ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Effect of Selective Serotonin Reuptake Inhibitors on Cognitive Function in Patients with Major Depressive Disorder.

Anshudeep Dodake[1]*, and Vijay Daberao[2].

[1]Department of Pharmacology, LTMMC&GH, Sion Mumbai, Maharashtra, India.
[2]Apollo Hospitals, Navi Mumbai, Maharashtra, India.

ABSTRACT

Major depressive disorder is commonly accompanied by deficits in attention, memory, and executive abilities that substantially impair everyday functioning. Although selective serotonin reuptake inhibitors are first-line pharmacotherapies, their net impact on cognition remains debated. In this prospective observational study, 40 patients meeting Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria for major depressive disorder were enrolled. Depression severity was quantified using the Hamilton Depression Rating Scale. Global cognition and domain-specific performance were evaluated with the Mini-Mental State Examination and standardized neurocognitive tests. Assessments were performed at baseline and after 8 weeks of treatment with standard selective serotonin reuptake inhibitor therapy. Within-group changes were analyzed using paired t-tests, with statistical significance defined as $p < 0.05$. Treatment was associated with a robust reduction in depressive symptom burden, with Hamilton Depression Rating Scale scores declining from 22.6 ± 4.2 to 12.1 ± 3.8 ($p < 0.001$). Parallel improvements were observed across cognitive domains, most prominently in attention, immediate memory, and executive functioning. Mini-Mental State Examination scores increased from 25.1 ± 2.8 to 27.4 ± 2.2 ($p = 0.002$). No clinically meaningful cognitive adverse effects were identified during follow-up. Eight weeks of selective serotonin reuptake inhibitor therapy resulted in significant alleviation of depressive symptoms along with measurable enhancement of cognitive performance. These findings support the view that effective antidepressant treatment may contribute to recovery of cognitive domains frequently compromised in major depressive disorder.

Keywords: major depressive disorder; selective serotonin reuptake inhibitors; cognition; antidepressant therapy.

https://doi.org/10.33887/rjpbcs/2024.15.6.118

Corresponding author

INTRODUCTION

Major Depressive Disorder is frequently associated with cognitive impairment, which significantly affects daily functioning. Although Selective Serotonin Reuptake Inhibitors are widely prescribed for MDD, their cognitive effects remain uncertain. As the first-line pharmacological treatment for depression, SSRIs have yielded conflicting evidence regarding their impact on cognitive domains: while some studies suggest improvements in psychomotor speed and delayed recall, others report patient complaints of memory loss during therapy (1,2).

This discrepancy highlights the need to clarify whether cognitive deficits are primarily attributable to the underlying pathophysiology of depression or represent adverse effects of pharmacological intervention (3,4). Furthermore, understanding the specific cognitive domains affected by SSRIs is essential for optimizing treatment adherence and clinical outcomes, as drug-induced memory loss can be a significant barrier to medication compliance (2).

Accordingly, the present study aims to evaluate the cognitive tolerability profile of SSRIs in long-term treatment, specifically examining the prevalence of cognitive symptoms such as fatigue, inattentiveness, and memory impairment in patients successfully treated with these agents (4). By systematically assessing these cognitive parameters, this research seeks to distinguish between residual depressive symptoms and medication-induced adverse effects, thereby informing clinical guidelines for the management of cognitive function in patients receiving SSRI therapy (3,5).

Literature Review

The cognitive profile of Major Depressive Disorder encompasses deficits in both 'hot' and 'cold' cognitive domains, with patients exhibiting small to moderate impairments in processing speed, attention, memory, and executive functions (6). These deficits are particularly concerning as cognitive dysfunction is identified as one of the residual symptoms of MDD that most strongly impairs quality of life, and persistent cognitive impairment may prevent full recovery even following the resolution of depressive episodes (7).

Furthermore, the limited literature evaluating this question may be restricted because these evaluations are not typically conducted from a neuropsychological perspective that includes a comprehensive assessment of cognitive domains such as executive functioning, attention, concentration, psychomotor speed, memory, and verbal and visuospatial memory (8). Consequently, the variability in methodological approaches and the specific cognitive domains assessed across studies has led to inconsistent findings regarding the efficacy of antidepressant treatments in improving cognitive performance (9). Notwithstanding the paucity of data showing beneficial effects of antidepressants on cognitive performance in non-elderly adult subjects with MDD, converging evidence supports the assumption that the clinical magnitude of antidepressant effects is also small in this population (7).

MATERIALS AND METHODS

This prospective, observational study was conducted in the Department of Psychiatry at a tertiary care hospital. We enrolled a total of 40 patients diagnosed with Major Depressive Disorder according to DSM-5 criteria. Eligible participants were adults aged 18–55 years who were newly initiated on selective serotonin reuptake inhibitors and provided written informed consent. Patients with comorbid psychiatric disorders, substance use disorders, neurological illnesses, or medications known to affect cognition were excluded. Baseline assessment was performed before starting SSRI therapy. Sociodemographic details and clinical history were recorded using a structured proforma.

Baseline assessment was performed before starting SSRI therapy. Sociodemographic details and clinical history were recorded using a structured proforma. Depression severity was assessed using the **Hamilton Depression Rating Scale (HDRS)**, and baseline cognitive function was evaluated using validated neuropsychological tools, including the **Mini-Mental State Examination (MMSE)** and domain-specific tests assessing attention, memory, executive function, and processing speed. All assessments were conducted by a trained clinical psychologist to ensure consistency.

Patients were initiated on standard therapeutic doses of commonly prescribed SSRIs such as sertraline, fluoxetine, escitalopram, or paroxetine, based on the clinician's judgment. Follow-up assessments were conducted after 8 weeks of continuous treatment. Cognitive tests and HDRS scoring were repeated at the same intervals to measure changes in cognitive performance and depressive symptoms. Medication adherence and adverse effects were monitored throughout the study period.

Data were compiled and analyzed using appropriate statistical software. Descriptive statistics were used to summarize demographic variables. Paired t-tests and repeated-measures analyses were applied to compare pre- and post-treatment cognitive scores. A p-value of <0.05 was considered statistically significant. All ethical guidelines were strictly followed.

RESULTS

This section presents the key findings from the study on the effect of Selective Serotonin Reuptake Inhibitors on cognitive function in patients with Major Depressive Disorder. The results cover participant demographics, changes in depression severity, and alterations in various cognitive domains after 8 weeks of SSRI treatment.

Baseline Characteristics of Study Participants

The study included a total of 40 participants (n=40). The mean age of the participants was 34.8 ±8.6 years. The cohort comprised 18 (45%) males and 22 (55%) females. Regarding educational background, 8 (20%) participants had less than 10 years of education, 14 (35%) had between 10 to 12 years, and 18 (45%) were graduates. At baseline, the mean Hamilton Depression Rating Scale score was 22.6 ±4.2, indicating a significant level of depression. The mean Mini-Mental State Examination score at baseline was 25.1 ±2.8, suggesting some degree of cognitive impairment in the study population.

Table 1: Baseline Characteristics of Study Participants (n = 40)

	Category	Number	Mean ± SD
Age	—	—	34.8 ± 8.6
Gender	Male	18	—
	Female	22	—
Education Level	<10th	8	—
	10th–12th	14	—
	Graduate	18	—
HDRS Score	—	—	22.6 ± 4.2
MMSE Score	—	—	25.1 ± 2.8

Change in Depression Severity After 8 Weeks of SSRI Therapy

Following 8 weeks of SSRI therapy, a statistically significant reduction in depression severity was observed across all measured parameters. The HDRS Total Score significantly decreased from a baseline of 22.6 ±4.2 to 12.1 ±3.8 after 8 weeks, reflecting a mean change of −10.5 ($p<0.001$*). All symptomatic sub-categories also showed significant improvement. Somatic symptoms decreased from 6.4 ±1.5 to 3.2 ±1.4 (mean change −3.2, $p<0.001$*). Cognitive symptoms, as assessed by HDRS, improved from 4.9 ±1.3 to 2.5 ±1.1 (mean change −2.4, $p<0.001$*). Emotional symptoms also showed a substantial reduction, moving from 11.3 ±2.8 to 6.4 ±2.0 (mean change −4.9, $p<0.001$*). These results indicate that SSRI treatment was effective in reducing the overall burden of depressive symptoms, including the cognitive aspects of depression.

ISSN: 0975-8585

Table 2: Change in Depression Severity After 8 Weeks of SSRI Therapy

Parameter	Baseline	8 Weeks	Mean Change	p-value
HDRS Total Score	22.6 ± 4.2	12.1 ± 3.8	−10.5	<0.001*
Somatic Symptoms	6.4 ± 1.5	3.2 ± 1.4	−3.2	<0.001*
Cognitive Symptoms	4.9 ± 1.3	2.5 ± 1.1	−2.4	<0.001*
Emotional Symptoms	11.3 ± 2.8	6.4 ± 2.0	−4.9	<0.001*

*Statistically significant

Cognitive Function Scores Before and After SSRI Treatment

The study also revealed significant improvements in various cognitive domains after 8 weeks of SSRI treatment. The MMSE Total Score increased from 25.1 \pm 2.8 at baseline to 27.4 ±2.2 at 8 weeks, representing a 9.1% improvement (p=0.002). Specific cognitive domains also demonstrated statistically significant enhancements. Attention & Concentration scores improved from 7.8 ±1.6 to 9.1 ±1.4, showing a 16.6% improvement (p=0.001*). Immediate Memory scores rose from 8.2 ±1.8 to 9.5 ±1.7, indicating a 15.8% improvement (p=0.003). Executive Function scores increased from 6.9 ±1.5 to 8.0 ±1.4, with a 15.9% improvement (p=0.004*). Lastly, Processing Speed improved from 7.5 ±1.3 to 8.4 ±1.2, an increase of 12.0% (p=0.006*). These findings collectively suggest that SSRI therapy not only alleviates depressive symptoms but also positively impacts multiple facets of cognitive function in patients with MDD.

Table 3: Cognitive Function Scores Before and After SSRI Treatment

Cognitive Domain	Baseline Score	8-Week Score	Improvement	p-value
MMSE Total Score	25.1 ± 2.8	27.4 ± 2.2	+9.1%	0.002*
Attention & Concentration	7.8 ± 1.6	9.1 ± 1.4	+16.6%	0.001*
Immediate Memory	8.2 ± 1.8	9.5 ± 1.7	+15.8%	0.003*
Executive Function	6.9 ± 1.5	8.0 ± 1.4	+15.9%	0.004*
Processing Speed	7.5 ± 1.3	8.4 ± 1.2	+12.0%	0.006*

*Statistically significant

DISCUSSION

Our present study evaluated the effects of Selective Serotonin Reuptake Inhibitors (SSRIs) on cognitive function in patients with Major Depressive Disorder (MDD) over an 8-week treatment period. The findings demonstrated a significant reduction in depressive symptoms along with notable improvements in multiple cognitive domains, including attention, memory, executive function, and processing speed. These results reinforce the hypothesis that treatment of mood symptoms with SSRIs indirectly contributes to cognitive enhancement, primarily by alleviating the cognitive load and emotional dysregulation associated with depression. (8,9)

Depression is widely recognized as a disorder with substantial neurocognitive involvement, and impairment in cognitive functions often persists even after mood improvement. In this study, patients showed a substantial reduction in HDRS scores by the eighth week, which paralleled improvements in cognitive test performance. This relationship suggests that part of the cognitive deficit in MDD may be state-dependent, influenced by the severity of depressive symptoms. Improvement in mood with SSRI therapy likely facilitates better concentration, increased motivation, and enhanced cognitive engagement, which collectively improve cognitive testing outcomes. (10,11)

The improvement across cognitive domains also highlights the potential neurobiological effects of SSRIs. Previous literature suggests SSRIs promote neuroplasticity, enhance serotonergic neurotransmission, and improve prefrontal cortical functioning—all of which may contribute to better

cognitive performance. Although SSRIs are primarily designed to target emotional dysregulation through serotonin reuptake inhibition, the indirect benefits on cognition observed here are consistent with similar clinical investigations showing enhanced neuropsychological functioning after antidepressant therapy.(12)

However, the magnitude of cognitive improvement varied across domains. Attention and immediate memory showed the most pronounced gains, while processing speed and executive function improved moderately. This pattern mirrors findings from earlier studies, which have shown that cognitive symptoms of MDD are multifactorial and do not uniformly respond to antidepressant therapy. Some cognitive deficits may persist despite adequate mood improvement, indicating the possibility of trait-related impairments independent of depressive severity.

While the study demonstrates positive cognitive outcomes following SSRI therapy, several limitations must be acknowledged. The sample size was relatively small (n=40), and the follow-up period of 8 weeks may not fully capture long-term cognitive effects. Additionally, different SSRIs were used based on clinical judgment, which may influence the consistency of outcomes. The absence of a control group or comparison with other antidepressant classes further limits generalizability. Despite these limitations, the study provides valuable evidence supporting the cognitive benefits of SSRIs in MDD patients. Overall, our findings suggest that SSRIs are not only effective in reducing depressive symptoms but may also play a meaningful role in improving specific cognitive domains. Future longitudinal studies with larger samples and controlled comparisons are needed to evaluate sustained cognitive changes and to explore whether some SSRIs offer superior cognitive outcomes compared to others.

The findings of this study have important clinical implications for the management of Major Depressive Disorder. Cognitive impairment is increasingly recognized as a core feature of MDD and often persists even after mood symptoms improve, affecting occupational performance, social functioning, and overall quality of life. The observed cognitive improvements with SSRI therapy highlight the value of selecting antidepressants that not only relieve depressive symptoms but also support cognitive recovery. Clinicians should routinely assess cognitive domains during follow-up visits and recognize early cognitive deficits as treatment targets. These results also underscore the importance of ensuring adequate treatment adherence and monitoring patient response over time. Given that improvement was most pronounced in attention and memory, SSRIs may be particularly beneficial for patients whose cognitive deficits interfere with daily tasks. Incorporating cognitive rehabilitation strategies and lifestyle interventions alongside SSRI therapy may further enhance treatment outcomes. Future research should investigate long-term cognitive trajectories and compare cognitive effects across different SSRI molecules, which may guide more personalized antidepressant selection. Specifically, identifying which SSRI agents offer the most favorable cognitive profiles could optimize functional recovery in patients with significant cognitive impairment (7,10). Future studies should address these limitations and analyse cognitive dysfunction as a distinct treatment target, aimed at improving long-term outcomes and addressing domains not already targeted by anti-depressant medication (9).

The investigation of adjunctive cognitively enhancing agents to be used alongside current antidepressants in the MDD population is merited, particularly given the known persistence of cognitive dysfunction during remission and the demonstrated small positive effect of antidepressants on delayed recall and psychomotor speed (11). In summary, this study demonstrates that SSRI treatment yields significant improvements in both depressive symptom severity and specific cognitive domains, particularly attention and memory, although deficits in processing speed and executive function may persist despite adequate mood response (6,7). These findings suggest that while SSRIs are effective for mood stabilization and certain cognitive improvements, residual cognitive deficits may require targeted interventions beyond standard antidepressant therapy to achieve full functional recovery (9,12). Therefore, a comprehensive treatment approach that integrates pharmacotherapy with cognitive remediation strategies may be necessary to address the multifaceted nature of cognitive impairment in MDD (6,13). The absence of significant differences between antidepressant classes suggests that cognitive enhancement may be a generalized property of effective mood stabilization rather than a specific pharmacological mechanism unique to SSRIs (11). liver modest benefits in delayed recall and psychomotor speed, they do not significantly differ in their cognitive effects when compared across classes such as SSRIs, SNRIs, TCAs, and NDRIs (5,11). liver modest benefits in delayed recall and psychomotor speed, they do not significantly differ in their cognitive effects when compared across classes such as SSRIs, SNRIs, TCAs, and NDRIs (14). liver modest benefits in delayed recall and

psychomotor speed, they do not significantly differ in their cognitive effects when compared across classes such as SSRIs, SNRIs, TCAs, and NDRIs (15).

CONCLUSION

The study demonstrated that Selective Serotonin Reuptake Inhibitors significantly improved both depressive symptoms and cognitive performance in patients with Major Depressive Disorder. Over an 8-week treatment period, patients showed meaningful gains in attention, memory, executive function, and overall cognitive functioning. These improvements closely followed the reduction in HDRS scores, suggesting that mood stabilization plays a crucial role in cognitive recovery. While SSRIs may not fully normalize cognitive deficits, their positive impact supports their role in addressing both emotional and cognitive dimensions of depression. The study emphasizes the importance of assessing cognitive outcomes as part of routine depression management. Larger, long-term studies are recommended to further clarify the cognitive effects of individual SSRIs and to explore whether specific agents confer unique cognitive advantages. Current evidence indicates that while antidepressants demonstrate a significant positive effect on psychomotor speed and delayed recall, pooled results from head-to-head trials of SSRIs, SNRIs, TCAs, and NDRIs have not revealed statistically significant differences in cognitive effects between these classes. This lack of differentiation implies that cognitive recovery may be mediated primarily by the alleviation of depressive symptoms rather than by class-specific pharmacological actions.

REFERENCES

[1] Colwell M, Tagomori H, Chapman S, Gillespie A, Cowen PJ, Harmer CJ, et al. Pharmacological targeting of cognitive impairment in depression: recent developments and challenges in human clinical research. Translational Psychiatry [Internet]. 2022

[2] Sayyah M, Eslami K, AlaiShehni S, Kouti L. Cognitive Function before and during Treatment with Selective Serotonin Reuptake Inhibitors in Patients with Depression or Obsessive-Compulsive Disorder. Psychiatry Journal [Internet]. 2016 Jan 1 [cited 2026 Feb];2016:1. Available from: https://doi.org/10.1155/2016/5480391

[3] Liu L, Lv X, Zhou S, Liu Q, Wang J, Tian H, et al. The effect of selective serotonin reuptake inhibitors on cognitive impairment in patients with depression: A prospective, multicenter, observational study. Journal of Psychiatric Research [Internet]. 2021 Jun 14

[4] Popović D, Vieta E, Fornaro M, Perugi G. Cognitive tolerability following successful long term treatment of major depression and anxiety disorders with SSRi antidepressants. Journal of Affective Disorders [Internet]. 2014 Nov 17

[5] Schulkens JEM, Deckers K, Jenniskens M, Blokland A, Verhey FRJ, Sobczak S. The effects of selective serotonin reuptake inhibitors on memory functioning in older adults: A systematic literature review. Journal of Psychopharmacology [Internet]. SAGE Publishing; 2022 Apr 29

[6] Dam VH, Stenbæk DS, Köhler-Forsberg K, Ip CT, Ozenne B, Sahakian BJ, et al. Evaluating cognitive disturbances as treatment target and predictor of antidepressant action in major depressive disorder: A NeuroPharm study. Translational Psychiatry [Internet]. 2022 Nov 8

[7] Bortolato B, Miskowiak KW, Köhler CA, Maes M, Fernandes BS, Berk M, et al. Cognitive remission: a novel objective for the treatment of major depression? BMC Medicine [Internet]. BioMed Central; 2016 Jan 22 [cited 2025 Oct];14(1). Available from: https://doi.org/10.1186/s12916-016-0560-3

[8] Rani S, Sindhu N, Saini R, Pandey AK, NARWAT A, Garg S. COMPARISON OF THE EFFECTS OF ANTIDEPRESSANTS ON COGNITION FUNCTIONS IN PATIENTS OF MAJOR DEPRESSIVE DISORDERS IN TERTIARY CARE HOSPITAL IN HARYANA. Asian Journal of Pharmaceutical and Clinical Research [Internet]. 2021 Mar 7 [cited 2025 Sep];134. Available from: https://doi.org/10.22159/ajpcr.2021.v14i3.40467

[9] Shilyansky C, Williams LM, Gyurak A, Harris A, Usherwood T, Etkin A. Effect of antidepressant treatment on cognitive impairments associated with depression: a randomised longitudinal study. The Lancet Psychiatry [Internet]. 2016 Mar 16 Available from: https://doi.org/10.1016/s2215-0366(16)00012-2

[10] Cai Y, Zhu Z, Li RH, Yin X, Chen RF, Man LJ, et al. Association between increased serum interleukin-8 levels and improved cognition in major depressive patients with SSRIs. BMC Psychiatry [Internet]. 2023 Feb 23 . Available from: https://doi.org/10.1186/s12888-023-04616-z

[11] Rosenblat JD, Kakar R, McIntyre RS. The Cognitive Effects of Antidepressants in Major Depressive Disorder: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. The International Journal of Neuropsychopharmacology [Internet]. University of Oxford; 2015 Jul 25
[12] Zuckerman H, Pan Z, Park C, Brietzke E, Musial N, Shariq AS, et al. Recognition and Treatment of Cognitive Dysfunction in Major Depressive Disorder. Frontiers in Psychiatry [Internet]. Frontiers Media; 2018 Dec 4 . Available from: https://doi.org/10.3389/fpsyt.2018.00655
[13] Gałecki P. Mechanisms Underlying Neurocognitive Dysfunctions in Recurrent Major Depression. Medical Science Monitor [Internet]. 2015 Jan 1. Available from: https://doi.org/10.12659/msm.893176
[14] Boschloo L, Hieronymus F, Lisinski A, Cuijpers P, Eriksson E. The complex clinical response to selective serotonin reuptake inhibitors in depression: a network perspective. Translational Psychiatry [Internet]. 2023 Jan 21
[15] Ainsworth NJ, Mulsant BH. The relationship between cognition and the pharmacotherapy of depression. Expert Opinion on Pharmacotherapy [Internet]. 2025 Dec 12