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# A Study to Assess the Effect of Selective Serotonin Reuptake Inhibitors (SSRIS) On the Cognition of Patients with Depression and Anxiety in Acute Phase of Treatment

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## I. Introduction

Depression and Anxiety disorders are caused due to abnormalities of the norepinephrine (NE) and serotonin (5HT) neurotransmitter systems. The majority of evidence supports under activation of serotonergic function and complex dysregulation of noradrenergic function, most consistent withover activation of this system [(1)]The increase in serotonergic function and decrease in noradrenergic function accompany treatment with antidepressants, and these alterations may be necessary for antidepressant efficacy. The selective serotonin reuptake inhibitors (SSRIs) have been the most widely used pharmacological agents for Depression and Anxiety disorders, Monotherapy with SSRIs is often recommended for patients diagnosed with these conditions. [(3)]

SSRIs were devoid of side effects associated with the earlier antidepressant drugs—the tricyclics (TCAs) and MAOIs. These included dry mouth, constipation, sedation, orthostatic hypotension, and tachycardia. [(4)]

Despite the potential usefulness of SSRIs, they could cause unwanted side effects such as headaches, weight gain, sexual dysfunction, changes in sleep patterns, and gastrointestinal problems. Originally, SSRIs did not appear to cause cognitive impairment, but nowadays there are conflicting evidences regarding this side effect and many patients complain of memory loss during their course of therapy with SSRIs.

Many antidepressant compounds increase synaptic levels of one or more monoamines that play acrucial role in modulating affection and cognition. [(6)] For this reason, antidepressant agents could improve the cognitive symptoms of depression. But few studies show SSRI use was associated with memory impairment, specifically poorer episodic, though not working or semantic memory. [(9)]

**AIM**

The aim of this study is to assess the effect of SSRI drugs on cognitive function of patients with Depression and Anxiety in acute phase of therapy.

## II. Methods:

**STUDY DESIGN:** It is aLongitudinal Observational Studyconducted atGovernmentHospital for Mental Care, Visakhapatnam

**STUDY SAMPLE:** The study sample consisted of 40 patients diagnosed with Depression and Anxiety according to ICD 10 Criteria attending King George Hospital and Government Hospital for Mental Care, Visakhapatnam.

SAMPLING METHOD: Convenience Sampling

**INCLUSION CRITERIA:**

- Age :18 to 60 years
- Diagnosis of Depression and Anxiety according to International Classification of Diseases-10 criteria.
- No diagnosed cognitive impairment or mental retardation
- The ability to write and read
- No visual or auditory impairment

**EXCLUSION CRITERIA:**

- Patients with medical or neurological illness
- History of loss of consciousness after head trauma or brain surgery.
- History of using psychoactive drugs within 14 days prior to the study.
- Individuals with memory loss complaints in daily functioning.
- Patients who are contraindicated to use SSRIs.

Patients fulfilling the inclusion criteria were taken up for the study. These cases are enrolled after taking informed consent from them to be included in the study. After a detailed history and mental status examination a diagnosis of Depression and Anxiety wasconfirmed according to International Classification of Diseases-10 criteria.

The patient's socio demographic data and illness history were collected in the first visit (week 0 of therapy) andMMSE (a 30-point test) was performed at weeks 0, 4, and8 of drug therapy. Each patient's drug regimen (type of drug and dosage) remained fixed throughout this 8-week period. Iffor any reason the patient needed a dose reduction or increaseor medication discontinuation, he/she would be excludedfromthe study.

**STUDY TOOLS:**

**Self-designed semi structured proforma** was used. It included the following:

a)Socio demographic data sheet

b) Clinical profile sheet

**Mini Mental Status Examination (MMSE):** The MMSE is a brief, quantitative measure of cognitive status in adults. It can be used to screen for cognitive impairment, to estimate the severity of cognitive impairment at a given point in time, to follow the course of cognitive changes in anindividual over time, and to document an individual's response totreatment. It includes tests of orientation, attention, memory, language and visual-spatial skills. It is a 30 points questionnaire and any score greater than or equal to 24 points (out of 30) indicates a normal cognition. Below this, scores can indicate severe (≤9 points), moderate (10–18 points) or mild (19–23 points) cognitive impairment.Its reliability based on Cronbach's Alpha is 81% and a cut-off point of22 showed a sensitivity of 90% and specificity of 93.5%.

**STATISTICAL ANALYSIS:**Statistical analysis of the data was carried out using SSPS software version 23.The data were analysed using repeated measures one-way ANOVA. Results with a $p$ value of less than 0.05 were considered significant. Correlationsof MMSE scores and age, sex, and level of education wereanalysed by Pearson correlation test, one-way ANOVA test, and paired sample $t$-test, respectively.

## III. Results:

Forty patients 18 women and 22 men, ages ranging from 20 to 60 years) participated in this study.They all completed the study and we had no dropout patients. All of them showed signs of response to treatment of their psychiatric disorder at week 8.

The mean age of the patients was found to be 30.85±8.58.

All the patients were literate.

12.5% were from a rural background.

30% were unemployed.

In order to analyse thecorrelation of level of education with MMSE scores, we grouped thepatients into four different groups. 2 patients were in the Tenth class group,6 patients were in the Intermediate group,29 patients were in the Graduate group and 3 patients were in the Post Graduate group.

The prescribed drugs for patients were Escitalopram for 28 patients (70%), Sertraline for 8 patients (20%) and fluoxetine for 4 patients (10%).

The results of means of MMSE scores at weeks 0,4, and 8 are 29.75,29.87 and 29.52.

With a $p$ value more than 0.05, the MMSE scores of patients did not lower significantly from their baseline after the acute phase of treatment.

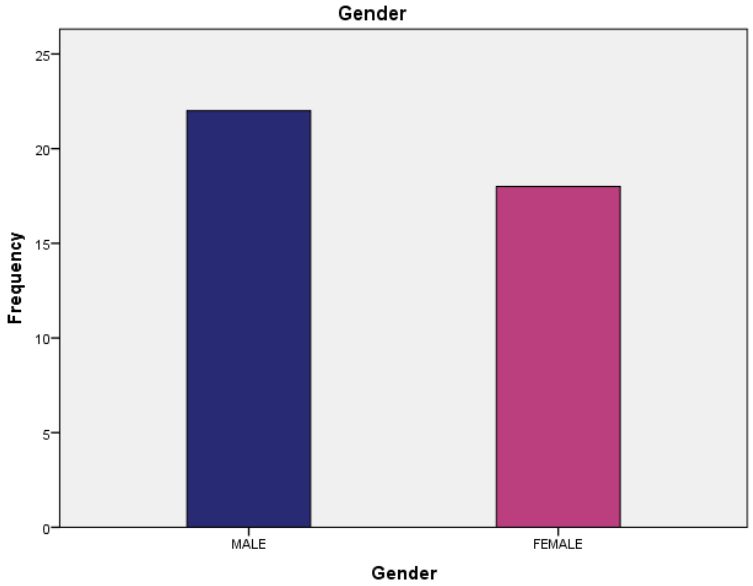
Correlation of age and MMSE scores was also assessed and the results showed no significant relationship between them, neither prior to therapy ($p$ value = 0.70) nor during it ($p$ value =0.84).

MMSE scores among male and female patients had a similar decline trend, when week 8 of the treatment was completed when compared with the baseline.

The level of education of patients showed no significant correlation with decline of cognitive function ($p$ value = 0.84)

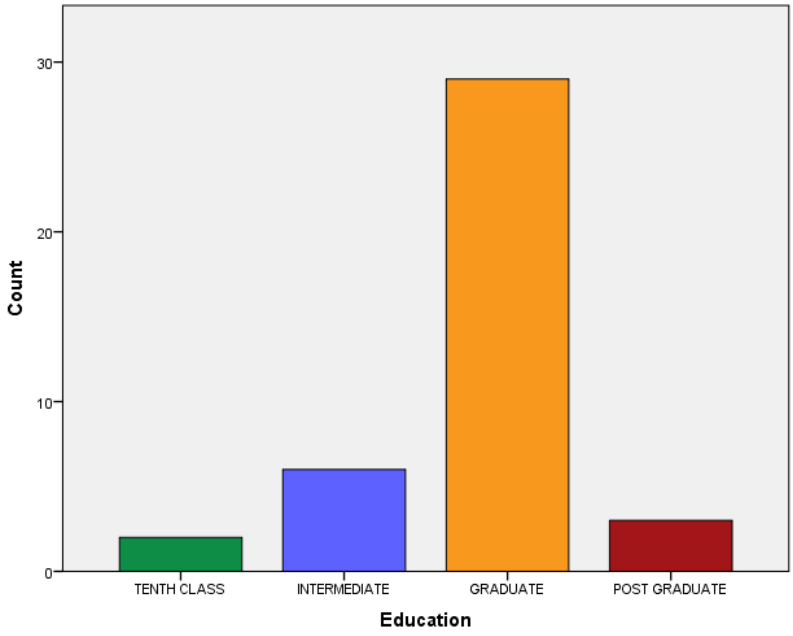
GENDER

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| MALE | 22 | 55.0 | 55.0 | 55.0 |
| FEMALE | 18 | 45.0 | 45.0 | 100.0 |
| Total | 40 | 100.0 | 100.0 | |



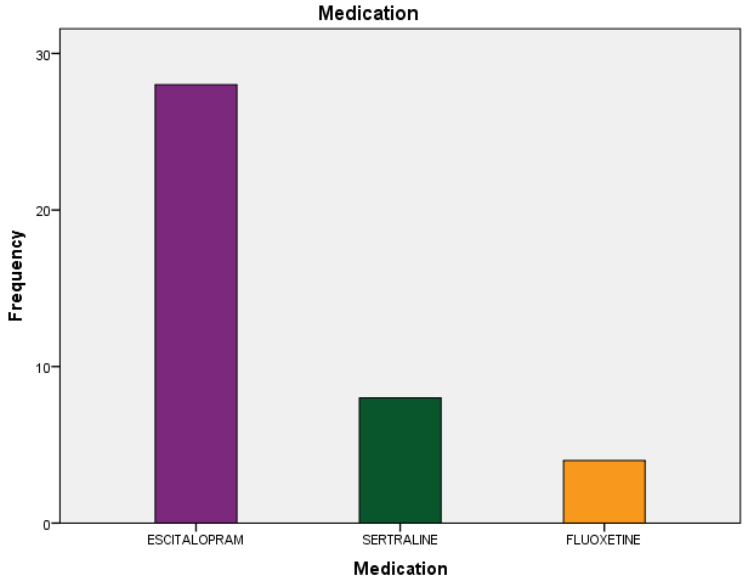

EDUCATION

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| TENTH CLASS | 2 | 5.0 | 5.0 | 5.0 |
| INTERMEDIATE | 6 | 15.0 | 15.0 | 20.0 |
| GRADUATE | 29 | 72.5 | 72.5 | 92.5 |
| POST GRADUATE | 3 | 7.5 | 7.5 | 100.0 |
| Total | 40 | 100.0 | 100.0 | |



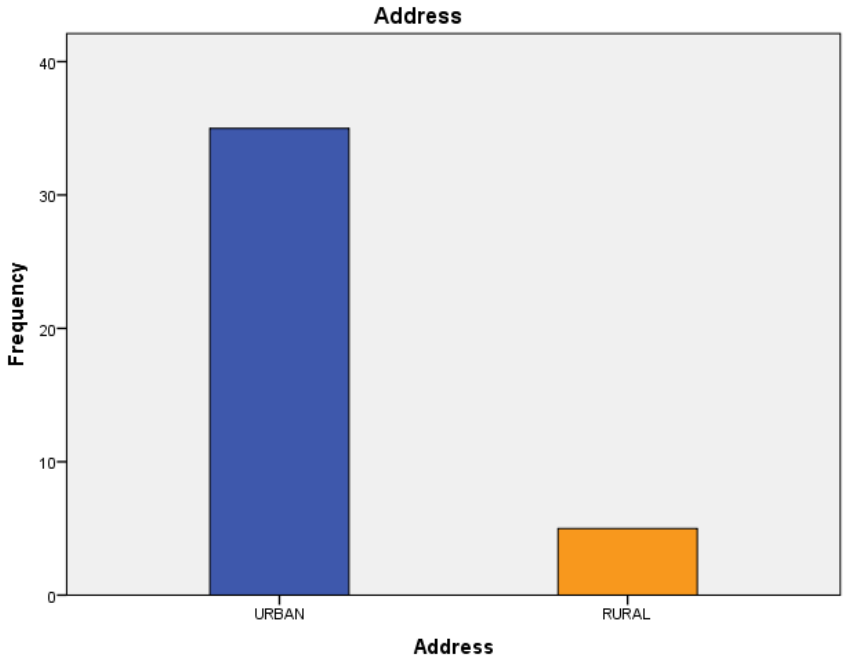
MEDICATION

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| ESCITALOPRAM | 28 | 70.0 | 70.0 | 70.0 |
| SERTRALINE | 8 | 20.0 | 20.0 | 90.0 |
| FLUOXETINE | 4 | 10.0 | 10.0 | 100.0 |
| Total | 40 | 100.0 | 100.0 | |




ADDRESS

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| URBAN | 35 | 87.5 | 87.5 | 87.5 |
| RURAL | 5 | 12.5 | 12.5 | 100.0 |
| Total | 40 | 100.0 | 100.0 | |



**MEAN OF MMSE AT WEEK 0,4,8**

| | | MMSE @ 0 WEEKS | MMSE @ 4 WEEKS | MMSE @ 8 WEEKS |
|---|---|---|---|---|
| N | Valid | 40 | 40 | 40 |
| | Missing | 0 | 0 | 0 |
| Mean | | 29.7500 | 29.8649 | 29.5250 |
| Std. Deviation | | .70711 | .41914 | .84694 |

**DIFFERENCE BETWEEN MEANS OF MMSE**

| | | Diff_mmse0and4 | Diff_mmse4and8 |
|---|---|---|---|
| N | Valid | 40 | 40 |
| | Missing | 0 | 0 |
| Mean | | -.1081 | .3243 |
| Std. Deviation | | .39326 | .66892 |

**AGE AND MMSE SCORE (Pearson correlation)**

**Correlations**

| | | Age | MMSE @ 0 WEEKS | MMSE @ 4 WEEKS | MMSE @ 8 WEEKS |
|---|---|---|---|---|---|
| Age | Pearson Correlation | 1 | -.222 | -.235 | -.211 |
| | Sig. (2-tailed) | | .169 | .162 | .191 |
| | N | 40 | 40 | 40 | 40 |

**SEXAND MMSE SCORES (ONE WAY ANOVA)**

| | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| MMSE @ 0 WEEKS | Between Groups | .400 | 1 | .400 | .796 | .378 |
| | Within Groups | 19.100 | 38 | .503 | | |
| | Total | 19.500 | 39 | | | |
| MMSE @ 4 WEEKS | Between Groups | .266 | 1 | .266 | 1.536 | .223 |
| | Within Groups | 6.058 | 35 | .173 | | |
| | Total | 6.324 | 36 | | | |
| MMSE @ 8 WEEKS | Between Groups | 1.225 | 1 | 1.225 | 1.740 | .195 |
| | Within Groups | 26.750 | 38 | .704 | | |
| | Total | 27.975 | 39 | | | |

**EDUCATION AND MMSE SCORES (Pearson correlation)**

**Correlations**

| | | Education | MMSE @ 0 WEEKS | MMSE @ 4 WEEKS | MMSE @ 8 WEEKS |
|---|---|---|---|---|---|
| Education | Pearson Correlation | 1 | .128 | .225 | .032 |
| | Sig. (2-tailed) | | .430 | .181 | .844 |
| | N | 40 | 40 | 40 | 40 |

## IV. Discussion:

Cognitive dysfunction subsequent to SSRI therapy remains controversial and different studies have reported inconsistent results. **(1)**

This study finding show that patients taking SSRIs experiencedmemory loss in the acute phase of treatment but it is not statistically significant. The reason forthe cognitive decline not being statisticallysignificant might be the low dose administration of the drugs.

The results did not vary with Age, gender and education of the patient.

The results of this study were similar to a study by Mehdi Sayyah et al. in which patients with OCD or depression and those who are naive to SSRI therapy, had a gradual decline in their memory function within the first 8 weeks of initiation of drug treatment with SSRIs**(1)**

A study by Popovic et al. showed that over 20% of patients with depression or anxiety disorders reported memory loss after 6 months of SSRI therapy. This was considered a side effect rather than a residual symptom of untreated depression and anxiety.**(4)**

Serretti et al. showed that using SSRIs even in healthy individuals leads to cognitive impairment. The memory loss caused by SSRIs has not yet been convincingly explained however, serotonin appears to play an important role in learning and memory.**(5)**

Serotonin transporter (SERT) expression has been found to be vital for memory development. Decreased expression of this transporter was found in memory impairments ,Alzheimer's disease and dementia.

Although these findings may partly explain the cause of memory loss due to SSRIs, more studies are needed to discover the exact mechanism responsible for this outcome.

Future studies with the help of other cognitive assessment tools can help to have a more accurateidentification of this problem.

**LIMITATIONS:**

- Small sample size
- Short follow up period
- Severity of the disease was not assessed

## V. Conclusion:

There is a decline in the cognition of patients with depression and anxiety in acute phase of treatment with SSRI's but the decline is not statistically significant.

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