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Original Research Article

## A comparative study to assess the effect of escitalopram and amitriptyline on psychomotor functions in patients of depression

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### ABSTRACT

**Background:** Depression is a most common and widespread of all psychiatric disorders. Treatment of depression includes the use of antidepressants commonly used clinically such as tricyclic antidepressants, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitor, and monoamine oxidase inhibitors. Certain antidepressants apart from improvement in the symptoms found to have detrimental effect on cognitive and psychomotor function. Objective of this study was to assess and to compare the effect of escitalopram and amitriptyline on cognitive and psychomotor functions

**Methods:** Effect of escitalopram and amitriptyline on psychomotor function was assessed by using Critical flicker fusion frequency (CFF) and Reaction time (RT) in patients of mild to moderate depression at the end of 2nd and 4th week of monotherapy.

**Results:** Patients in both the group have their RT remained significantly higher ( $p < 0.001$ ) in comparison with control and CFF remained significantly lower at the end of both the week. There was a significant rise in CFF in escitalopram group as compared to amitriptyline ( $p < 0.001$ ). Escitalopram showed a significant improvement in Visual reaction time (VRT), Auditory reaction time (ART) and Choice reaction time (CRT) ( $p < 0.001$ ) compared to amitriptyline at both the follow ups.

**Conclusions:** Findings of this study support the use of Selective serotonin reuptake inhibitor (SSRI) i.e. escitalopram which had shown less impairment of psychomotor function in patients of Depression as compared to amitriptyline (Tricyclic antidepressant), in special subgroups of population who operate machinery, drive vehicle or require alertness for the work.

**Keywords:** Reaction time, CFF, Antidepressants, Cognitive functions

### INTRODUCTION

Depression is a most common and widespread of all psychiatric disorders characterized by depressed mood most of the time for at least 2 weeks and or loss of interest or pleasure in most of the activities. In addition, depression is characterized by disturbances in sleep, appetite as well as deficit in cognition; thoughts of guilt, worthlessness and suicide are also common.<sup>1</sup> Antidepressants are commonly

used medication for depression they belong to tricyclic antidepressants, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitor, and monoamine oxidase inhibitors.

Depression related cognitive impairment is a condition that is under-recognized, undiagnosed and undertreated.<sup>2</sup> Cognitive impairment ranges from deficit in short term, long term memory or alteration in decision making process and impairment of information processing.

The largest population-based study to date of late onset depressive illness (65-84 years) documented severe cognitive impairment in ten per cent of depressed patients.<sup>3</sup> Approximately 70% of elderly depressed patients have measurable cognitive deficits, although a physician may be unaware of any overt signs.<sup>4</sup> It is well established that antidepressants can improve patient's well-being and functioning but many have demonstrable detrimental effect on range of cognitive functions. The optimum profile of antidepressant includes no detrimental effect on cognitive and psychomotor functions.<sup>5</sup>

With moves towards continuation and maintenance therapy for depression antidepressants with relatively non-sedating, non-cognition impairing profiles such as SSRIs (Selective serotonin reuptake inhibitors) are preferred in patients of depression.<sup>6</sup> However, Antidepressant like escitalopram and other SSRI's are known to improve cognition and memory in some studies cognition and memory parameters declined in some other studies.<sup>7-9</sup> The Tricyclic antidepressants (TCAs) have very potent antihistaminic and anticholinergic effects.<sup>10</sup> Both antihistaminic and anticholinergic activities of TCAs can cause psychomotor impairment by retarding the throughput of sensorimotor information particularly during continuous manual control operations, such as car driving. Development of tolerance to many of the cognitive and psychomotor deficits induced by antidepressants especially TCAs are seen in multiple dose healthy volunteer studies however, these studies have usually employed in a doses of less than or equal to 75 mg/day and volunteer studies with higher doses have all involved nocturnal dosing.<sup>11</sup> Similarly, it would be unwise to generalize the finding of the rapid development of tolerance to sedative TCAs in healthy volunteers to depressed patients. Apart from the development of tolerance there is also the question of whether antidepressant's psychomotor impairing effects can emerge or intensify after days or weeks of continuous dosing.

Use of antidepressants having cognitive and psychomotor function impairing properties may raise a concern amongst employees of some critical job that require high level of alertness such as drivers students, factory workers, machinery operators.<sup>12,13</sup> In view of long term medication, it is important to evaluate the effect of these antidepressants on cognitive and psychomotor functions which would help in making choice of drug based on the individual patient requirement.

This study was carried out to evaluate the effect of long-term administration of escitalopram and amitriptyline on psychomotor functions in patients of depression.

## **METHODS**

This was an open label prospective comparative clinical study designed to evaluate and the effects of escitalopram and amitriptyline on psychomotor function patients of

mild to moderate depression and to compare the same with unmedicated healthy adult volunteers. The study was conducted at Psychiatry department of MGM hospital Kamothe Navi Mumbai from January 2013 to June 2013.

### ***Inclusion criteria***

The inclusion criteria for the study was as follows: Patients of either sex, patients within the age limit of 18-60 years, a known cases of mild to moderate Depression diagnosed by DSM-IV criteria and HDRS scale, patients who were on monotherapy with either escitalopram 20 mg and amitriptyline 75 mg once a day and patients who were willing to participate in the study and willing to give written informed consent.

### ***Exclusion criteria***

The exclusion criteria for the study was as follows: Patients who were on any other medications (antihypertensive, sedative and systemic steroid etc.) that are known to affect cognitive and psychomotor functions, patients with serious systemic disorders (diabetes, hypertension etc), patients with any psychiatric illness or any other CNS disorder that will interfere with cognitive and psychomotor functions except depression, patients who were not willing to participate and not given written informed consent and patients with severe depression with HDRS score >17.

### ***Methodology***

Outpatient department (OPD) patients diagnosed with depression according to DSM-IV criteria and HDRS scale score were enrolled into the study. Before beginning of the study, the enrolled patients were explained about the importance of this study and informed consent was obtained from each patient and they were familiarized with Critical flicker fusion frequency test (CFFT) and Reaction time performance (RT) tests.

Tests were carried out between 10:00 to 1:00 p.m. tests were being carried out at the end of 2nd and 4th week of monotherapy. Patients personal data like name, age, registration number, educational status day and general and systemic examinations were carried out to exclude any systemic disease. Other things like symptoms, illness duration, past history, family history, past drug history were also being noted.

Test performed were: CFF; RT performance test- Visual reaction time (VRT), Auditory reaction time (ART), Choice reaction time (CRT).

### ***Critical Flicker-Fusion test***

It was assessed by the CFF apparatus (Techno Electronics, Lalbaugh Lucknow-226001). The apparatus is housed in a metal cabinet having two sloping sides the light source

flickers at the rate set by the experimenter. The flicker frequency range of the instrument is 5-50 Hz. the CFF.

Subjects were asked to indicate when a red-light-emitting flickering source increasing in frequency, is perceived to become a continuous signal. They were also required to distinguish the threshold at which a flickering signal was perceived from a continuous signal, when frequency decreased. This fusion and flicker are a reliable measure of cortical alertness and arousal and reasonably stable in a given subject. Decreases in thresholds is indicative of altered Central nervous system (CNS) function.<sup>14</sup>

#### *Determination of 'critical fusion frequency'*

The 'flicker per second' knob of the instrument was kept at minimum frequency of 5 Hz. The volunteers were told to view a flickering light source through the eyepiece. They were allowed adaptation to the least flicker frequency for 1 minute. Then frequency was increased slowly by rotating the flicks per second knob clockwise. The frequency increase was stopped as soon as patient responded by pressing the response switch, when he saw fusion i.e. no more flickering or a steady light source. Frequency from the dial setting was noted. Three such readings were taken and the score was calculated as the mean of these 3 readings.<sup>15</sup>

#### *Determination of 'critical flicker frequency'*

After determination of critical fusion frequency, the flicks per second knob was adjusted to maximum frequency of 50 Hz, after 1 minute adaptation frequency was decreased slowly, by rotating the flicks per second knob anticlockwise. The frequency reduction was stopped as soon as the subject responded when he saw flickering. Three reading were taken and the score was calculated as the mean of these 3 readings.<sup>16</sup>

Mean of both (a) and (b) was then calculated.

Mean CFF value is decreases with age, also with the antidepressants impairing cognitive and psychomotor function and hypnotics,<sup>16</sup>while CNS stimulant drugs increases critical flicker fusion frequency.<sup>16,17</sup>

#### **Reaction time performance test**

RT performance was assessed using (Digital Display Multiple Choice 4-visual  $\pm$ 4 Aural Type MCR-444) Lalbaugh Lucknow-2220. It measures reaction time, i.e. time interval after which subject responds to stimulus either visual/auditory.

Four different stimuli of different colours and four aural stimuli of different tones, with independent operation were provided. Chronoscope is a four figure 7 segment L.E.D Display with a minimum count of 00.10 seconds and The techno digital display multiple choice is a compact portable unit with sloping operating panel. On both sides

for ease of operation, a removable partition effectively shields the operation side from each side. It operates from 220 V 50 Hz AC.



**Figure 1: Techno flicker fusion apparatus.**



**Figure 2: Techno digital display multiple choice.**

Experimenter's side contains a) red, green, yellow and amber coloured L.E.D.'s lights or any four different colours b) the bottom row has eight press buttons four for visual stimuli four for auditory stimuli. Subject's side contains: red, green, yellow and amber coloured visual stimuli (or matching different colours) and eight press buttons four for visual four for aural stimuli.

Sensory component is an important aspect of psychomotor performance. Detection, perception, and recognition of a stimulus are three levels of information processing which together account for the majority of sensory activity. Thus, RT performance measures the processing of sensory information.

RT is impaired /increased with drugs declining cognitive functions, depression, with increasing age (time taken to respond to stimuli is increased with cognitive and psychomotor impairment could be due to drug or depression itself).<sup>17</sup> Certain antidepressants, caffeine and CNS stimulant such as amphetamine produces reduction in reaction time.<sup>18,19</sup>

In the present study, patients were included in such a way so as to exclude any extraneous influence on psychomotor function like drugs (example: antiepileptic, sedative-hypnotics, antipsychotic) and diseases (serious systemic disorder, for example diabetes mellitus.) Thus, the changes

observed in the study if any could be attributed to two factors, first the effect of drugs on psychomotor function parameters and second improvement in the disease, i.e. depression.

**Statistical analysis**

Data presented using charts and descriptive statistics such as mean, Standard deviation (SD), Standard error (SE). Further statistical analysis was being done using one-way ANOVA, followed by Tuckey’s Post-hoc Test. The significance level was set at 5%, p-value less than 0.05 was considered as a significant.

**RESULTS**

Table 1 shows the division of enrolled subjects into 03 groups with 20 participants in each group.

**Table 1: Division of enrolled subjects in various groups (n-number of subjects).**

Group 1 (n=20)	Group 2 (n=20)	Group 3 (n=20)
Healthy adult volunteers	Escitalopram 20 mg OD	Amitriptyline 75 mg OD

**Table 2: Sociodemographic profile of study participants.**

Demographic variables	Escitalopram (n=20)	Amitriptyline (n=20)	Control (n=20)
<b>Sex</b>			
Male	09 (45)	10 (50)	11(55)
Female	11 (55)	10 (50)	09 (45)
<b>Age group</b>			
18-40	08 (40)	11 (55)	
41-60	12 (60)	09 (45)	11 (55)
<b>Occupation</b>			09 (45)
Student	02 (10)	0 (25)	
Household	04 (20)	04 (20)	04 (20)
Factory worker	05 (25)	05 (20)	03 (15)
Labourer	04 (20)	04 (20)	03 (15)
Office worker	05 (15)	02 (10)	04 (20)
Others	-	-	02 (10)

Table 2 depicts the sociodemographic division of the enrolled participants into different groups. In this study there were 50% males and 50% females subjects. Out of 60 study subjects almost, 50% were in the age group of (18-40) and 50 % were in the age group of (41-60).

Table 3 showed, at 2nd and 4th week of monotherapy when both the drug groups compared with control, mean CFF, Mean VRT and mean CRT was decreased significantly (p<0.001).

Mean CFF in escitalopram group increased significantly when compared with amitriptyline (p<0.05) at 2nd week (30.83±0.28) and 4th week (31.63±0.29) of treatment. Mean VRT, ART and CRT increased significantly in amitriptyline group as compared to escitalopram and control group (p<0.05).

**Table 3: Effect on CFF and RT at the end of 2<sup>nd</sup> and 4<sup>th</sup> week between various groups (Mean±SEM).**

Test group	Control (n=20)	Escitalopram (n=20)		Amitriptyline (n=20)	
		2 <sup>nd</sup> week	4 <sup>th</sup> week	2 <sup>nd</sup> week	4 <sup>th</sup> week
<b>CFF</b>	33.34±0.17	30.83±0.28 <sub>ac</sub>	31.63±0.29 <sup>ad</sup>	25.28±0.33 <sub>b</sub>	25.40±0.31 <sup>b</sup>
<b>VRT</b>	163.06±2.69	234.20±1.63 <sup>ac</sup>	229.00±1.74 <sup>ad</sup>	278.58±6.72 <sup>b</sup>	274.77±3.98 <sup>b</sup>
<b>ART</b>	111.27±4.48	206.52±2.35 <sup>ac</sup>	198.00±2.31 <sup>ad</sup>	259.96±2.81 <sup>b</sup>	258.25±3.01 <sup>b</sup>
<b>CRT</b>	335.20±12.95	395.07±5.18 <sup>ac</sup>	391.10±5.29 <sup>ad</sup>	505.38±6.27 <sup>b</sup>	503.91±6.33 <sup>b</sup>

Time in mseconds. and frequency in Hz. CFF- critical flicker frequency RT-Reaction Time, VRT- visual reaction time ART- Auditory reaction time CRT-Choice reaction time. <sup>a</sup>p<0.001 as escitalopram compared with control at both the weeks. <sup>b</sup>p<0.001as amitriptyline compared with control at both the weeks. <sup>c</sup>p<0.001 as compared with amitriptyline at 2nd week. <sup>d</sup>p<0.001 as compared with amitriptyline 4th week.

**DISCUSSION**

Depression affects 121 million people worldwide; it has life-time prevalence of 16.2% and 12 months prevalence of 6.6% in developed countries, and is a leading cause of disability worldwide.<sup>20</sup> As far as the burden of depression in India is concerned, many studies have estimated the prevalence of depression in community samples and the prevalence rates have varied from 1.7 to 74 per thousand in Indian population.<sup>21,22</sup> The largest population-based study to date of late onset depressive illness (65-84 years) documented severe cognitive impairment in ten per cent of depressed patients.<sup>3</sup> Approximately 70% of elderly depressed patients have measurable cognitive deficits, although a physician may be unaware of any overt signs.<sup>4</sup> It is well established that antidepressants can improve patient’s well-being and functioning but many have demonstrable detrimental effect on range of cognitive functions. The optimum profile of antidepressant includes no detrimental effect on cognitive and psychomotor functions.<sup>5</sup>

Studies are available which show the effect of antidepressants on cognitive and psychomotor function but most of these studies were single-dose studies and healthy



volunteers were used as a study subjects.<sup>23</sup> Few studies reveal the effect of Selective serotonin reuptake inhibitors on cognitive and psychomotor performance in depressed patients.<sup>23,24</sup>

In the present study, at 2nd and 4th week of monotherapy, when both the drug groups compared with control, mean CFF of all patients was significantly less compared to control. Present results are in agreement with the effect of fluoxetine belonging to the class of SSRI, on cognitive and psychomotor performance in comparison with control as measured by CFF is in commensurate with findings of Sabbe et al in which they had assessed sensory-motor programming, coordination, initiation and execution of muscle commands and feedback processing.<sup>25</sup> The performances of patients receiving fluoxetine were compared to a control group of 22 individuals. The significant slowing of motor processes in the depressed inpatients decreased but did not disappear after treatment. At the end of treatment significant differences persisted between the patient group and the control group. Significant slowing of motor processes were observed in depressed inpatients receiving fluoxetine decreased but did not disappear at the end of 6th week.<sup>25</sup>

Escitalopram showed a significant decrease in mean RT performance i.e. VRT, ART and CRT at the end of 2nd and 4th week when compared with amitriptyline. Present results with escitalopram improving Mean reaction times and CFF compared to amitriptyline at 2nd and 4th week are in agreement with the conclusion of Fairweather et al.<sup>26</sup> This study compared fluoxetine versus amitriptyline showed similar results as the psychometric test battery showed that, compared to fluoxetine, amitriptyline, as expected, produced impairments in cognitive function and psychomotor performance. The relative impairment of cognitive and psychomotor skills following the tricyclic antidepressant amitriptyline and the lack of such activity after administration of the selective serotonin reuptake inhibition, fluoxetine are important considerations when prescribing antidepressants, especially when the safety and wellbeing of ambulant patients is essential. Escitalopram group showed a significant increase in mean CFF compared with amitriptyline at both the follow ups.

This study shows that, there was impairment in CFF and RT performance in amitriptyline group compared to escitalopram belonging to SSRI and healthy control group. Thus, amitriptyline produces significant impairment in cognitive and psychomotor functions. Escitalopram had produced lesser impairment in CFF and RT performance compared to amitriptyline.

Findings of this study supports the use of escitalopram (SSRI) compared to Amitriptyline (TCA) which had shown less impairment of psychomotor function (CFF) - a central integrative component in patients of mild to moderate depression. These findings are significant and of a clinical importance. Drugs which have low behavioural toxicity should therefore be preferred as they are less

disruptive of patient's everyday activities produce better quality of life and are not counter-therapeutic. It may be preferred in patients who operate machinery, drive vehicle, or require alertness for the work. However, our findings need confirmation by using larger number of patients with longer follow up.

## CONCLUSION

This study supports the use of escitalopram over amitriptyline specially in context with their use in patients require alertness at work, operate machinery with mild to moderate depression considering the less behavioral toxicity and detrimental effects on psychomotor functions. However, our findings need further review and confirmation with frequent follow-ups and larger multi center studies.

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