Neuropsychological Profile of Cenobamate: Evidence from a Real-World Cohort with Drug-Resistant Epilepsy

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AIMS

Antiseizure medications (ASMs) can impair cognitive domains such as attention, executive function, and memory, potentially affecting adherence and quality of life. Cenobamate (CNB) has been approved as adjunctive therapy for drug-resistant focal-onset seizures[1]. CNB's impact on cognitive functions is a relevant concern but has been poorly explored, with only preliminary data indicating a low incidence of related adverse effects[2,3]. Our study investigates potential cognitive and affective changes associated with adjunctive CNB treatment through comprehensive neuropsychological evaluations.

MATERIALS AND METHODS

We consecutively enrolled 25 individuals (15 females; mean age: 43±14.3 years). Inclusion criteria were: age ≥18 years; diagnosis of drug-resistant epilepsy; stable ASMs polytherapy regimen for at least six months; eligibility to receive CNB as adjunctive therapy; availability of baseline cognitive assessment performed within 12 months prior to CNB initiation. CNB was titrated according to recommended schedule.

All participants underwent a neuropsychological battery at baseline and follow-up visits within a predefined window of 3 to 12 months after reaching target-dose of CNB (200 mg): **Rey Auditory Verbal Learning Test** (RAVLT I and D) and **Rey–Osterrieth Complex Figure Test**; **Digit Span Forward and Backward**; **Weigl Colour-Form Sorting Test** and **Stroop Colour and Word Test**; **FAS Verbal Fluency Test**; **State-Trait Anxiety Inventory** and **Beck Depression Inventory-II** (BDI-II); **Quality of Life in Epilepsy Inventory – 31 items** (QOLIE-31); **Difficulties in Emotion Regulation Scale 36** (DERS-36); **Barratt Impulsiveness Scale** (BIS-11); **Apathy Evaluation Scale** (AES).

Longitudinal changes between baseline and follow-up were analyzed using linear mixed models with random intercepts, with model assumptions verified and FDR correction. Descriptive statistics, mean score changes, and Hedges'-corrected Cohen's *d* were calculated to estimate effect size.

RESULTS

The **mean observation period** between baseline (BL) and follow-up (FU) assessments was **9.4±2.9 months**. At follow-up, 17 (68%) subjects experienced a >50% reduction in seizure frequency, 4 (16%) became seizure-free and 4 (16%) showed no change. Significant improvements between baseline and follow-up visit emerged in several neuropshycological outcomes, as summarized in Table 1.

	Baseline	Follow-up	IC 95%	Estimated Difference			
Test	**M(sd)**	**M(sd)**	**min/max**	**Δ FU-BL**	**p-value**	**Cohen d**	**n**
RAVLT I	30,4(8,7)	33,6(11)	1,5/5,6	3,57	0.0007	0.64	22
BDI – II	17,44(10,07)	13,03(10,20)	-8,10/-0,72	-4.41	0.019	-0.44	25
QOLIE-31	48,45(15,48)	53,28(16.21)	1,31/9,03	5,17	0.008	0.51	25
DERS-36	89,6(28,76)	78,8(26,76)	-14,39/-5,23	−9.8	<0.001	-1,36	25
AES	46,44(13.85)	38,14(9,44)	-15,86/-7,21	-11.5	<0.001	-0.99	25
BIS-11	68,04(8,42)	62,23(7,99)	−7.45, −4.17	-5.81	<0.001	-1.36	25

Table 1. *Changes in neuropsychological test scores between baseline and follow-up. Mean (M) and standard deviation (sd) values are reported for each time point, along with estimated differences (Δ), 95% confidence intervals (CI), p-values, and Hedges'-corrected Cohen's d effect sizes.*

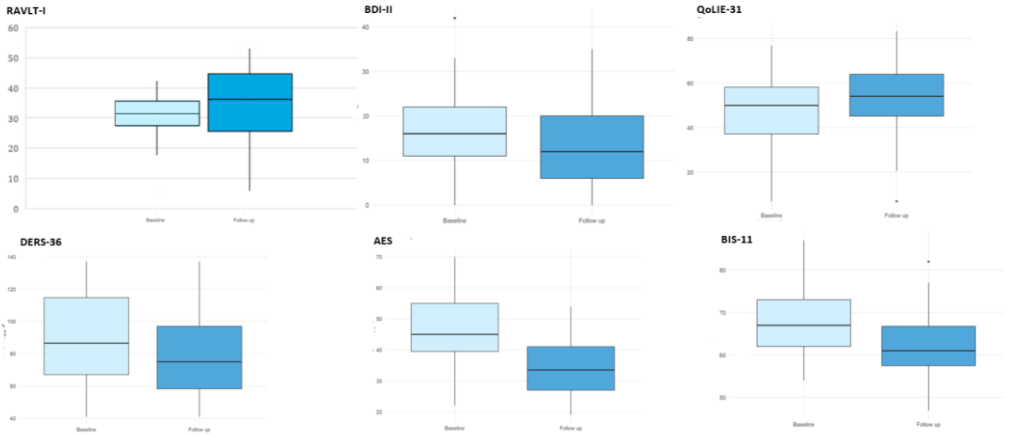

Figure 1. *Boxplots of neuropsychological test scores at baseline and follow-up*

DISCUSSION AND CONCLUSION

Our study demonstrates significant improvements in **immediate verbal memory, depressive symptoms, emotion regulation, impulsivity, apathy,** and **quality of life** following adjunctive cenobamate therapy. All other neuropsychological domains remained stable, suggesting favourable cognitive safety profile for CNB. These effects occurred alongside reductions in seizure burden, which is known to correlate with cognitive status. In this real-world cohort, adjunctive CNB therapy was associated with clinical seizure reduction and stable or improved cognitive and affective performances. These results support the cognitive safety and potential benefits of CNB within ASMs polytherapy, although larger studies are needed to confirm these results.

References

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