Section: Miscellaneous

Original Research Article

THE EFFECT OF BRIVARACETAM MONOTHERAPY ON COGNITION IN PATIENTS WITH EPILEPSY: A PROSPECTIVE STUDY

Balachandran M[1], Thelengana A[2], Roghan Balaji R[3], Reveda M[3], Rajalakshmi M[4], Reenaa Mohan[5]

[1]*Assistant Professor, Department of Neurology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.*
[2]*Associate Professor, Department of General Medicine, Sri Venkateshwaraa Medical College Hospital & Research Centre, Puducherry, India.*
[3]*Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.*
[4]*Associate Professor, Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.*
[5]*Assistant Professor, Department of Community Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.*

Received *: 10/09/2025*
Received in revised form *: 30/10/2025*
Accepted *: 15/11/2025*

Corresponding Author:
Dr.Balachandran M,
Assistant Professor, Department of Neurology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry, India.
Email:mbalachandran31@gmail.com

DOI: 10.70034/ijmedph.2025.4.355

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 1981-1983

ABSTRACT

Background: Cognitive impairment is a common comorbidity in epilepsy. Antiseizure medications (ASMs) can impact cognition positively or negatively. Brivaracetam (BRV), a selective synaptic vesicle protein 2A (SV2A) ligand, is known for its favorable neuropsychiatric profile. Limited data exist regarding its short-term effects on cognition. **Objective:** To prospectively evaluate cognitive outcomes after 1 month of brivaracetam monotherapy in patients with epilepsy.
Materials and Methods: Forty-six patients with epilepsy, newly initiated on BRV monotherapy, underwent cognitive assessment before treatment and after 1 month using standardized neuropsychological tests. McNemar's test assessed pre–post differences.
Results: No statistically significant changes in cognitive performance were observed across all domains ($p > 0.05$). Minor numerical differences suggested cognitive stability.
Conclusion: Brivaracetam monotherapy does not impair cognition in the short term and can be considered a cognitively safe ASM.
Keywords: Brivaracetam, epilepsy, cognition, monotherapy, antiseizure medication, neuropsychology.

INTRODUCTION

Epilepsy is often associated with cognitive and behavioral comorbidities, which can result from seizures, interictal discharges, and ASM therapy. Preserving cognition while controlling seizures is a key therapeutic goal. Older ASMs such as topiramate or valproate may impair attention, memory, and psychomotor function,[1-4] whereas newer ASMs, including brivaracetam (BRV), have been suggested to have minimal cognitive impact.[5,6] BRV is a high-affinity SV2A ligand, rapidly absorbed, with linear pharmacokinetics and minimal drug interactions.[7,8]
This study prospectively evaluated short-term cognitive outcomes (1 month) in patients with epilepsy on BRV monotherapy.

MATERIALS AND METHODS

Study Design and Participants
This was a prospective observational study conducted at a tertiary epilepsy center. The study was conducted after obtaining approval from the Institutional Ethics Committee. Informed consent was taken from all study participants. Forty-six patients aged ≥12 years, newly initiated on BRV monotherapy, were included.
Inclusion Criteria
Patients eligible for the study were those with epilepsy who was newly initiated on brivaracetam monotherapy, aged 12 years or older, and who provided written informed consent either personally or via their guardians.

Exclusion Criteria

Patients were excluded if they refused consent, were younger than 12 years, had gross baseline mental subnormality, or suffered from severe internal organ disease. Additionally, individuals with alcohol or substance abuse or with major neurological or psychiatric comorbidities including autism, cerebral palsy, severe depression, or encephalopathy or those with associated speech or hearing impairments were excluded from participation.

Drug Administration

Brivaracetam was initiated at 50 mg twice daily and titrated as clinically indicated. Compliance was ensured through follow-up visits.

Cognitive Assessment

Cognitive tests were performed before treatment and 1 month after initiation of brivaracetam monotherapy. A comprehensive battery of standardized neuropsychological assessments was used to evaluate multiple cognitive domains. Attention and processing speed were assessed using the Trail Making Test Part A (TMT-A),[9] while executive function and mental flexibility were evaluated with the Trail Making Test Part B (TMT-B)9 and the Verbal Fluency Test (VFT).[10] Psychomotor speed and working memory were measured with the Digit Symbol Substitution Test (DSST),[11] and selective attention and inhibitory control were assessed using the StroopColor-Word Test.[12] Frontal lobe executive functions were screened with the Frontal Assessment Battery (FAB),[13] and global cognitive function was evaluated using the Addenbrooke's Cognitive Examination III (ACE-III).[14]

Each test was administered according to standardized protocols, and scores were categorized as normal or abnormal based on established normative data. This battery was chosen because it provides a multidimensional assessment of cognition, capturing attention, executive function, memory, psychomotor speed, and global cognitive status. Using a combination of brief screening tools (FAB, ACE-III) and domain-specific tests (TMT, DSST, Stroop, VFT) allows detection of subtle changes in cognitive performance after short-term pharmacotherapy.

Statistical Analysis: McNemar's test compared categorical pre- and post-treatment outcomes. Significance threshold: $p < 0.05$. Percentage differences and 95% confidence intervals were calculated.

RESULTS

Patient Characteristics

A total of 46 patients completed the study, comprising 24 females (52.2%) and 22 males (47.8%), with a mean age of 37.8 ± 11.9 years. All patients were newly initiated on brivaracetam monotherapy, with an average dose of 100 ± 30 mg/day, ranging from 50 to 200 mg/day over the 1-month follow-up period. Comorbid conditions were present in a small proportion of patients, including hypertension (13%) and diabetes (8.7%). No concomitant anti-seizure medications were used, as all participants were on BRV monotherapy, and no adverse events or discontinuations were reported during the study period.

Cognitive Outcomes

Table 1 shows cognitive outcomes before and 1 month after BRV monotherapy.

Interpretation of Findings

Across all cognitive assessments, no significant differences were observed between pretest and post-test results after 1 month of brivaracetam monotherapy ($p > 0.05$). The Verbal Fluency Test demonstrated complete stability, with no change in the distribution of normal or abnormal scores. Although slight numerical declines were noted in the Trail Making Test Part B, Digit Symbol Substitution Test, and Addenbrooke's Cognitive Examination III (ACE-III) scores, these changes were not statistically significant. Overall, cognitive performance remained stable across attention, executive function, and global cognitive domains, suggesting that brivaracetam monotherapy does not adversely affect cognitive function in patients with epilepsy over the short-term follow-up period.

Table 1: Cognitive Outcomes Before and After Brivaracetam Monotherapy (n = 46)

Clinical outcomes	Pretest n (%)	Post test n (%)	McNemar's test (*p* value)	Difference %	95% Confidence Interval
Trail A Normal Abnormal	 43(93.5) 3(6.5)	 42 (91.3) 4(8.7)	1	2.17%	2.04% to 6.39%
Trail B Normal Abnormal	 41(89.1) 5(10.9)	 38(82.6) 8(17.4)	0.25	6.52%	-0.61% to 13.66%
Digit symbol substitution test Normal Abnormal	 41(89.1) 5(10.9)	 39(84.8) 7(15.2)	0.5	4.35%	-1.55% to 10.24%
Stroop colour word score Normal Abnormal	 38(82.6) 8(17.4)	 10(78.3) 36(21.7)	0.62	4.35%	-4.08% to 12.78%
Verbal fluency test Normal Abnormal	 41(89.1) 5(10.9)	 41(89.1) 5(10.9)	1	0.00%	6.03% to 6.03%

Frontal Assessment Battery Normal Abnormal	39(84.8) 7(15.2)	38(82.6) 8 (17.4)	1	2.17%	-5.18% to 9.53%
Addenbrooke cognition examination (ACE-III) Normal Abnormal	39(84.8) 7(15.2)	37(80.4) 9(19.6)	0.625	4.35%	-4.08% to 12.78%

DISCUSSION

This prospective study evaluated the cognitive effects of BRV monotherapy in patients with epilepsy. Over the 1-month follow-up, no statistically significant changes were observed across multiple cognitive domains, including attention, executive function, memory, psychomotor speed, and global cognition. These findings are consistent with previous studies reporting a favorable cognitive profile for BRV, even compared with older ASMs known to cause cognitive slowing.[1-8]

The cognitive neutrality of BRV is likely related to its selective binding to synaptic vesicle protein 2A (SV2A), which modulates neurotransmitter release without broadly affecting excitatory or inhibitory signaling in the CNS.[5,6]Unlike topiramate or valproate, which interferes with GABAergic and glutamatergic pathways leading to sedation and attentional deficits,[1-4]BRV avoids these off-target effects. Its rapid CNS penetration and linear pharmacokinetics minimize fluctuations in plasma and brain concentrations, reducing the risk of transient cognitive impairment.[5,6]

Comparative studies suggest BRV may be particularly beneficial for patients with preexisting cognitive vulnerabilities, including working-age adults, students, and individuals with epilepsy-related cognitive deficits.[,2,7,8]Unlike older ASMs, which can induce daytime sleepiness, slowed psychomotor function, and impaired executive function,[1-4]BRV allows seizure control without sacrificing cognitive performance. This is supported by the stability observed across TMT, DSST, VFT, Stroop, FAB, and ACE-III scores.[9-14]

The absence of significant cognitive change in short-term BRV therapy has practical implications for clinical decision-making. Preserving cognition while achieving seizure control is critical, particularly in populations for whom cognitive performance directly impacts quality of life. Thus, BRV may offer a clinically meaningful advantage as monotherapy, especially for individuals at risk of cognitive decline from other ASMs.

However, the study has limitations. The small sample size and lack of a control group may limit detection of subtle cognitive changes or rare adverse events. Additionally, the 1-month follow-up may not capture cumulative or delayed cognitive effects. Future research should include longer-term studies, larger samples, and quantitative computerized cognitive assessments to enhance sensitivity in detecting minor changes.[9-14]

In conclusion, BRV monotherapy is associated with stable cognitive performance across attention, executive, memory, psychomotor, and global domains in patients with epilepsy. Its favorable cognitive profile, combined with efficacy and tolerability, underscores BRV's potential as a first-line monotherapy or alternative for patients sensitive to cognitive side effects of other ASMs.

CONCLUSION

In conclusion, BRV monotherapy is associated with stable cognitive performance across attention, executive, memory, psychomotor, and global domains in patients with epilepsy. Its favorable cognitive profile, combined with efficacy and tolerability, underscores BRV's potential as a first-line monotherapy or alternative for patients sensitive to cognitive side effects of other ASMs.

Conflicts of interest: Nil

Sources of funding: Nil

REFERENCES

1. Mula M, Trimble MR. Antiepileptic drug-induced cognitive adverse effects: potential mechanisms and prospects for intervention. CurrOpin Neurol. 2009;22(2):159–165.
2. Meador KJ, et al. Cognitive effects of antiepileptic drugs. Epilepsy Behav. 2007;11(1):1–10.
3. Loring DW, Meador KJ. Cognitive side effects of antiepileptic drugs. Epilepsy Behav. 2001;2(4):209–215.
4. Aldenkamp AP, et al. Cognitive effects of antiepileptic drugs in children. Epilepsia. 2004;45(9):1017–1024.
5. Abou-Khalil B, et al. Brivaracetam as adjunctive therapy for uncontrolled partial-onset seizures: a randomized, double-blind, placebo-controlled trial. Epilepsia. 2014;55(1):57–66.
6. Biton V, et al. Efficacy and tolerability of brivaracetam in adults with refractory partial-onset seizures. Epilepsy Res. 2016; 124:16–24.
7. French JA, et al. Long-term safety and efficacy of brivaracetam in patients with epilepsy. Epilepsia. 2017;58(5):1031–1040.
8. Sills GJ. The mechanisms of action of brivaracetam. Epilepsy Res. 2008;80(1):10–17.
9. Reitan RM. Trail Making Test: Manual for Administration and Scoring. Tucson, AZ: Reitan Neuropsychology Laboratory; 1992.
10. Lezak MD, et al. Neuropsychological Assessment. 5th ed. Oxford University Press; 2012.
11. Wechsler D. Wechsler Adult Intelligence Scale–Fourth Edition (WAIS–IV). San Antonio, TX: Pearson; 2008.
12. Stroop JR. Studies of interference in serial verbal reactions. J Exp Psychol. 1935;18(6):643–662.
13. Dubois B, et al. The FAB: a frontal assessment battery at bedside. Neurology. 2000;55(11):1621–1626.
14. Hsieh S, et al. Validation of the Addenbrooke's Cognitive Examination III in frontotemporal dementia and Alzheimer's disease. Dement GeriatrCognDisord. 2013;36(3–4):242–250.