Study of difference in cognitive functions after a single manic episode versus recurrent episodes in euthymic bipolar 1 patients

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ABSTRACT

Background: Neurocognitive deficits have been substantially documented in patients with bipolar disorder in the euthymic state. The assessment of cognitive change from first episode mania is crucial in understanding whether cognitive deficits are progressive or already present from the first diagnostic episode of bipolar I disorder. The objective of the study is to assess and compare the cognitive function in bipolar I patients with one manic episode and recurrent episodes currently in remission.

Methods: A cross sectional observational study consisting of 3 groups was carried on eighty cases each of bipolar 1 disorder patients in euthymic phase with one manic, more than 3 manic episodes and controls. These were subjected to the neuropsychological assessment and then compared.

Results: The patients with recurrent episodes group shows poor performance upon digit span test, visuospatial memory test, verbal learning and memory test, color stroop test and trail making test than patients with single manic episode and healthy controls upon these cognitive tests.

Conclusions: The present finding suggest that there is impairment in various cognitive domains like executive function, attention, memory even in bipolar patients after single manic episode.

Keywords: Bipolar 1 disorder, Euthymia, Neuropsychological assessment

INTRODUCTION

Bipolar disorder (BD) is a complex and chronic mental disorder characterized by recurrent episodes of depression and mania (hypomania). It is the sixth leading cause of disability worldwide among young adults (i.e. 15-44 years of age).

The chances of recurrences are common after the first manic episode with more than one-half of the patients experiencing a mood event within 12 months and the rate of recurrence increase with the number of episodes.

First-episode mania (FEM) is a crucial time for the trajectory of cognitive change. Hence, identifying cognitive deficits that may be present prior to the effects of multiple episodes and prolonged exposure to psychotropic treatment is theoretically important, whilst also informing approaches to early intervention.

Neurocognitive deficits have been substantially documented in patients with bipolar disorder in the euthymic state, and exist in the areas of executive functioning, verbal and visual memory, attention, and visuospatial ability.
The assessment of cognitive change from first episode mania is crucial in better understanding whether cognitive deficits are progressive or already present from the first diagnostic episode of bipolar I disorder. Hence, we conducted this study to look for cognitive deficits early in the illness i.e. after first manic episode to identify an opportunity for early psychological intervention and to monitor treatment.

METHODS

A cross sectional comparative observational study was carried out at department of psychiatry, SMS medical college and hospital, Jaipur. The study included total 240 subjects, 80 in each group. First group consisted of 80 patients of bipolar disorder having 1 episode of mania and the second subgroup had 80 patients having recurrent i.e. more than or equal to 3 episodes of mania and third sub group was control group (80) which included normal and healthy persons. Then each participant in the study were subjected to instruments of study and statistical analysis was done.

Selection criteria

Inclusion criteria

- Patients under follow up with diagnosis of bipolar disorder I as per criteria given by ICD-10
- Euthymic patient (YMRS≤6 and HDRS ≤8)
- Euthymic for at least 3 months prior to participation in the study
- Age 18-45 yr of either sex
- Provision of informed consent
- Literate enough to understand the neuropsychological tests.

Exclusion criteria

- A history of neurological disorder, mental retardation/learning disability, severe psychotic illness, significant head injury, any significant medical illness.
- Current drug abuse or dependency problem except nicotine within a 3month period.
- ECT sessions within 3month period prior to the study.

Tools for study

- Consent form: This form was formatted in Hindi language and were given to all participants of this study. The written consent was taken from each subject before screening procedure.
- Screening proforma: The proforma was included all exclusion criterions with the Yes/No option before each question.
- Socio-demographic profile: This was included name, age sex, father’s/husband’s name, address, marital status, education, occupation, type of family and monthly income of the participant.
- Clinical profile performa: This was included history of psychiatric illness and medications given.
- Young Mania Rating Scale (YMRS): The Young Mania Rating scale is an eleven-item clinician administered scale used to measure the severity of mania; it is not a diagnostic instrument. Each item is rated based on the individual’s subjective report over the previous forty-eight hours, as well as on the behavioral observations of the clinician. The rating of each item is on a scale of 0 to 4 (absent to overtly present), except for four of the items, which receive double the weighting and are rated on a scale of 0 to 8. This rating scale was used to assess for presence of manic symptoms and the total score was used in the analyses. A score of 6 or less typically characterizes euthymia and patients with score >6 are excluded from the study.6
- Hamilton Rating Scale for Depression (HAM-D): This scale contains 17 variables, some defined in terms of a series of categories of increasing intensity while others by a number of equal valued terms. A score of 8 or less typically characterizes an asymptomatic state and patients with score >8 are excluded from study.7
- Neuropsychological tests assessment:
  - Attention and concentration: The forward digit span test and the trail making test A.
  - Executive function: The trail making test part B, the backward digit span test and the Stroop colour test.
  - The verbal learning and memory test: The verbal learning and memory test in Hindi.
  - Visuospatial working memory matrix.

RESULTS

On comparing the three groups, there was no significant difference found in the sociodemographic profile of the patients and the controls.

All groups significantly differ from each other in DSTFWD as (Control>Group 1>Group 2) (p<0.01) (Table 1). Significant difference was observed according to DSTBWD test among the groups (p=0.001). On applying post HOC Test TUKEY test, mean DSTBWD were significantly lower in group 1 and 2 as compared to control group. No significant difference was observed in group 1 and group 2 (p=0.107) (Table 2).

Significant difference was observed according to Visuospatial test among the groups (p=0.001). On applying post HOC test TUKEY test, MEAN Visuospatial were significantly lower in group 2 as compared to group 1 and control group. No significant difference was observed in control group and group 1 (p=0.28) (Table 3).
Table 1: Digit span test (forward).

| Group   | N   | Mean | Std. deviation | p Value ls | C vs 1 | C vs 2 | 1 vs 2 |
|---------|-----|------|----------------|------------|--------|--------|--------|
| Control | 60  | 6.40 | 1.028          |            |        |        |        |
| Group 1 | 60  | 5.2  | 1.412          | <0.001s    | s      | S      | S      |
| Group 2 | 60  | 4.02 | 1.186          |            |        |        |        |
| Total   | 180 | 5.21 | 1.556          |            |        |        |        |

Table 2: Digit span test (backward).

| Group   | N   | Mean | Std. deviation | p Value ls | C vs 1 | C vs 2 | 1 vs 2   |
|---------|-----|------|----------------|------------|--------|--------|----------|
| Control | 60  | 5.37 | 1.089          |            |        |        |          |
| Group 1 | 60  | 4.13 | 0.747          | <0.001s    | s      | S      | NS (0.107) |
| Group 2 | 60  | 3.8  | 0.819          |            |        |        |          |
| Total   | 180 | 4.43 | 1.119          |            |        |        |          |

Table 3: Visuospatial test.

| Group   | N   | Mean | Std. deviation | p Value ls | C vs 1 | C vs 2 | 1 vs 2   |
|---------|-----|------|----------------|------------|--------|--------|----------|
| Control | 60  | 7.93 | 1.056          |            |        |        |          |
| Group 1 | 60  | 7.40 | 2.125          | <0.001s    | NS (0.28) | S      | S        |
| Group 2 | 60  | 5.52 | 2.347          |            |        |        |          |
| Total   | 180 | 6.95 | 2.180          |            |        |        |          |

Table 4: Color stroop test.

| Group   | N   | Mean | Std. deviation | p Value ls | C vs 1 | C vs 2 | 1 vs 2 | 0.01    |
|---------|-----|------|----------------|------------|--------|--------|--------|---------|
| Control | 60  | 273.33 | 35.291         |            |        |        |        |         |
| Group 1 | 60  | 311.83 | 50.760         | <0.001s    | <0.001s | <0.001s | 0.01   |         |
| Group 2 | 60  | 337.50 | 57.339         |            |        |        |        |         |
| Total   | 180 | 307.56 | 55.161         |            |        |        |        |         |

Table 5: Trail making test A.

| Group   | N   | Mean | Std. deviation | p Value ls | C vs 1 | C vs 2 | 1 vs 2 | S       |
|---------|-----|------|----------------|------------|--------|--------|--------|---------|
| Control | 60  | 84.15 | 17.333         |            |        |        |        |         |
| Group 1 | 60  | 93.67 | 28.461         | <0.001s    | NS (0.052) | S      | S      |         |
| Group 2 | 60  | 153.50 | 19.207        |            |        |        |        |         |
| Total   | 180 | 110.44 | 37.883        |            |        |        |        |         |

Table 6: Trail making test B.

| Group   | N   | Mean | Std. deviation | p Value ls | C vs 1 | C vs 2 | 1 vs 2 | S       |
|---------|-----|------|----------------|------------|--------|--------|--------|---------|
| Control | 60  | 93.50 | 32.408         |            |        |        |        |         |
| Group 1 | 60  | 164.17 | 66.391        | <0.001s    | S      | S      | S      |         |
| Group 2 | 60  | 292.50 | 50.711        |            |        |        |        |         |
| Total   | 180 | 183.39 | 97.311        |            |        |        |        |         |
Significant difference was observed according to color stroop test total among the groups (p<0.001). On applying post HOC Test TUKEY test, mean color stroop test total were significantly more in group 2 compared to group 1 and also significantly more in group 1 as compared to control. (Mean stroop test total was Group 2>group 1>control) (Table 4).

Significant difference was observed according to seconds spend in doing TMT A among the groups (P<0.001S). On applying post HOC Test TUKEY test, Mean TMT A (seconds spend) were significantly higher in group 2 as compared to group 1 and control group. No significant difference was observed in control group and group 1 (Table 5). Significant difference was observed according to trail making test B among the groups (p<0.001). On applying post HOC Test TUKEY test, mean TMT B Sec were significantly more in group 2 as compared to group 1, and also it was significantly more in group 1 and 2 as compared to control group (mean TMT B is Group 2>Group 1>Control) (Table 6).

**DISCUSSION**

Present study reports that euthymic bipolar disorder patients perform poorer upon digit span test, visuospatial memory test, verbal learning and memory test, color stroop test and trail making test. The patients with recurrent episodes group shows even poorer performance than patients with single manic episode and healthy controls upon these cognitive tests. These findings indicate that both the groups had poorer performance upon new learning and recall, attention, the ability to shift strategy, selective inhibition, working memory and psychomotor speed. Significant differences in attention and executive function were found between patients and controls and in those patients who had had just 1 manic episode compared to those who had 3 or more which means the number of manic episodes predicted poor cognitive performance, suggesting that the recurrence of mania may have a long-term neuropsychological impact.

This is in line with the study conducted by Hellvin T et al, which concluded that BD patients early in their disease course showed impairments in psychomotor speed, attention, learning and memory, executive functioning, and IQ. Madalina Vrabie et al, also found that an increased number of past manic episodes was the strongest correlated event with the poorest outcomes in verbal memory testing.

**CONCLUSION**

The present finding suggests that there is impairment in various cognitive domains like executive function, attention, memory even in bipolar patients after single manic episode or immediately after onset of illness. Thus, by properly managing the severity of illness would prevent further cognitive decline and thus the functional outcome.

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**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

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