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Analysis of Cognitive Status Before and After Cannabidiol Treatment in Adult Patients with Focal Drug-Resistant Epilepsy

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Abstract

Objective: The aim of this study is to assess the cognitive status in adult patients with focal drug-resistant epilepsy before and after the use of cannabidiol (CBD).

Method: A prospective, observational, open-label, prospective cohort study was conducted with an uncontrolled before-after design. Patients aged 18 to 60 years, recruited from a public hospital in Buenos Aires, Argentina. The follow-up period for each subject was 6 to 9 months. We analyzed by specific domain: episodic memory verbal and non-verbal, language, executive functions and attention.

Results: Forty-four patients were included. They were separated into three groups regarding treatment efficacy: responders (n = 38), non-responders (n = 5) and worsening (n = 1).

In the responders group we found statistically significant improvements in verbal memory, visual memory, language, sustained attention and alternating attention. In the non-responders and worsening group, we found significant improvements in verbal memory and visual memory.

Conclusion: Our results suggest that, unlike conventional anti-seizure therapies, CBD does not have a negative impact on the cognitive status of patients. Notably, we found an improvement in verbal and visual memory, language and attention.

Keywords: *Epilepsy; Cannabidiol; Cognition*

Introduction

In patients with drug-resistant epilepsy the cognitive domains frequently reported to be affected are memory, attention, language and executive functions [1-7]. There are different hypotheses about the relationship between cognitive impairment in this type of epilepsy. Some research [8] describes static factors, as brain lesions (developmental or acquired), and dynamic factors, as active epilepsy, seizures and epileptic discharges, even after a first crisis [9], effects of anti-seizure medications, and psychiatric comorbidities [10-12]. These factors are not necessarily independent of each other. Furthermore, the age of epilepsy onset [8] and disease duration [13] are also relevant variables in studies of cognitive impairment in epilepsy. In addition, the presence of psychiatric comorbidities can negatively impact cognitive performance [14-16].

There is limited research on the effects of CBD on cognition in adult patients with epilepsy. A 2021 systematic review by Lattanzi., *et al*. examined the use of CBD in patients with various epileptic conditions, no cognitive adverse effects were found in either adult or pediatric populations [17]. Similar results were reported by other authors [18-20].

CBD is currently the only cannabinoid drug that has demonstrated anticonvulsant activity in well-designed randomized placebo-controlled trials [21-23]. Our group recently demonstrated the efficacy and tolerability of cannabidiol (CBD) in adult patients with treatment-resistant focal epilepsy [24]. In the same population, we also found a beneficial effect of CBD on symptoms of depression and anxiety [16].

Aim of the Study

The aim of the present work was to investigate the cognitive status, in each cognitive domain, memory, attention, language and executive functions before and after treatment with CBD in patients with drug-resistant epilepsy. We analyzed the same population that was studied to evaluate the efficacy of CBD treatment [24] and the impact of psychiatric comorbidities [16].

Materials and Methods

Prospective, observational, open cohort study, evaluated using an uncontrolled before-after design (time series). Patients aged 18 - 60 years, recruited at the Neurosciences Section, Epilepsy, of the Hosp. El Cruce "N. Kirchner" of Florencio Varela (HEC), were included. The neuropsychological assessment was conducted at baseline (month 0) prior to initiating CBD treatment and was repeated after six months of treatment (endpoint).

A commercial preparation of standardized cannabidiol (standardized hemp seed) oil (Hemp Oil RSHO-X 21 mg CBD c/1 ml, 236 ml) was used for CBD treatment.

An electronic medical record (OPEN MRS) made for patients with epilepsy and the digitized medical record of the HEC was accessed. The medical records detailed: demographics, seizure type, seizure frequency, current treatment, pharmacological history of antiepileptic drugs received, neuropsychological reports, and additional reports of imaging and neurophysiology studies.

Inclusion criteria:

- Adult patients aged 18 - 60 years, with drug-resistant epilepsies defined as those who did not respond to traditional and new antiepileptic drugs, and/or ketogenic diet, and/or vagus nerve stimulation, and who are not candidates for surgery or did not respond to surgery.
- Seizure frequency is greater than or equal to 2 seizures per month in the last 4 months, as defined by the patient according to their seizure diary.
- Included in the CBD trial [24]. All patients were evaluated with the Neurosciences Service protocol (video-EEG, brain MRI, neuropsychological evaluation, psychiatric evaluation) [25].
- Patients who completed the following questionnaires during their first and last visit: Quality of Life in Epilepsy Inventory-10 (QOLIE-10) [26]; Beck Depression Inventory - II (BDI II) [27]; Beck Anxiety Inventory (BAI) [28].
- Patients who have completed minimum primary level of schooling education.
- Signed informed consent form.

Exclusion criteria:

- Epileptic seizures secondary to metabolic, toxic, infectious, infectious, psychogenic, drug abuse and acute illness-related disorders.
- Patients who are pregnant or breastfeeding.
- Cardiac, renal, hepatic, pancreatic or hematologic dysfunction.
- Patients with chronic liver disease.
- Hypersensitivity to any of the components of CBD.
- Progressive or degenerative neurological disease.
- Use of cannabidiol during the last month (commercial or artisanal) in regular intake.
- Presence of status epilepticus in the last year.
- Lennox Gastaut Syndrome; Syndrome Dravet; encephalopathy epileptic.
- Psychosis.

Neuropsychological assessment

Neuropsychological assessment was performed with the protocol of our center [2] (Table 1). The assessment was carried out before starting treatment with CBD, at baseline (month 0) and was repeated after six months of treatment (endpoint). Neuropsychological performance was compared with normative data adjusted for age, sex, and level of formal education. Raw scores obtained from each cognitive test were transformed into Z scores for individual analyses. Tests were subsequently grouped according to the cognitive domain assessed. Participants were classified as having normal cognitive performance when all test scores were above a Z score of −1, and as abnormal when at least one score was below a Z score of −1.5. Each assessment session began with a semi-structured clinical interview, followed by administration of the neuropsychological test battery. The total duration of the assessment was approximately two hours, including scheduled breaks between tasks. All evaluations were conducted by the same examiner (IM) and supervised by a neuropsychology team blinded to participants' group allocation (pre- or post-treatment).

Verbal memory

The Rey auditory-verbal learning test (RAVLT) [29] is a task that assesses verbal memory and consists of reading a list of 15 words that the patient must repeat in order to achieve learning.

At the end, a second list (B) of interferences is presented, which the patient must repeat and then repeat the first list (A) again to assess immediate recall. After 30 minutes, the patient is asked to recall list A, assessing delayed recall. The last stage of this test (Recognition) consists of multiple-choice recognition of five alternatives.

Visual memory

Rey Complex Figure Test (RCF) [30] assesses non-verbal material memory. The test requires the copying of a complex, abstract figure. After copying, the figure must be reproduced immediately (immediate recall) and after 30 minutes (delayed recall). Finally, a multiple-choice recognition task is performed (recognition).

Language

Boston Abbreviated Test, Verbal Fluency. The Boston Naming Test (abbreviated) [31] is a visual confrontation naming task in which the patient is presented with 60 printed pictures of increasing complexity according to frequency of use. The patient must denominate

the figure presented. This allows lexical access to be assessed. Verbal fluency (VF) is the ability to produce spontaneously fluent speech, and to search for words without glitches or pauses. Within VF, both Phonological Verbal Fluency (PFF) and Semantic Verbal Fluency (SVF) are assessed [32]. In both, the patient is asked to evoke words in one minute with certain restrictions: in PFVF he/she must say as many words beginning with a letter (i.e. P) as possible, except for proper nouns. During the FVS assessment, he/she must say as many words as possible that belong to a certain category (i.e. animals).

Executive functions

INECO Frontal Screening (IFS) [33] is a screening tool for executive functioning, which consists of several tasks: motor series, conflicting instructions, go no-go, digits backwards, months backwards, Corsi cubes, proverbs and the Hayling Test. The executive functions assessed by this screening test are: programming, sensitivity to interference, inhibitory control (motor and verbal), working memory (visual and verbal) and abstract thought. The Trail Making Test (TMT) [34,35] part B consists of interleaving numbers and letters in increasing order. As previously mentioned, this test assesses visual-motor tracking ability, speed of response, and specifically alternating attention and working memory.

Attention

TMT and Span Digits direct [36]. The TMT is a test that consists of two parts: A and B. In part A, 25 randomly distributed numbers must be linked in an increasing and consecutive manner.

This task assesses visual-motor tracking ability, speed of response, attentional sustainment and working memory. Span, patients are asked to repeat a series of digits that gradually become longer. The maximum number of digits that the patient can repeat in the correct order constitutes the raw score.

Intelligence quotient

WASI test [36]. It is a scale for estimating global cognitive performance that includes two subtests of the WAIS (Wechsler Adult Intelligence Scale) for the Executive Scale: Block Design and Progressive Matrices Test, and two subtests for the Verbal Scale: Vocabulary and Analogies.

Cognitive domain	Test
Verbal memory	Rey Auditory Verbal Test (RAVLT)
Visual memory	Rey Complex Figure Test (RCF)
Language	Boston test; Semantic verbal fluency (SVF)
Executive Functions	Ineco Frontal Screening (IFS); Phonemic verbal fluency task; Backward digit span
Attention	Trail Making Test; Digit span (DGS)
Intelligence Quotient	Wechsler Abbreviated Scale of Intelligence (WASI Test)

Table 1: *Standardized cognitive assessment protocol.*

Statistical analyses

To analyse the impact of CBD treatment on cognitive functions, R 4.4.2 [37] software was used and two statistical tests were employed to compare pre- and post-treatment measurements. First, the paired Student's t-test, a parametric test suitable for comparing means of dependent measurements, was applied. Secondly, as an alternative in case the assumptions of normality in the distribution of the

differences between the assessments were not met, the non-parametric Wilcoxon test was applied. The Wilcoxon test, based on the analysis of ranges, allows the assessment of significant changes without relying on the assumption of normality of the data.

Results

Demographic and clinical data

The data presented corresponds to the 44 patients who completed the clinical trial. Age at seizure onset was between 19 and 60 years (mean 35, SD 10), with 66% being female. The mean baseline seizure frequency per month at the first visit was 51 (SD 63), with a median of 33. Twenty-three (52%) had focal seizures that progressed to bilateral, with a mean of 3.5 (SD 6). The median time with epilepsy was 21 years (SD 14). In regards to etiology, 20 patients (46%) had cortical developmental malformations, four (9%) hippocampal sclerosis, three (7%) gliosis on brain MRI without other lesion, one (2%) tumor (primitive neuroectodermal tumors or gangliogliomas), one (2%) inflammatory etiology, one (2%) vascular malformation, one (2%) tuberous sclerosis complex and 13 (30%) non-lesional epilepsy.

In terms of schooling, 6 patients (13.63%) have completed primary level, 35 patients (79.55%) started and/or completed secondary school, and 3 patients (6.82%) have higher education.

After treatment with CBD, to assess seizure frequency, patients were categorized into three groups based on the percentage change in seizure frequency: Responders: Decrease number of seizures 50% or more, (38 patients, 86%); Non-responders: Decrease number of seizures between 0-50%, (5 patients, 11%) and Worsening: increase number of seizures, (one patient, 2%).

In regards to psychiatric aspects [16], depression prior to CBD treatment, 22 of 44 patients (50%) met the criteria for depression according to the Beck Depression Inventory-II (BDI-II).

Following 6 months of CBD treatment, a significant improvement ($p = 0.001$) was observed in 21 (95.4%) of the patients with depression. The quality of life was evaluated with QOLIE-10, before CBD treatment, the median score for the entire population was 24.5 points, indicating normal quality of life. After CBD treatment, 30 patients (68%) reported an improvement in QOLIE, 4 (9%) remained unchanged, and 10 (22.7%) experienced a decline. The patient who experienced an increase in seizure frequency after CBD treatment did not exhibit any changes in QOLIE-10 scores.

A significant direct relationship was found between BDI-II and QOLIE-10 scores at baseline and the final trial visit ($p < 0.036$ and < 0.001, respectively), indicating that improvement in depressive symptoms correlates with improved quality of life.

In relation to anxiety symptoms, analyzed with HADS before CBD treatment, 24 (54.5%) patients exhibited anxiety symptoms. After 6 months of CBD treatment, 17 (71%) patients in the anxiety symptom group showed a significant improvement, 4 (16.6%) patients remained unchanged, and 3 (12.5%) experienced an increase in anxiety symptoms.

Cognitive results

For the analysis of baseline and control outcomes, patients were separated into the previously mentioned groups: responders ($n = 38$) and non-responders ($n = 5$). The worsening group consists of only one patient, which is why it is excluded from the statistical analysis (Table 2).

Analysis by domains

Prior to CBD treatment, a substantial proportion of participants exhibited deficits in several cognitive domains. Specifically, [36.96%] demonstrated impairments in immediate verbal recall, while [32.61%] and [8.70%] showed deficits in delayed verbal recall and verbal recognition, respectively. Similarly, [67.39%], [65.22%], and [70.45%] displayed impairments in immediate visual recall, delayed visual recall, and Boston Naming Test performance, respectively.

Following CBD treatment, significant improvements were observed. For instance, the proportion of participants without deficits in immediate verbal recall increased to [63.04%], while those without deficits in delayed verbal recall and verbal recognition rose to [91.30%] and [95.65%], respectively. Similar trends were observed in other cognitive domains, such as semantic fluency ([41.30% to 60.87%]), Trail Making Test B ([72.09% to 40.91%]), and digit span ([47.83% to 58.70%]) (Table 2).

Of the initial 44 patients, 2 patients were excluded: one due to a worsening of her general condition, for reasons other than epilepsy and CBD treatment, and one due to missing data.

The results presented correspond to the remaining 42 patients.

Analysis of changes in cognitive performance pre- and post-treatment with CBD using paired t-tests revealed statistically significant improvements ($p < 0.05$) in the following cognitive domains and their respective tasks (Table 2).

Verbal memory

Significant improvements were observed in all lists of the Rey Verbal Learning Test (RAVLT): List 1 ($p < 0.001$), List 2 ($p < 0.001$), List 3 ($p < 0.001$), List 4 ($p < 0.001$) and List 5 ($p < 0.001$). Significant improvements in immediate recall ($p < 0.001$), delayed recall ($p < 0.001$) and recognition ($p = 0.01$) were also found in this same test.

Visual memory

The analysis also indicated statistically significant improvements in the Rey-Osterrieth Complex Figure (RCF) in both immediate recall ($p < 0.001$) and delayed recall ($p < 0.001$).

Attention

Finally, a statistically significant improvement was found in the Trail Making Test part B (TMT B) task ($p = 0.02$)

Task	P Value	Cohen	Statistical	P Value Adjusted
RAVLT 1 before-after	0.00	0.74	T paired	0.00 (*)
RAVLT 2 before-after	0.00	0.69	T paired	0.01 (*)
RAVLT 3 before-after	0.00	0.77	T paired	0.00 (*)
RAVLT 4 before-after	0.00	0.68	T paired	0.00 (*)
RAVLT 5 before-after	0.00	0.73	Wilcoxon	0.01 (*)
RAVLT B before-after	0.79	-0.16	Wilcoxon	1
RAVLT immediate recall before-after	0	0.92	T paired	0.00 (*)
RAVLT delayed recall before after	0	0.86	T paired	0.00 (*)
RAVLT recognition before after	0.00	0.551316	Wilcoxon	0.012702 (*)
RCF immediate recall before after	0	0.71	T paired	0.00 (*)
RCF delayed recall before after	0	0.81	T paired	0.00 (*)
RCF recognition before-after	0.11	0.28	Wilcoxon	1
Boston Test before-after	0.07	0.26	Wilcoxon	1
SVF before-after	0.75	0	Wilcoxon	1
IFS before-after	0.23	-0.23	Wilcoxon	1
TMT B before-after	0.00	0.36	Wilcoxon	0.02 (*)

Reverse digits before-after	0.26	0	Wilcoxon	1
Phonological fluency before after	0.58	0	Wilcoxon	1
DGS before-after	0.09	0.15	Wilcoxon	1
TMT A before-after	0.00	0.31	Wilcoxon	0.09
Copy of RCF before-after	0.06	0.02	Wilcoxon	1

Table 2: *Results before-after treatment with CBD.*

RAVLT: Rey Auditory Verbal Learning Test; RCF: Rey Complex Figure; SVF: Semantic Verbal Fluency; IFS: INECO Frontal Screening; TMT: Trail Making Test; DGS: Digit span.

Due to the continuous nature of the scores obtained in the cognitive assessments, linear models implemented in R statistical software were used to investigate the relationship between cognitive performance and mental health. The independent variables analyses were: years of epilepsy evolution, scores on depressive symptomatology scales (Beck Depression Inventory-II), scores on anxiety symptomatology scales (Beck Anxiety Inventory) and scores on quality of life scales (QOLIE-10). The results are presented in table 3.

Verbal memory

Analysis indicated positive relationships between several variables and performance on specific verbal memory subtests. Specifically, a greater number of years since epilepsy diagnosis was associated with better performance on Trial 5 ($\beta = 0.03$, $p = 0.03$). Similarly, greater perceived treatment efficacy was related to better recall in Trial 2 ($\beta = 1.04$, $p = 0.02$). Similarly, higher levels of anxiety were associated with better performance on Trial 6 ($\beta = 0.45$, $p = 0.04$), and better quality of life was linked to better recall on Trial 4 ($\beta = 0.68$, $p = 0.01$).

Visual memory

For visual memory, positive associations were observed between years since epilepsy diagnosis and immediate recall ($\beta = 0.04$, $p = 0.03$), as well as between anxiety and both immediate ($\beta = 0.52$, $p = 0.04$) and delayed recall ($\beta = 0.56$, $p = 0.02$). These findings suggest that longer duration of epilepsy and higher levels of anxiety were related to better performance on these visual memory tasks.

Attention

Time since diagnosis of epilepsy was positively and significantly associated with performance on alternating attention ($\beta = 0.11$, $p = 0.00$) and sustained attention ($\beta = 0.13$, $p = 0.00$) tasks. This means that, in the present analysis, patients with a greater number of years since epilepsy diagnosis tended to show better performance on these specific tests of attention.

In addition to statistically significant associations ($p < 0.05$), trends towards statistical significance ($0.05 \leq p < 0.08$) were observed in the following relationships.

Verbal memory

A trend towards a proportional relationship was found between treatment efficacy and performance on Trial 3 ($\beta = 0.84$, $p = 0.078$). This suggests that greater perceived treatment efficacy may be associated with better recall on this specific verbal memory subtest, although this trend did not reach statistical significance.

Language

A trend towards an inversely proportional relationship between treatment efficacy and performance on the visual naming task of the Boston Test was identified ($\beta = -1.37$, $p = 0.06$). This suggests that greater perceived treatment efficacy may be associated with lower performance on this language task, although this relationship did not reach statistical significance in the present study.

There was a trend towards an inversely proportional relationship between years since epilepsy diagnosis and performance on the semantic fluency task (β = -0.02, p = 0.07). This preliminary finding suggests that longer duration of epilepsy may be related to lower semantic verbal fluency.

Model	Years of Epilepsy	Effectiveness	Beck (Depression)	HADS (Anxiety)	QOLIE (Quality of Life)
RAVLT 1	NS	NS	NS	NS	NS
RAVLT 2	NS	0.02 (1.40)	NS	NS	NS
RAVLT 3	NS	0.078 (0.84)	NS	NS	NS
RAVLT 4	NS	NS	NS	NS	0.01 (0.68)
RAVLT 5	0.03 (0.02)	NS	NS	NS	NS
RAVLT B	NS	NS	NS	NS	NS
RAVLT Immediate	NS	NS	NS	0.04 (0.45)	NS
RAVLT Delayed	NS	NS	NS	NS	NS
RAVLT Recognition	NS	NS	NS	NS	NS
RCF Immediate	0.03 (0.03)	NS	NS	0.04 (0.52)	NS
RCF Delayed	NS	NS	NS	0.02 (0.56)	NS
RCF Recognition	NS	NS	NS	NS	NS
BOSTON	NS	0.06 (-1.37)	NS	NS	NS
SVF	0.075 (-0.01)	NS	NS	NS	NS
IFS	NS	NS	NS	NS	NS
TMT B	0.00 (0.10)	NS	NS	NS	NS
Reverse digits	NS	NS	NS	NS	NS
Phonological fluency	NS	NS	NS	NS	NS
DGS	NS	NS	NS	NS	NS
TMT A	0.00 (0.13)	NS	NS	NS	NS
RCF Copy	NS	NS	NS	NS	NS

Table 3: *p-values of the linear models (estimate).*

RAVLT: Rey Auditory Verbal Learning Test; RCF: Rey Complex Figure; SVF: Semantic Verbal Fluency; IFS: INECO Frontal Screening; TMT: Trail Making Test; DGS: Digit span; (*): Statistically significant; NS: not significant; (#): tendency to be statistically significant.

Discussion

Our group has reported that adjuvant treatment with CBD in drug-resistant focal epilepsy is safe, effective and well tolerated at low initial doses [8]. Also, we observed a significant improvement in quality of life, anxiety and depression [9].

In adult populations with focal drug-resistant epilepsy, there are few publications assessing the cognitive effects of CBD [17-20]. Our study is the first in the Spanish-speaking population to analyze cognitive status pre- and post-treatment with CBD.

The results of this study reveal a complex picture of the impact of adjunctive CBD treatment and the influence of clinical and mental health variables on cognitive functions in patients with drug-resistant epilepsy. Prior to CBD treatment, a substantial proportion of

participants exhibited deficits in various cognitive domains. We found significant improvements in multiple cognitive domains following CBD intervention, including verbal memory (all components tested), visual memory (immediate and delayed recall) and alternating attention. These findings suggest a potentially beneficial effect of CBD on several areas of cognition in this group of patients. Similar results were found in another study [41]. Other authors did not find these benefits, but did not report negative cognitive changes due to use of CBD [18,38]. Another relevant aspect of our research is that we found no negative effects on cognition in the study population, which is usually observed with most anticonvulsant drugs.

Furthermore, linear models explored associations between patients' baseline characteristics and their cognitive performance. Surprisingly, the variable that showed the most consistent influence was time of epilepsy evolution, which was positively associated with better performance on specific verbal and visual memory tasks, as well as on both measures of attention. This counterintuitive relationship may reflect the possible influence of compensatory mechanisms developed over time or the heterogeneity of the sample in relation to disease progression and its cognitive effects. Notably, in contrast to literature-based expectations [10,12,39-42], depressive symptomatology did not appear to demonstrate a significant relationship with cognitive performance.

Larger numbers of participants, multicenter studies and longer follow-up are needed to confirm these findings and to be able to analyze the implication of seizure control on cognitive functioning, as well as the maintenance of these improvements over time and the influence of other variables (quality of life, behavior, Antiseizure medications). This is also why before and after cognitive assessments should be a necessary requirement in future clinical trials to generate more robust results.

Conclusion

This study suggests that adjunctive CBD treatment was associated with significant improvements in several cognitive domains, including verbal memory, visual memory and alternating attention, in patients with drug-resistant epilepsy. Depressive symptomatology did not demonstrate a significant influence on cognitive performance in this sample. These results highlight the potential usefulness of CBD as an adjunctive therapy to improve cognition in this population.

Bibliography

1. Lezak MD., *et al*. "Neuropsychological assessment, 5th edition". Oxford University Press (2012).

2. Oddo S., *et al*. "Mesial temporal lobe epilepsy and hippocampal sclerosis: Cognitive function assessment in Hispanic patients". *Epilepsy and Behavior* 4.6 (2003): 717-722.

3. Reyes A., *et al*. "Moving towards a taxonomy of cognitive impairments in epilepsy: application of latent profile analysis to 1178 patients with temporal lobe epilepsy". *Brain Communications* 4.6 (2022): 1-17.

4. Lomlomdjian C., *et al*. "The right hemisphere's contribution to discourse processing: A study in temporal lobe epilepsy". *Brain and Language* 171 (2017): 31-41.

5. Múnera CP., *et al*. "Memory for emotional material in temporal lobe epilepsy". *Epilepsy and Behavior* 52 (2015): 57-61.

6. Múnera CP., *et al*. "Episodic and semantic autobiographical memory in temporal lobe". *Epilepsy* (2014): 157452.

7. Jones-gotman M., *et al*. "The contribution of neuropsychology to diagnostic assessment in epilepsy". *Epilepsy and Behavior* 18.1-2 (2010): 3-12.

8. Witt JA and Helmstaedter C. "Cognition in the early stages of adult epilepsy". *Seizure* 26 (2015): 65-68.

9. Pugh R., *et al*. "Cognitive and psychological dysfunction is present after a first seizure, prior to epilepsy diagnosis and treatment at a first seizure clinic". *Epilepsia Open* 9.2 (2024): 717-726.

10. Salpekar JA and Mula M. "Common psychiatric comorbidities in epilepsy: How big of a problem is it?" *Epilepsy and Behavior* 98 (2018): 293-297.

11. Jansen C., *et al*. "Interictal psychiatric comorbidities of drug-resistant focal epilepsy: Prevalence and influence of the localization of the epilepsy". *Epilepsy and Behavior* 94 (2019): 288-296.

12. González Stivala E., *et al*. "Comorbid impulsivity after one year of epilepsy surgery". *Epilepsy and Behavior* 124 (2021): 108331.

13. Oyegbile TO., *et al*. "The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy". *Neurology* 62.10 (2004): 1736-1742.

14. Yogarajah M and Mula M. "Social cognition, psychiatric comorbidities, and quality of life in adults with epilepsy". *Epilepsy and Behavior* 100.B (2019): 106321.

15. Mula M., *et al*. "Neuropsychiatric and cognitive comorbidities in epilepsy". *Continuum (Minneap Minn)* 28.2 (2022): 457-482.

16. Lamonarca JA., *et al*. "Psychiatric comorbidities before and after cannabidiol oil treatment in patients with refractory focal epilepsy". *Epilepsy and Behavior* 160 (2024): 110032.

17. Lattanzi S., *et al*. "Highly purified cannabidiol for epilepsy treatment: a systematic review of epileptic conditions beyond Dravet syndrome and Lennox-Gastaut syndrome". *CNS Drugs* 35.3 (2021): 265-281.

18. Gaston TE., *et al*. "Effects of highly purified cannabidiol (CBD) on fMRI of working memory in treatment-resistant epilepsy". *Epilepsy and Behavior* 112 (2020): 107358.

19. Rosenberg EC., *et al*. "Quality of life in childhood epilepsy in pediatric patients enrolled in a prospective, open-label clinical study with cannabidiol". *Epilepsia* 58.8 (2017): e96-e100.

20. Thompson MD., *et al*. "Cognitive function and adaptive skills after a one-year trial of cannabidiol (CBD) in a pediatric sample with treatment-resistant epilepsy". *Epilepsy and Behavior* 111 (2020): 107299.

21. Franco V and Perucca E. "Pharmacological and therapeutic properties of cannabidiol for epilepsy". *Drugs* 79.13 (2019): 1435-1454.

22. Devinsky O., *et al*. "Effect of cannabidiol on drop seizures in the Lennox-Gastaut syndrome". *New England Journal of Medicine* 378.20 (2018): 1888-1897.

23. Miller I., *et al*. "Dose-ranging effect of adjunctive oral cannabidiol vs placebo on convulsive seizure frequency in Dravet syndrome: a randomized clinical trial". *JAMA Neurology* 77.5 (2020): 613-621.

24. Kochen S., *et al*. "Cannabidiol as an adjuvant treatment in adults with drug-resistant focal epilepsy". *Epilepsy and Behavior* 144 (2023): 109210.

25. Oddo S., *et al*. "Surgical strategies for epilepsy in developing countries: experience with SEEG in temporal lobe epilepsy". *Annals of Epilepsy and Seizures* 3.1 (2021).

26. Viteri C., *et al*. "Validación de la versión española del cuestionario de calidad de vida en epilepsia QOLIE-10". *Neurologia* 23.3 (2008): 157-167.

27. Beck AT., *et al*. "Psychometric characteristics of the scale for suicide with psychiatric outpatients". *Behaviour Research and Therapy* 35.11 (1997): 1039-1046.

28. Beck AT., *et al*. "Use of the beck anxiety and depression inventories for primary care with medical outpatients". *Assessment* 4.3 (1997): 211-219.

29. Burin DI., *et al*. "Evaluación neuropsicológica del envejecimiento: normas según edad y nivel educacional". *Revista Neurológica Argentina* 28.3 (2003): 148-152.

30. Lu PH., *et al*. "Effectiveness of the Rey-Osterrieth complex figure test and the Meyers and Meyers recognition trial in the detection of suspect effort". *Clinical Neuropsychology* 17.3 (2003): 426-440.

31. Allegri RF., *et al*. "Spanish Boston Naming Test norms". *Clinical Neuropsychologist* 11.4 (1997): 416-420.

32. Butman J., *et al*. "Spanish verbal fluency. Normative data in Argentina". *Medicina (B Aires)* 60.5 (2000): 561-564.

33. Torralva T., *et al*. "INECO Frontal Screening (IFS): A brief, sensitive, and specific tool to assess executive functions in dementia". *Journal of the International Neuropsychological Society* 15.5 (2009): 777-786.

34. Reitan RM and Tarshes EL. "Differential effects of lateralized brain lesions on the trail making test". *Journal of Nervous and Mental Disease* 129 (1959): 257-262.

35. Tombaugh TN. "Trail Making Test A and B: Normative data stratified by age and education". *Archives of Clinical Neuropsychology* 19.2 (2004): 203-214.

36. Wechsler D. Wechsler Abbreviated Scale of Intelligence WASI (1999).

37. R Core Team. _R: A Language and Environment for Statistical Computing_. R Foundation for Statistical Computing, Vienna, Austria (2024).

38. Martin RC., *et al*. "Cognitive functioning following long-term cannabidiol use in adults with treatment-resistant epilepsy". *Epilepsy and Behavior* 97 (2020): 105-110.

39. Lombardi N., *et al*. "To what extent does depression influence quality of life of people with pharmacoresistant epilepsy in Argentina?" *Epilepsy and Behavior* 69 (2019): 133-138.

40. Alessio LD., *et al*. "Psychiatric outcome of epilepsy surgery in patients with psychosis and temporal lobe drug-resistant epilepsy: A prospective case series". *Epilepsy and Behavior* 37 (2014): 165-170.

41. Metternich B., *et al*. "Cognitive and behavioral effects of cannabidiol in patients with treatment-resistant epilepsy". *Epilepsy and Behavior* 114 (2021): 107558.

42. Scévola L., *et al*. "To what extent does depression influence quality of life of people with pharmacoresistant epilepsy in Argentina"? *Epilepsy and Behavior* 69 (2017): 133-138.

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