed by Miyake et al. the suicidal behaviour in MDD is a major clinical challenge for the clinician. The cognitive inflexibility is a very important cognitive factor which interact with other clinical factors in MDD to produce suicidal behaviour. There is need to do large sample size, prospective study to understand the predictive and causative value of cognitive inflexibility to help clinician in managing and preventing suicide in MDD and other Psychiatric disorder.

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