Epilepsy & Behavior 94 (2019) 137–143

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

The neuropsychological profile of parietal and occipital lobe epilepsy

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ARTICLE INFO

Article history:
Received 28 November 2018
Revised 22 February 2019
Accepted 22 February 2019
Available online 22 March 2019

Keywords:
Posterior epilepsy
Cognitive dysfunction
Visuospatial deficits
Lurian model
Functional systems
Epileptic networks

ABSTRACT

Despite the extensive body of research in clinical neurology on the functional organization of posterior cortices, parietal and occipital lobe epilepsy (PLE and OLE) have not as yet received the attention afforded frontal and temporal lobe epilepsy (FLE and TLE), perhaps due to their low prevalence. Posterior epilepsies however, represent a challenge for epileptology in general and neuropsychological differential diagnosis in particular. Our main purpose was to examine the likely existence of a pattern of cognitive dysfunction characterizing patients suffering from seizures with a parietal and/or occipital ictal onset. We hypothesized that such patients would present difficulties in the visuospatial and visuoconstructive domains, since spatial analysis and synthesis is an inherent feature of posterior cortical systems. Participants were 14 patients with epilepsy and 14 healthy controls matched for demographic characteristics (gender, age, and education level). We used an extensive battery of neuropsychological tests to assess auditory-verbal memory and learning, episodic memory, attention and working memory, verbal abilities, haptic perception, arithmetic abilities, and executive functions. Special attention was given to visuospatial abilities. Depression and anxiety symptoms were assessed through a self-administered questionnaire. Nonparametric (Mann–Whitney *U* test) statistical tests were conducted. We found that patients with epilepsy performed significantly worse in visuoconstruction, verbal, and executive functions compared to their healthy matches. Finally, we interpret our findings from the perspective of Luria of mental functions organized into functional systems and the current trends in epileptology to view epilepsy as a system (network) problem.

1. Introduction

The neuropsychology of parietal and occipital lobe epilepsy remains relatively unexplored, as the low prevalence of these conditions prevents the recruitment of patients to form adequately large samples. Parietal lobe epilepsy (PLE) represents only 5–6% of patients suffering from focal epilepsies, while occipital lobe epilepsy (OLE) represents 5–8% [1–3]. In a series of surgical cases, PLE represented 5% of patients with focal epilepsy [4], while others [1] provided an estimate of 6.3%.

The topography of PLE's epileptogenic networks comprises areas such as the posterior central sulcus, superior and inferior parietal lobule, as well the internal parietal cortex surface. Seizures in the parietal lobe typically have a focal onset and give rise to somatosensory symptoms, suggesting an activation of the posterior central sulcus, as well the motor cortex [1,5], while loss of consciousness is not common. Some instances of paresthesia (e.g., numbness, tickling), sense of burning or limp movement have been reported [6–8], as well as aberrant body image perception, such as a sense of floating [9–12]. Other rare symptoms are vertigo, mood changes [13], and gustatory hallucinations [14]. Finally, patients with chronic PLE may rarely present aphasia, alexia, dyscalculia, and hemineglect [2,15,16]. OLE usually manifests with visual symptoms such as amaurosis, myoclonus, diplopia [17–19], and visual hallucinations [12]. Sometimes posterior seizures tend to spread to adjacent brain areas, thus confounding their clinical presentation and site of anatomical origin [2,12,20,21]. For instance, ictal activity with an occipital onset may spread to the frontal lobes (in one-third of cases), as well as to multiple other cortical sites simultaneously (in one-third of cases) [3].

Apart from the presence of interictal cognitive dysfunction, focal neuropsychological deficits may also be part of patients' ictal clinical semiology. The limited research on this topic suggests a connection between seizures emanating from the right parietal lobe and deficits in spatial and construction abilities and less often visual neglect or anosognosia, while seizures with a left parietal onset may induce problems in the domains of reading, writing, and calculation, or more generally affecting verbal abilities [22]. Occipital lobe seizures have typically been linked to visuoperceptual deficits and visual hallucinations. Posterior seizures, however, may also present a pattern of generalized cognitive dysfunction or even neuropsychological impairment typical of temporal lobe dysfunction due to the effects of seizure propagation [2].

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https://doi.org/10.1016/j.yebeh.2019.02.021
1525-5050/

Thus, neuropsychological disturbances may have a diffuse character, analogous to seizures clinical semiology and electroencephalography (EEG), often giving rise to a frontal- or a temporal-like pattern of dysfunction [15,16]. Finally, parietal damage has been linked to disturbances in spatial abilities, orientation, haptic perception, construction apraxia, and neglect [23], while occipital damage may lead to cerebral blindness, visual agnosia [24], simultagnosia [25], and visual hallucinations [26].

Our goal in undertaking the present investigation was to test for possible neuropsychological markers characterizing PLE and OLE in order to provide neuropsychological data to inform the process of differential diagnosis. We hypothesized that patients with seizures in posterior brain areas would present difficulties in their analytic–synthetic abilities concerning visuospatial processing and visuoconstruction based on the aforementioned literature.

2. Material and methods

2.1. Participants

Twenty-eight individuals participated in the present study: 14 with epilepsy and 14 healthy controls, matched on demographic characteristics (gender, age, and education level). The total sample comprised 14 women and 16 men, between 17 to 57 years of age and an educational level ranging from secondary school to university. The average age was 32.3 years (S.D. = 11) and the mean years of education completed 14.7 (S.D. = 2.2) for the control group. For the group with epilepsy the average age and the mean years of education completed were 32 (S.D. = 10.9) and 13.9 (S.D. = 2.3), respectively.

All participants were right-handed, with the exception of one ambidextrous individual (in the group with epilepsy). Hand preference was assessed with Annett's Handedness Questionnaire [27]. All patients suffered a structural etiology (four individuals had an arteriovenous malformation, six a focal cortical dysplasia, one a cavernoma, one a calcification, one a dysembryoplastic neuroepithelial tumor, and one a gliosis) and were taking antiepileptic drugs (AEDs); AED treatment varied from one to five drugs per patient (one drug: n = 4, two drugs: n = 4, three drugs: n = 5 and five drugs: n = 1). The AEDs used were the following: carbamazepine (n = 5), oxcarbazepine (n = 4), levetiracetam (n = 8), lamotrigine (n = 2), perampanel (n = 2), gabapentin (n = 1), topiramate (n = 2), lacosamide (n = 3), phenobarbital (n = 1), pregabalin (n = 1), clobazam (n = 1), and sodium valproate (n = 1). Lesions were localized in the parietal lobe (n = 4), the occipital lobe (n = 6), and parietooccipital areas (n = 3), while one patient suffered an occipital lesion extending slightly anteriorly and involving a small portion of the posterior temporal cortex.

Sensory symptoms, automatisms, and less often, autonomic symptoms represented the main ictal clinical manifestations. The majority of patients mentioned auras like numbness, dizziness, blurring, sense of burning, and vomiting. More details regarding the group with epilepsy are listed in Table 1.

Both groups had no history of psychiatric or other neurological problems. All participants were oriented to time and space and presented good oral and written language comprehension. They also gave written informed consent to take part in the study and were treated in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

2.2. Material

A host of neuropsychological tests was used to assess auditory and verbal memory and learning, episodic memory, attention and working memory, verbal abilities, haptic perception, arithmetic abilities, and executive functions. We explored visuospatial and visuoconstruction abilities more extensively than the other cognitive functions. Depression and anxiety symptoms were assessed through a self-administered questionnaire.

2.2.1. Memory tasks

Verbal memory, specifically learning, storage, and recall of new information, was assessed via a List learning and a Story learning test from a Greek neuropsychological test battery [28]. Variables of interest were immediate recall, delayed recall, and recognition in the former and immediate recall and delayed recall in the latter. The Taylor Complex Figure Test was given for the assessment of visuospatial perception and memory, including planning and organization, and variables of interest were figure copy, immediate recall, delayed recall, and recognition [29,30].

2.2.2. Attention and working memory tasks

Digit span forward and spatial span forward were used for measuring selective attention, phonological, and visual short-term memory and digit span and spatial span backwards for measuring phonological and visual working memory, respectively [31]. Trail Making Test (TMT) Part A was used to assess attention and psychomotor speed and Part B to assess mental flexibility and shifting [32,33]. Variables of interest were the correct responses on the span tests and the time needed to completion on the TMT tasks.

Table 1
Demographic and seizure information regarding the group with epilepsy.

Epilepsy group									
Sex	Age	Educational level attained	Etiology	Age of onset	Last seizure	Symptoms	Aura	L.O.C.	Secondarily generalized seizures
Male	25	University	Calcification	<1	2014	Numbness on L side, blurring, tonic–clonic seizures	No	Yes	No
Male	25	University	Arteriovenous malformation	14	2008	Blurring, tonic–clonic seizures	Yes	Yes	No
Male	35	High school	Arteriovenous malformation	5	2017	Absence, tongue numbness, blurring, jaw contractions	Yes	Yes	Yes
Female	29	High school	Cavernoma	6	2017	Sense of burning and pinching on L side, absence	Yes	No	No
Female	34	High school	Focal cortical dysplasia	<1	2011	Dizziness, loss of consciousness and contractions	Yes	Yes	No
Female	35	High school	Gliosis	26	2017	Tremor and yelling during sleep	No	No	Yes
Female	44	High school	Arteriovenous malformation	21	2017	Muscle contractions, tremor, aberrant hand perception	Yes	Yes	No
Male	45	University	Focal cortical dysplasia	8	2017	Blurring, eye pinching, myoclonus	Yes	No	No
Male	17	High school	Focal cortical dysplasia	<1	2017	Absence (petit mal), head twisting	No	No	No
Male	29	University	Arteriovenous malformation	15	2014	Visual disturbances, disturbances in speech	Yes	Yes	No
Male	19	Currently a university student	Dysembryoplastic neuroepithelial tumor	14	2017	Loss of control of the right side (paralysis), tremor, myoclonus	No	No	No
Female	22	University	Focal cortical dysplasia	13	2014	Delusions, déjà vu, perspiration, vomiting	Yes	No	No
Male	32	Currently a university student	Focal cortical dysplasia	16	2017	High eye pressure, dizziness, quick thoughts, tonic–clonic seizures	Yes	Yes	No
Female	57	Middle School	Focal cortical dysplasia	27	2017	Numbness, blindness, tremor	Yes	Yes	No

2.2.3. Verbal abilities tasks

We evaluated confrontation naming with a Picture Naming test [28]. No semantic or phonological cues were given. Vocabulary knowledge and word comprehension was evaluated using a Greek Vocabulary test, in multiple choice format [34]. Variables of interest were the number of correct answers for each test.

2.2.4. Construction ability tasks

Visuoconstruction ability was examined by means of the Clock Drawing Test, the Block Design subtest of the Wechsler Adult Intelligence Scale fourth edition (WAIS-IV) and the copy trial of the Taylor Complex Figure Test [30,35,36]. Clock Drawing also requires knowledge of numbers, abstract reasoning, and working memory [37]. Participants were asked to draw a clock indicating a particular time.

2.2.5. Visuospatial perception tasks

Several tests were used for the assessment of visuospatial abilities. More specifically, we examined visual neglect (Pair Cancelation and Line Bisection), visual tracking (Pair Cancelation), distance estimation (Line Bisection), perception of direction and angular relations (Judgment of Line Orientation), mental rotation and perceptual organization (Hooper Visual Organization Test) [31], right–left discrimination (Right–Left Discrimination Test), and body orientation/orientation of personal space (Semmes Body Placement) [38]. Finally, different aspects of object and space perception were assessed by means of the Visual Object and Space Perception (VOSP) battery [39]. This battery also contains a screening test for patients' visual ability.

2.2.6. Haptic perception task

The ability to recognize objects through touch was assessed with the haptic recognition task, from the Fuld Object–Memory Evaluation [40,41]. Participants were asked to identify 10 common objects, e.g., scissors, small ball, through tactile sense with their eyes closed. The variable of interest was the number of correct responses.

2.2.7. Executive functions tasks

The Wisconsin Card Sorting Test (WCST) was administered for the assessment of abstract thinking, concept formation and switching [42], organized behavior, and inhibition. Perseveration and impulsivity were also assessed with this test. We used the short form of the WCST, utilizing 64 cards. The Verbal Fluency Test (semantic and phonological conditions) evaluates ease and speed of word generation as well as strategies to optimize performance [28]. Variables of interest for the WCST were the number of correct answers, the number of categories completed and the number of perseverative errors, and for the Verbal Fluency Test the number of correct answers in the semantic and the phonological conditions.

2.2.8. Mental arithmetic

The Arithmetic function scale from the Luria-Nebraska Neuropsychological Battery was used to evaluate participants' arithmetic abilities (knowledge of numbers and arithmetic rules, recognition of arithmetic symbols, and the calculation of written or mental problems) and the likely presence of dyscalculia, while short-term auditory memory, symbol formation, and crystallized knowledge were also assessed. The test includes two conditions, one assessing the understanding of numbers and number values and another assessing math problems [43,44].

2.2.9. Assessment of depression and anxiety

The Hospital Anxiety and Depression Scale is a self-report questionnaire measuring signs of depression and anxiety on a Likert scale. It includes two cutoff scores, one suggesting a possible diagnosis (≥8–10) and another suggesting a definite diagnosis (≥11) [45–47].

2.3. Procedure

Individual meetings were held for every participant in a quiet place without external distractions, lasting about 2 to 3 h on average with a short break. Participants were asked to try their best. These tests were administered to all participants in the same order to avoid potential differences in order effects.

3. Results

Analyses were conducted with SPSS statistical software (version 23.0). First, we grouped all test variables into nine cognitive domains, namely, memory, attention, working memory, verbal abilities, visuospatial perception, construction ability, executive functions, arithmetic abilities, and tactile perception. We then converted test raw scores into z-scores and calculated the sums of those in each cognitive domain, yielding nine composite domain scores. Z-scores were based on performance of both groups (raw scores of all participants for each test were simultaneously converted to z-scores). We applied nonparametric tests (Mann–Whitney *U* tests for group comparisons and Spearman coefficients for correlations) because of the small size of the sample with epilepsy.

For the group comparisons, group was the independent variable, and the nine composite domain scores were the dependent variables. Statistical significance was set at $\alpha = 0.05$. Mann–Whitney *U* tests showed significant differences between the two groups in construction ability ($U = 55.000$, $p = 0.048$), verbal abilities ($U = 46.000$, $p = 0.016$), and executive functions ($U = 40.000$, $p = 0.007$), with the group with epilepsy performing significantly more poorly than controls, but no differences on memory ($U = 64{,}000$, $p = 0.125$), attention ($U = 64{,}000$, $p = 0.125$), working memory ($U = 77.000$, $p = 0.346$), visuospatial perception ($U = 60.000$, $p = 0.085$), arithmetic ($U = 76.000$, $p = 0.317$), and tactile perception ($U = 82.500$, $p = 0.502$). Additionally, we found no group difference on depression ($U = 66.000$, $p = 0.14$) and anxiety ($U = 63.500$, $p = 0.11$) scales. Table 2 lists mean ranks by group for each cognitive domain and mood score.

We also examined which particular tests differentiated the groups (patients vs. healthy controls) in the aforementioned cognitive domains in which statistically significant differences were found (visuoconstruction, verbal, and executive functions). In these analyses, group was the independent variable and the dependent variables were all neuropsychological test variables included in the cognitive domains in which we found a significant group difference. We found no group difference on Clock Drawing ($p = 0.81$), Block Design ($p = 0.17$), and the copy trial of the Taylor Complex Figure Test ($p = 0.08$), but patients did more poorly than the healthy group on Picture Naming ($p = 0.04$). Furthermore, all three variables of interest on the Wisconsin Card Sorting Test – number of correct responses ($p = 0.01$), number of categories

Table 2
Cognitive performance and mood (mean ranks) by group.

Cognitive domain	Mean ranks	
	Control	Epilepsy
Memory	16.93	12.07
Attention	16.93	12.07
Working memory	16.00	13.00
Verbal abilities*	18.21	10.79
Visuospatial perception	17.21	11.79
Visuoconstruction abilities*	17.57	11.43
Executive function**	18.64	10.36
Arithmetic	12.93	16.07
Tactile perception	15.61	13.39
Mood		
HADS – Anxiety	12.04	16.96
HADS – Depression	12.21	16.79

* $p < 0.05$.
** $p < 0.01$.

Table 3
Group comparisons (patients vs. healthy controls) on individual test variables from the cognitive domains in which patients with epilepsy were impaired.

Cognitive domain test		U	z	*p*-Value	Group with epilepsy		Healthy group	
					Mean	SD	Mean	SD
Visuoconstruction ability	Taylor Complex Figure–Copy	61.50	−1.7	0.08	35.0	1.5	32.3	5.1
	Clock Drawing	64.00	−1.9	0.81	14.7	0.5	14.2	0.9
	Block Design (WAIS-IV)	67.50	−1.4	0.17	40.2	12.7	33.3	10.1
Verbal abilities	Picture Naming	55.00	−2.3	**0.04**	39.8	0.3	39.3	0.6
	Greek Vocabulary Test	57.00	−1.8	0.06	31.8	7.0	26.7	7.0
Executive functions	WCST[a] # of Correct responses	43.00	−2.5	**0.01**	51.2	7.4	42.2	9.9
	WCST # of Categories	43.00	−2.6	**0.008**	4.1	1.2	2.7	1.4
	WCST # of Perseverative errors	38.00	−2.8	**0.004**	1.2	2.0	6.3	4.9
	Verbal Fluency – Semantic	64.50	−1.5	0.13	23.6	7.7	18.3	7.0
	Verbal Fluency – Phonological	63.00	−1.6	0.11	12.3	4.8	9.7	4.3
	Trail Making Test Part B	56.50	−1.9	0.06	66.8	18.9	112.4	80.7

[a] WCST = Wisconsin Card Sorting Test.

($p = 0.008$), and number of perseverative errors ($p = 0.004$) – yielded significantly lower scores in the group with epilepsy, while the remaining tests of executive function showed no statistical difference. Table 3 presents Mann–Whitney *U* values for group (epilepsy vs. healthy control) comparisons on individual test variables.

In addition to the aforementioned group comparisons, we explored the number of patients whose performance was poorer than a large normative dataset to determine whether the present group differences might also reflect clinically significant impairment. Indeed, we found that 12 participants in the group with epilepsy had impaired performance (score less than one standard deviation from the normative group mean) on the Wisconsin Card Sorting Test number of correct responses compared to Greek normative data and seven achieved significantly fewer categories, but none showed pathological scores in the perseverative errors. Thus, in light of our clinical sample's demonstrated structural brain pathology (magnetic resonance imaging [MRI]), seizure history, and AED medication, the significantly decreased psychometric performance, which emerged in the present group comparisons, likely reflects neuropsychological impairments.

In order to explore the potential cognitive effects of seizure laterality, we compared subgroups with epilepsy (independent variable), namely those with right localization (seven patients) and those with left localization (seven patients); cognitive domain scores were the dependent variables. No statistically significant differences were found between the two subgroups. Table 4 presents the group (right vs. left hemisphere epilepsy foci) comparisons.

Finally, we explored the potential relationship between the number of AEDs and patients' cognitive performance using Spearman correlation coefficients. We found a large negative association of number of AEDs and visuoconstruction ability ($rs = -0.55$) and arithmetic ($rs = -0.68$), wherein, the more AEDs currently being taken, the worse the performance on these tests. However, Bonferroni correction ($p = 0.005$) showed no statistically significant correlations between cognitive domains and the number of AEDs. Table 5 presents Spearman correlation coefficients for AED load and each cognitive domain.

Table 4
Comparisons of patient groups based on seizure location (right hemisphere, left hemisphere) on cognitive domains and mood.

Cognitive function	U	z	*p*-Value
Memory	22.00	−0.32	0.81
Attention	17.00	−0.96	0.38
Working memory	15.00	−1.21	0.26
Verbal abilities	13.00	−1.47	0.17
Visuospatial perception	12.00	−1.60	0.13
Visuoconstruction abilities	14.00	−1.34	0.21
Executive functions	24.00	−0.06	1.00
Arithmetic	22.00	−0.32	0.80
Tactile perception	20.00	−0.68	0.71
HADS – Anxiety	22.00	−0.32	0.81
HADS – Depression	17.00	−0.96	0.38

4. Discussion

We explored neurocognitive functioning in patients with posterior epilepsies (PLE and OLE) in order to detect potential specific markers of cognitive dysfunction. Our findings suggest that posterior epilepsies are associated with impairment in visuoconstruction, verbal skills, and executive functions. While the former was expected, impairment in the latter two cognitive domains was unexpected as they are typically mediated by anterior brain regions.

4.1. Visuoconstruction

The present study focused on visuoconstructive praxis, the ability to plan and execute the necessary movements for organizing a series of items in space, usually in a drawing or in a picture copy situation. This ability is the coproduct of visuospatial, motor, and executive processing skills. Indeed, apraxic symptoms may arise as a result of a breakdown in visuospatial perception or problem-solving processes [48], and may reflect either a state inducing general cognitive dysfunction or brain damage [48,49]. Alternatively, construction apraxia may be a selective deficit of construction ability, despite intact visual perception [50].

Our findings are consistent with current literature on visuoconstruction deficits arising from parietal and occipital lesions. Damage to the right parietal lobe and often a disconnection between parietoccipital cortices and subcortical structures has been linked to construction apraxia [50]. Disturbances in visuoconstruction ability have been observed among patients with benign Rolandic epilepsy [51], while others have reported deficits in spatial and construction abilities in cases with seizures emanating from the right parietal lobe [22]. In addition, problems in visual attention, naming, and praxis in children with parietooccipital epilepsy have been reported [52].

Table 5
Relationship between cognitive domains and antiepileptic drug (AED) load values.

Cognitive functions	Number of AEDs	
	Spearman r	*p*-Value
Memory	−0.38	0.18
Attention	−0.35	0.22
Working memory	−0.34	0.23
Verbal abilities	−0.55	**0.04**
Visuospatial perception	−0.33	0.24
Visuoconstruction abilities	−0.27	0.34
Executive function	−0.44	0.11
Arithmetic	−0.68	**0.008**
Tactile perception	−0.36	0.21

Note. Bonferroni correction: $p < 0.0056$.

4.2. Verbal abilities

Picture naming, a task on which the present patient sample was impaired, requires perceiving and recognizing an object, finding the word it denotes and generating its appropriate utterance. The majority of errors made by the patients were semantic in nature (e.g., *nail* instead of *screw*, *shark* or *dog fish* instead of *swordfish*), one was perceptual (*coil* instead of *snake*) and one anomic (*bird that talks* instead of *parrot*). Most studies have linked temporal lobe epilepsy (TLE) and temporal lobectomy of the dominant hemisphere to deficits in verbal abilities, especially naming and verbal memory [53–58], while language comprehension [59], naming, and verbal fluency deficits have also been found in patients with benign Rolandic epilepsy [60–62].

On the other hand, consistently with our results, one study has reported that seizures of the left parietal lobe may induce deficits in language and general verbal abilities [22]. Indeed, semantic errors can be viewed as emanating from the aberrant functioning of a variety of cognitive mechanisms (e.g., problems in semantics or difficulties accessing vocabulary stores), and as such, from damage in various brain areas including Wernicke's area, the superior temporal and adjacent occipital cortex, the posterior middle and inferior temporal gyrus, and the angular and supramarginal gyrus, the latter two being associated with language perception [63]. Specifically, the angular gyrus is likely involved in the transfer of visual information to Wernicke's area [64] and has also been implicated in number processing [65], memory recall, spatial knowledge [66], attention, and social cognition [67]. Finally, impaired naming may result from disruption to processing of incoming information, semantic representations, or at the output level (e.g., word utterance) [68].

The relationship between drug polytherapy and both verbal abilities and arithmetic may have influenced the present findings. Interestingly, however, attention, vigilance, and psychomotor speed were not associated with polytherapy. This is in contrast to the findings regarding their vulnerability to the effects of AEDs reported elsewhere [22,69]. Last but not least, epilepsy onset in childhood may have influenced learning in school and resulted in lower academic skills, including writing, spelling, and even general vocabulary knowledge.

4.3. Executive functions

In the present study, we assessed abstract thinking, concept formation, mental flexibility, problem solving and the implementation of strategies, verbal fluency, organization, use of feedback, and inhibition. Our patients with epilepsy demonstrated defective use of strategies and mental flexibility, and an increased tendency toward perseveration.

Many studies have reported executive dysfunction in patients with FLE (e.g., [70,71]). For instance, studies have reported problems in concept formation, mental flexibility, and inhibition in patients with seizures of dorsolateral prefrontal origin [22,72]. Indeed, a functional MRI (fMRI) study during Wisconsin Card Sorting Test performance identified a network with increased activity comprising the frontoparietal and striatal areas including right ventral prefrontal cortex (RVPC), right dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC), and the temporoparietal junction [73].

On the other hand, patients with chronic mesial TLE (MTLE) may present executive dysfunction as well [74–77]. Executive deficits in TLE may reflect neural noise propagation (the spread of epileptic spike activity from the temporal to the frontal lobe territories through their direct and reciprocal connections) [78]. This perspective is supported by the finding of executive improvement among patients with TLE after removal of the epileptogenic zone.

Direct and reciprocal connections have also been found between the frontal cortex and parietal and occipital areas reinforcing the speculation of neural noise propagation. Different researchers have studied the frontoparietal networks related to the functions of grasping, spatial attention, and orientation [79–81], and the occipitofrontal and frontoparietoccipital networks such as the top-down modulation [82] and visually guided reaching in monkeys [83], respectively. In the present study, however, topographic heterogeneity in the distribution of epileptogenic zones renders the interpretation of functional–anatomical correlations difficult.

In addition, early seizure onset may affect executive performance as seizure activity in a still developing brain may interfere with central nervous system (CNS) maturation dynamics. This is especially the case with respect to the frontal lobes, which mature through the sequential establishment of corticocortical connections, dominating postnatal cerebral development from birth to age of 16 years [84]; thus, early seizure onset may lead to inadequate network construction, although the main mechanism underlying this construction still remains unclear [85,86]. Five of our patients had developed epilepsy before seven years of age. Chronic epileptic activity may potentially affect cognitive functions, since the more complex a function is the more vulnerable it would be to aberrant brain activity. Finally, given the complexity of executive functions and the reliance of many tests on additional cognitive functions (low specificity of many tests), we cannot rule out the possibility that other factors reduced performance on executive functions tests.

4.4. Visuospatial functions

No group difference in visuospatial functions was identified in the present study. Similarly, normal visual discrimination in all five resected patients with posterior intractable epilepsy was found in another study, while three out of five patients presented deficits in visuospatial orientation, four in visuoconstruction ability, and all of them in naming [52]. Possible explanations accounting for this lack of group differences are the heterogeneity of epileptic foci and the absence of serious structural brain damage in the present sample. Furthermore, two patients with posterior cortical atrophy developed strategies and achieved higher scores on two tasks of object and space perception despite their parietal dysfunction, indicating that the evaluation of the aforementioned functions can be influenced by other cognitive functions [87]. In addition, no specific pattern of cognitive deficits in patients with MTLE was found, suggesting the need for a detailed cognitive assessment, especially in cases of imminent surgery [74]. Cognitive measures for visuospatial and visuoperceptual functions vary in sensitivity and validity. For instance, the Judgment of Line Orientation is capable of detecting visuospatial deficits [88] and the Hooper Visual Organization Test of detecting impairments in visual organization and visuospatial ability [89], while the Pair Cancelation Test is more sensitive to frontal and subcortical impairment and Line Bisection to posterior damage [31]. Finally, as mentioned previously, several studies have reported generalized cognitive dysfunction in parietal and occipital epilepsy, sometimes imitating the cognitive profile typical of MTLE (medial temporal lobe epilepsy) most likely resulting from the spread of epileptic spike activity to other brain regions, thus rendering differential diagnosis quite challenging [2,15,16].

4.5. Connection with Luria's theory

Our findings are in line with Luria's theory of brain functioning. Luria proposed that cognitive functions are organized in complex functional systems located in different brain regions inter- or intrahemispherically [2]. They constitute dynamic systems that interact and are nonlinearly organized in space–time patterns [90]. Thus, damage to a particular brain area may disrupt a functional system in any of its constituent parts, giving rise also to secondary systemic abnormalities. The neurocognitive impairment of our group with epilepsy can be interpreted in light of this model, where location of damage does not completely coincide with the location of the disturbed function, but with one of the many factors participating in its integrity.

Modular views of the brain suggesting a compartmentalization of mental processes by strictly attributing them to specific areas or hemispheres have been criticized by many researchers, as they offer a simplified approach to complex functional brain dynamics. Moscovitch has implied that after early processing stages, both hemispheres encode the same information, but in their own way according to their functional characteristics and processing properties [91]. Moreover, the idea that every brain area is responsible for a specific cognitive function has been criticized by Hécaen and Albert who suggested that every function includes distant areas, which collaborate and contribute based on its own specialization [92]. Finally, epilepsy categorization based on anatomic segregation has been disputed because of the dynamic function of the brain, which involves complex neuronal pathways that cannot be delineated by artificial anatomic boundaries [12].

Luria's theory is consistent with current views of epilepsy as a network disorder and the clinical concept of the functional deficit zone [2]. New trends emphasize the role of epileptic networks underlying seizures indicating a complex set of network dynamics pre-, inter-, and postictally [93]. Additionally, a description of abnormal functional and structural brain connections is essential for understanding the developing mechanisms of epilepsy [94]. Finally, several studies have cautioned against the inefficiency of looking at epilepsy as a circumscribed focal phenomenon, as it usually also involves distant areas that produce interictal or ictal activity [2,95,96].

4.6. Limitations

The clinical heterogeneity of epilepsy and the difficulty of controlling for seizure frequency as a possible factor affecting cognitive functioning may have limited the validity of the present results. Furthermore, not all tests administered had been standardized for the Greek population but had only been translated and adapted to the Greek language, perhaps limiting their reliability.

4.7. Conclusions

Patients suffering posterior epilepsies (PLE and OLE) demonstrated an unexpected neuropsychological profile. Specifically, they were impaired on visuoconstruction, verbal abilities, and executive function, with intact memory, attention, visuospatial abilities, arithmetic, and tactile perception. Thus, differentiating posterior epilepsies from others, based on cognitive performance appears to be an elusive goal. Instead, this nonspecificity corroborates the idea of mental functions as functional networks and epilepsy as a network disorder. Further investigations should focus on specific epileptic networks. An assessment of seizure frequency and severity as factors that may influence cognitive functioning would also be an important step in future studies.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations of conflict of interest

None.

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