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ORIGINAL COMMUNICATION

Neuropsychological profile of adult patients with nonsymptomatic occipital lobe epilepsies

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Abstract To explore the neuropsychological and neurobehavioral profile in adult patients affected by nonsymptomatic (cryptogenic and idiopathic) occipital lobe epilepsy (OLE), with normal intelligence, we enrolled 20 adult patients with nonsymptomatic OLE and 20 age-, sex-, and education-matched healthy subjects. All participants underwent neuropsychiatric assessment scales, and standardized neuropsychological tests tapping memory, executive functions, constructional, visuospatial and visuoperceptual skills. After Bonferroni correction for multiple comparisons, patients performed significantly worse than controls on several tests tapping complex visuospatial skills and frontal lobe functions. The analysis of single patients' performance revealed that a significantly higher number of OLE patients achieved age- and education-adjusted pathological scores on three tests (Benton Judgment of Line Orientation Test, Freehand Copying of Drawings Test, color-word interference task of Stroop test) with respect to controls. Patients did not differ from control subjects on neuropsychiatric aspects. The direct comparison between OLE subtypes showed that cryptogenetic OLE patients tended to achieve lower scores than idiopathic OLE patients on most tests, but no difference between the two groups was fully significant. In summary, patients with nonsymptomatic OLE can be affected by clinically relevant impairments in selected neuropsychological domains: complex visuospatial skills and executive functions. It could be speculated that frontal and visuospatial cognitive deficits might be the result of epileptic activity spreading within a neural network that includes structures far beyond the occipital lobe.

Keywords Epilepsy · Occipital lobe epilepsy · Visuoconstructional functions · Visuoperceptual abilities · Frontal lobe functions · Neural networks

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Introduction

Occipital lobe epilepsies (OLE) are a group of seizure disorders originating in the occipital lobes. The cardinal ictal symptoms are visual (elementary or complex visual hallucinations, blindness, visual illusions and palinopsia) and oculomotor (tonic deviation of eyes, nystagmus and repetitive eyelid closure or eyelid fluttering). Seizures may spread to anterior regions, generating additional ictal symptoms and secondarily generalized tonic–clonic seizures [1–10].

In population studies of newly diagnosed epilepsy, OLE has been identified in 1.2–2.6 % of the patients [11, 12].

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The International Classification of Epilepsies and Epileptic Syndromes [13] distinguished idiopathic, symptomatic and cryptogenic OLE. In symptomatic forms a structural or metabolic etiopathogenic factor can be identified (e.g., dysplastic, vascular, metabolic, neoplastic), while in idiopathic and cryptogenic epilepsies such factors are lacking. Idiopathic epilepsies are usually age-dependent and present with quite typical natural history, seizure types and EEG features; cryptogenic epilepsies, conversely, do not possess such clinical identity and most probably are symptomatic forms in which the etiopathogenic factor cannot be identified.

Previous studies demonstrated that children with idiopathic OLE show cognitive defects in the visuoperceptual domain but also lower performance on attention and memory tests with respect to normally developed children; moreover, OLE children appear to be at risk for poor scholastic achievement, anxiety and depressive disorders [14, 15]. Since occipital lobes are involved in both low level and high level visual processing, it has been hypothesized that in OLE patients seizures might alter the normal functioning of occipital circuitries and might lead to cognitive visuoperceptual and visuoconstructional deficits [15]. Only one study has been performed in adult OLE patients, in which subtle difficulties in low-level visuoperceptual abilities (i.e. Perceptive Differences Test, and Object Denomination Test, and Famous Faces Test) have been detected, without significant differences between symptomatic and idiopathic/cryptogenic OLE patients [16]. No systematic neuropsychological investigation, including high-level visuospatial cognition, visuoconstructional skills, memory and frontal/executive functions, is available in adult OLE patients yet. Moreover, the behavioral profile of adult OLE patients has not systematically explored, although comorbid behavioral symptoms such as depression or anxiety have often been reported in patients with epilepsy, particularly in patients with temporal lobe epilepsy and frontal lobe epilepsy [17, 18].

To the aim of filling this gap, in this study we investigated the neuropsychological and behavioral profile of adult patients with OLE. In our study we included only patients suffering from idiopathic and cryptogenic forms (here collectively termed "nonsymptomatic") [16], in order to exclude the possible effect of definite organic lesions on neuropsychological and behavioral profile.

Neuropsychological and behavioral profile of "nonsymptomatic" OLE patients was characterized by means of standardized tests for high-level visuospatial cognition, visuoconstructional skills, memory and frontal lobe functions, and by several validated rating scales for behavioral disturbances, anxiety, depression and apathy.

Methods

Subjects

We screened for the study consecutive outpatients referring to the Epilepsy Center of the Department of Neurological Sciences, "Federico II" University, Naples, Italy, with diagnosis of OLE, i.e., with epileptic seizures having a clear occipital ictal onset as demonstrated by clinical and EEG data. To enter the study, patients had to fulfill the following criteria: diagnosis of idiopathic or cryptogenic OLE according to criteria from ILAE classification of the epilepsies and epileptic syndromes [13], i.e., OLE patients with normal neurological evaluation, normal MRI, normal hematology and biochemistry screening for metabolic disorders; active epilepsy, i.e. recurrent seizures within the five years prior to the study [19]; adult age (>18 years) and educational level equal to or higher than elementary school; normal intelligence (score adjusted for age and education on Raven Coloured Progressive Matrices, RCPM above 18.96) [20]; absence of major depression according to DSM-IV criteria [21]; no medication but antiepileptic drugs (AEDs).

Twenty patients (12 idiopathic OLE and 8 cryptogenic OLE; 12 females and 8 males; age range 18–50 years; education range 5–18) matched inclusion and exclusion criteria. Age at seizure onset ranged from 7 to 21 years (mean 12.5 $\pm$ 3.9 years), and the duration of illness from 6 to 38 years (mean 16.1 $\pm$ 8.2 years). All patients were treated with AEDs at the moment of study entry; 13 patients were seizure free, with seizure control achieved for at least 1 year, while the remaining seven still presented seizures despite taking AEDs.

Number of lifetime seizures (from onset of epilepsy to the last recorded seizure) ranged from 7 to 800, whereas mean yearly seizure frequency (i.e., number of seizures/years of clinically documented seizures) ranged from 1 to 40 (Table 1).

In all patients seizure onset was marked by visual semiology (elementary visual hallucinations in 13 patients, blindness or field defect in 3; both in 4). In all patients initial visual aura was followed, more or less frequently, by other ictal phenomena consisting in one or more of the following: eye deviation, often associated with ipsilateral turning of the head (15 patients), loss of contact (16 patients), motor seizures (unilateral tonic or clonic seizures: 7 patients). In 18 of 20 patients secondarily generalized tonic–clonic seizures had occurred at least once. Post-ictal symptoms, represented by headache and/or vomiting and/or sleep, were reported in 16 patients (clinical details are reported in Table 1).

All OLE patients were completely independent in instrumental activities of daily living assessed by means of

Table 1 Patients' demographic, clinical, EEG data

Pt	Sex	Age	OLE syndrome	Age at onset (years)	Type of visual aura	Possible additional ictal symptomatology[a]				Post-seizure symptoms	Total number of seizures[c]	Yearly seizure frequency from onset	Seizure frequency in the last year	Interictal EEG epileptic findings[d]		AED treatment at study entry (mg/day)
						Eye deviation	Loss of contact	Motor seizures[b]	SGTCS					Side of occipital paroxysmal activity	Spreading	
1	M	22	IG	14	Blind	Right	Yes	Yes	Yes	H	15	3	0	Left	Yes	VPA (1,500)
2	F	34	C	21	Hall	Right	Yes	No	Yes	H	50	4	5	Left	No	LEV (3,000), CBZ (600), CNZ (1)
3	F	23	IP	16	Hall	Right	Yes	Yes	No	No	15	3	0	Left	Yes	LTG (250)
4	M	18	IG	8	Hall	Left	Yes	Yes	No	No	12	2	0	Right	Yes	VPA (600)
5	F	41	C	15	Blind	No	Yes	No	Yes	H	50	2	6	Left	Yes	OXC (1,050), TPM (200)
6	F	32	C	14	Hall	Left	No	No	Yes	S	250	14	12	Right	No	LTG (450), CBZ (800)
7	F	22	IG	11	Blind, Hall	No	No	No	Yes	H	10	1	5	Left	No	LEV (2,000)
8	M	50	C	18	Hall	No	Yes	No	Yes	No	50	2	0	Bilateral	Yes	OXC (1,500), LEV (3,000)
9	M	28	IG	13	Blind	Left	Yes	No	Yes	S	12	1	0	Right	No	CBZ (400)
10	F	26	IP	15	Hall	Left	Yes	No	Yes	H, S	13	1	0	Right	Yes	LEV (2000)
11	F	24	IG	7	Hall	Left	Yes	Yes	Yes	H, S, V	30	2	0	Bilateral	Yes	LEV (2500)
12	F	27	IG	11	Hall	Left	No	Yes	Yes	H	8	1	0	Right	Yes	PB (100)
13	F	30	C	9	Hall	Left	Yes	No	Yes	No	800	40	20	Right	Yes	OXC (1,500), CNZ (3)
14	F	24	IG	18	Blind	No	Yes	No	Yes	No	7	1	0	Bilateral	Yes	TPM (100)
15	M	26	IG	11	Blind, Hall	No	Not	No	Yes	H	15	1	0	Left	Yes	CBZ (400)
16	M	25	IG	7	Hall	Right	Yes	No	Yes	H, S, V	15	1	0	Left	Yes	LEV (1500)
17	M	25	IG	7	Blind, Hall	Right	Yes	No	Yes	H, S, V	12	1	0	Left	No	LEV (1,000)
18	M	50	C	12	Hall	Right	Yes	No	Yes	H	100	3	0	Bilateral	No	OXC (1,800), LEV (3,000)
19	F	19	C	11	Hall	Left	Yes	Yes	Yes	S	300	37	20	Right	Yes	OXC (1,350), CLB (10)

Table 1 continued

Pt	Sex	Age	OLE syndrome	Age at onset (years)	Type of visual aura	Possible additional ictal symptomatology[a]				Post-seizure symptoms	Total number of seizures[c]	Yearly seizure frequency from onset	Seizure frequency in the last year	Interictal EEG epileptic findings[d]		AED treatment at study entry (mg/day)
						Eye deviation	Loss of contact	Motor seizures[b]	SGTCS					Side of occipital paroxysmal activity	Spreading	
20	F	26	C	12	Hall	Left	Yes	Yes	Yes	H	150	11	12	Right	Yes	LTG (250), VPA (1,100)

OLE occipital lobe epilepsy, *C* cryptogenic, *IG* idiopathic-gastaut type, *IP* idiopathic-photosensitive type, Type of visual aura: *Blind* blindness or visual field defect, *Hall* elementary hallucinations, *AED* antiepileptic drug, *VPA* valproic acid, *LEV* levetiracetam, *CBZ* carbamazepine, *CNZ* clonazepam, *LTG* lamotrigine, *OXC* oxcarbazepine, *TPM* topiramate, *PB* phenobarbital

[a] Occurred and witnessed in at least one occasion

[b] Unilateral tonic or clonic seizures; *SGTCS* secondary generalized tonic–clonic seizures; post-seizure symptoms: *H* headache, *S* sleep, *V* vomiting

[c] As occurred in the time period since the first seizure (epilepsy onset) to the last recorded seizure

[d] Seizure frequency refers to number of episodes occurred in the last year

[e] Detectable paroxysmal activity (as spikes, spike-wave or sharp-slow-wave complexes) at least in one of available EEGs

the Lawton Instrumental Activities of Daily Living (IADL) Scale [22].

For each patient enrolled in the study, we selected an age-, sex- and education- matched control subject (12 females and 8 males) not affected by any known neurological or psychiatric disorder, with normal intelligence (score adjusted for age and education on RCPM above 18.96) [20] and without major depression according to diagnostic criteria of DSM-IV. No significant differences between the OLE group and the control group were found on age at evaluation (mean age 28.6 ± 9.1 vs. 28.9 ± 9.6; $P = 0.906$), and educational level (mean education 10.9 ± 3.8 vs. 11.1 ± 3.8; $P = 0.869$). The present study was reviewed and approved by the appropriate Local Ethics Committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consent was obtained from all subjects after the nature of the study was fully explained to them.

Procedures

After having given written informed consent, all participants underwent a battery of standardized neuropsychological tasks and several neuropsychiatric assessment scales. All tests and questionnaires were administered by the same expert examiner, blinded to clinical and instrumental data.

Neuropsychological assessment

Visual exploration was assessed by the Star Cancellation Test [23]. Visuospatial perception was assessed by Benton Judgment of Line Orientation Test [24]. Visuoconstructional skills were explored by means of two tests: Freehand Copying of Drawings (CD) and Copying of Drawings with Landmarks (CDL; both tests included in the Mental Deterioration Battery) [20]. *Frontal Lobe/Executive Functions* were evaluated by means of Wisconsin Card Sorting Test (WCST) [25], phonological fluency task [20], copying of the Rey-Osterrieth Complex Figure (ROCF) [26–28], and Stroop Color-Word Test (in its classic version based on card presentation, and consisting of two nonexecutive tasks, reading and color-naming, and one color-word interference task [29]; for the purpose of this study, only the interference task in which the subject has to name the color of the ink in which a word is printed was analyzed).

Long-term memory was assessed by means of Rey's auditory 15 word learning test, including immediate and delayed recall of word lists [20], and by delayed recall of ROCF [26–28].

Behavioral assessment

All patients and control subjects underwent the following behavioral assessment scales: the Hospital Anxiety and Depression Scale (HADS) [30], the Apathy Evaluation Scale (AES) [31], and the Neuropsychiatric Inventory (NPI) [32], a validated informant-based interview to identify neuropsychiatric disturbances such as delusions, hallucinations, agitation, depression, apathy, disinhibition, irritability, motor disturbances, night time behavior and eating.

Statistical analysis

Normal subjects and OLE patients were compared for their mean scores on all tests and questionnaires, and also for the number of pathological performances on each test with respect to age- and education adjusted normative data. To avoid any statistical bias related to the relatively small sample sizes and to the non-normal distribution of scores, we used nonparametric statistical tests: the differences in continuous variables between groups were assessed using a Mann–Whitney U test, the distribution of dichotomous variables in the two groups were compared by Fisher's exact test. We applied Bonferroni corrections on post hoc tests to reduce the risk of type 1 error for multiple comparisons, by dividing the P value by the number of neuropsychological variables considered ($0.05/15 = 0.003$ for neurobehavioral variables; $0.05/11 = 0.004$ for neuropsychological variables). The same procedure was adopted to compare cryptogenic and idiopathic OLE patients. Moreover, in nonsymptomatic OLE patients, Spearman's correlation coefficients (rho) were computed to search for associations between clinical aspects (age at onset, frequency of seizures at study entry, total number of seizures, mean yearly seizure frequency and duration of seizure disorder) and behavioral and neuropsychological measures.

Results

Neuropsychological results: OLE patients versus healthy controls

The neuropsychological results were summarized in Table 2. Although OLE patients generally achieved lower scores than the normal subjects, after Bonferroni correction the differences between the two groups were significant only on color-word interference task of Stroop test, copy and delayed recall of ROCF, BJLOT, CD and CDL.

With respect to the control group, a significantly higher number of OLE patients achieved age- and education-adjusted pathological scores on the Benton Judgment Lines Orientation Test (15/20 vs. 6/20; Fisher's exact test 0.010), on Freehand Copying of Drawings Test (6/20 vs. 0/20; Fisher's exact test 0.020), and on the color-word interference task of Stroop test (7/20 vs. 0/20; Fisher's exact test 0.008).

Behavioral results: OLE patients versus healthy controls

After Bonferroni correction, no significant differences between OLE group and control subjects were found on HADS, NPI total and subscales score and AES (Table 3).

Correlation analysis

In nonsymptomatic OLE group, older age at epilepsy onset was significantly associated with higher NPI delusions score ($r = 0.580$, $P = 0.015$), NPI euphoria score ($r = 0.559$, $P = 0.020$), NPI disinhibition score ($r = 0.559$, $P = 0.020$) and NPI irritability score ($r = 0.495$, $P = 0.043$). Longer duration of nonsymptomatic OLE significantly correlated with a lower score on the Stroop color-word interference test ($r = -0.573$, $P = 0.008$). Both total number of seizures and mean yearly seizure frequency did not correlate with neuropsychological or neurobehavioral variables.

Comparison of cryptogenic versus idiopathic OLE patients

The neuropsychological scores obtained by cryptogenic and idiopathic OLE patients are summarized in Table 4. Cryptogenic OLE patients tended to achieve lower scores than the normal subjects, but after Bonferroni correction no difference between the two groups was significant.

The number of pathological scores on neuropsychological tests did not differ significantly in the two patient groups.

The scores on HADS, NPI total and subscales score and AES were quite similar in the two patient groups, and the difference between the groups were very far from significant for all items (not shown).

Discussion

The present study showed that adult patients with nonsymptomatic OLE showed lower scores than a group of matched normal controls on several tests. In the same cognitive domains, a high proportion of patients enrolled in the present study achieved pathological scores with respect to Italian normative data. These novel findings would thus demonstrate that, although we had excluded from our

Table 2 Neuropsychological scores (mean ± SD) in OLE patients and control subjects, percentage of subjects scoring under age- and education-adjusted cut-off values within each group, and summary of statistical comparisons

Neuropsychological parameter	OLE patients ($n = 20$)	Controls ($n = 20$)	U	P	Cut-off value
Frontal function					
WCST—global score	71.3 ± 36.5 (35 %)	58.5 ± 31.3 (20 %)	136.5	0.086	90.6
Phonological fluency	28.4 ± 11.1 (25 %)	37 ± 10.8 (5 %)	104.5	0.009	17.35
Stroop test: interference	21 ± 9.1 (35 %)	32.5 ± 7.7 (0 %)	72.0	<0.001*	10
Memory					
Immediate recall	49.2 ± 8.9 (15 %)	57.5 ± 8.7 (5 %)	96.0	0.004	28.53
Delayed recall	11.4 ± 2.1 (0 %)	13.2 ± 1.8 (0 %)	98.5	0.005	4.69
ROCF—delayed recall task	13.6 ± 6.6 (66.7 %)	20.6 ± 5 (30 %)	69.5	0.001*	9.46
Visual spatial functions					
Star cancellation task	54.7 ± 0.7 (5 %)	54.8 ± 0.4 (0 %)	198.5	0.968	51
BJLOT	20.2 ± 7.9 (75 %)	26.5 ± 2.9 (30 %)	93.5	0.003*	17
Freehand Copying of Drawings Test	11.6 ± 1.9 (30 %)	13.7 ± 0.6 (0 %)	67.0	<0.001*	7.18
CDL	66.5 ± 4.5 (15 %)	69.6 ± 1.4 (0 %)	80.0	<0.001*	61.85
ROCF—copy task	31.5 ± 6.4 (28 %)	34.0 ± 3.1 (10 %)	69.5	0.001*	28.87

In brackets the percentage of subjects who scored under cut-off value in each group

WCST Wisconsin Card Sorting Test, *ROCF* Rey-Osterrieth Complex Figure test, *BJLOT* Benton Judgment of line orientation test, *CDL* Copying of Drawings with Landmarks Test, *U* Mann–Whitney *U* test

* $P = 0.004$ after Bonferroni correction

Table 3 Behavioral comparisons between patients with OLE and control subjects

Neuropsychiatric parameter	Patients with OLE ($n = 20$)	Controls ($n = 20$)	U	P	Cut-off value
HADS total score	9 ± 5.3 (30 %)	7.6 ± 6.2 (20 %)	159.0	0.277	10
NPI-delusions	0.3 ± 0.8	0 ± 0	150.0	0.557	
NPI-hallucinations	–	–	–	–	
NPI-agitation/aggression	0.7 ± 2.9	0 ± 0	160.0	0.775	
NPI-depression or dysphoria	0.6 ± 1.2	0 ± 0	120.0	0.133	
NPI-anxiety	1.7 ± 2.5	0 ± 0	90.0	0.014	
NPI-elation or euphoria	0.3 ± 1.4	0 ± 0	160.0	0.775	
NPI-apathy or indifference	1.8 ± 4.2	0 ± 0	140.0	0.373	
NPI-disinhibition	0.3 ± 1.4	0 ± 0	160.0	0.775	
NPI-irritability or lability	0.9 ± 2.9	0 ± 0	140.0	0.373	
NPI-motor disturbances	–	–	–	–	
NPI-night-time behavior	0.9 ± 2.9	0 ± 0	140.0	0.373	
NPI-appetite and eating	0.6 ± 0.2	0 ± 0	160.0	0.775	
Apathy Evaluation Scale	27.7 ± 8.2 (5 %)	26.5 ± 3.6 (0 %)	160.5	0.289	38

In brackets the percentage of subjects who have a pathological score in each group is reported

HADS Hospital Anxiety and Depression Scale, *NPI* neuropsychiatric inventory, *U* Mann–Whitney *U* Test

sample patients affected by possible cognitive deterioration, OLE patients may show clinically relevant impairments of selected neuropsychological functions: complex visuospatial skills, constructional abilities, and executive functions. Therefore, we demonstrated that these patients show a wider range of cognitive impairments than what has been reported before [16], although the cognitive defects were not severe enough to hamper patients' daily living or working activity. However, it is possible that such cognitive deficits may impact Quality of Life (QoL), i.e., self-perceived well-being, as suggested by a recent study in epileptic subjects [33]. This issue has not been explored in the present study and deserves further research.

The comparison between cryptogenic and idiopathic OLE patients did not show robust differences between the two groups, confirming and extending previous

Table 4 Neuropsychological scores (mean ± SD) in patients with cryptogenetic or idiopathic OLE, percentage of subjects scoring under age- and education-adjusted cut-off values within each group, and summary of statistical comparisons

Neuropsychological parameter	Patients with cryptogenetic OLE ($n = 7$)	Patients with idiopathic OLE ($n = 13$)	*U*	*P*	Cut-off value
Frontal function					
WCST—global score	88 ± 26.5 (42.9 %)	68.8 ± 33.3 (30.8 %)	29.0	0.211	90.6
Phonological fluency	28.7 ± 13.5 (14.3 %)	28.2 ± 10.2 (30.8 %)	44.0	0.938	17.35
Stroop test: interference	13.6 ± 8.7 (57.1 %)	25 ± 6.6 (23.1 %)	14.5	0.011	10
Memory					
Immediate recall	44.9 ± 9 (14.3 %)	51.5 ± 8.3 (15.4 %)	28.5	0.183	28.53
Delayed recall	10.6 ± 2.6 (0 %)	11.7 ± 1.6 (0 %)	36.5	0.485	4.69
ROCF—delayed recall task	9.8 ± 5.1 (66.7 %)	15.5 ± 6.5 (66.7 %)	17.0	0.083	9.46
Visual spatial functions					
Star cancellation task	54.9 ± 0.4 (0 %)	54.7 ± 0.8 (7.7 %)	44.0	0.938	51
BJLOT	13.7 ± 8.3 (85.7 %)	23.7 ± 5.1 (69.2 %)	12.0	0.006	17
Freehand Copying of Drawings Test	8.3 ± 2.2 (57.1 %)	9.9 ± 1.5 (15.4 %)	22.5	0.067	7.18
CDL	64.3 ± 5.9 (28.6 %)	67.8 ± 3.3 (7.7 %)	23.0	0.081	61.85
ROCF—copy task	28.1 ± 10.1(33.3 %)	33.2 ± 2.6 (25 %)	21.0	0.180	28.87

In brackets the percentage of subjects who scored under cut-off value in each group

WCST Wisconsin Card Sorting Test, *ROCF* Rey-Osterrieth Complex Figure test, *BJLOT* Benton Judgment of line orientation test, *CDL* Copying of Drawings with Landmarks Test, *U* Mann–Whitney *U* Test

observations on symptomatic and nonsymptomatic OLE patients [16]. For this reason, we will adopt a conservative approach and will not discuss further the possible distinction between cognitive and behavioral profile of nonsymptomatic OLE subtypes.

The presence of visuospatial impairment on BJLOT is in line with previous findings described in adults [15] and children with OLE [14, 15]. However, evidence from visuoconstructional tests would suggest that functional impairments can be found in cognitive domains involving larger neural networks. In particular, recent neurofunctional studies demonstrated that drawing involves both posterior and anterior cortical areas [34], and constructional apraxia can be frequently associated with parieto-occipital lesions [35]; on this basis, the visuoconstructional deficits found in OLE patients might be ascribed to an alteration of circuitries projecting from the occipital cortex towards the parietal and frontal cortexes.

In the present study OLE patients showed worse performance than controls on delayed figure recall tapping visual long-term memory. This result might depend on their specific difficulty in processing visuospatial stimuli revealed by reduced performance on BJLOT and FCDT. This deduction seems to be supported by our findings that OLE patients did not show significant difficulty on performing cognitive tasks consisted of verbal stimuli (i.e., immediate and delayed recall of words list).

Moreover, patients with OLE were more impaired on the Stroop test with respect to normal subjects. Performance on the Stroop test is considered to be a measure of "cognitive" inhibition and has been described to be sensitive to lesions of the lateral and superior medial regions of the frontal lobes; instead, there is no specific association between performance on the Stroop test and lesions of the orbitofrontal cortex [36]. On this basis, we argue that impaired performance on the Stroop test is not related to behavioral disinhibition, that it is one clinical expression of orbitofrontal lesions [37, 38], but it might reflect poorer inhibitory "cognitive" control and suggest dysfunction of lateral and superior medial frontal regions. Interictal EEG findings in our series support this hypothesis: in fact, in 70 % of our patients (14/20) the interictal occipital paroxysmal activity spreads more or less frequently to the frontal lobes or shows a generalized diffusion. This finding might explain why cognitive disturbances in OLE patients are not strictly limited to altered function of the occipital lobes.

As for clinical aspects, the present study showed no association between age at onset and cognitive deficit as previously reported [15]. However, we found a significant association between duration of epilepsy and poor performance on the Stroop Test, evaluating inhibitory control; this finding may indicate that the frontal functions deteriorate with increasing duration of OLE and are in line with the idea of a relationship between progression of epilepsy and cognitive decline reported in a previous review [39].

The present study was the first to explore the possible presence of behavioral and psychological disturbances in adults with OLE. Our findings showed no significant

differences between OLE patients and control subjects in total scores on depressive and anxiety symptoms. However, correlation analysis indicated a significant association between age at onset of OLE and severity of euphoria, irritability, delusions and disinhibition. This might suggest that, although not different from those found in normal subjects, behavioral disorders thought to be related to frontal lobe dysfunctions [40] are more frequent in patients with higher age at onset.

Taken together, the impairments in complex visuospatial skills and frontal lobe functions suggest that seizures arising from the occipital lobes may alter functioning of cortico-cortical networks interconnecting occipital lobe with other cerebral regions. Although it is not possible in our patients to pinpoint the spatio-temporal dynamics of propagation of the epileptic discharges from the occipital focus towards the anterior regions, it could be hypothesized that such spreading occurred along the occipito-frontal (inferior occipital-frontal fasciculus) and/or dorsal (superior longitudinal fasciculus) visual pathways [41, 42]. Since these visual pathways reach different frontal and parietal neural targets, modulating different functions, it is likely that epileptic activity traveling along these connections might result in impairment of selective functions like the ones observed in our series.

In the present study, we did not compare performance of OLE patients with that of patients affected by other kinds of epilepsy (e.g., temporal or frontal lobe epilepsy), so we cannot infer whether the present visuospatial and executive deficits are specific for OLE patients. By comparing the profile of the OLE group to the other clinical groups it will be possible to verify whether a neurocognitive profile of OLE may play a role in future diagnostic classification systems.

All patients in our sample presented active epilepsy, with recurrent seizures in the last five years originating from the occipital lobes; in none of them were any brain structural abnormalities found. Consequently, the behavioral and cognitive defects observed in our study are most probably related to epilepsy itself. However, since all patients in our study were treated with AEDs, the possible role of drug treatment as a factor or a cofactor influencing behavioral and cognitive status must be taken into consideration. Several conflicting reports focused on potential effects of AEDs on neuropsychological functioning [43–46]. AEDs might exert differential, reversible, and sometimes cumulative cognitive adverse consequences through several possible causal mechanisms [47]. The possible contribution of AEDs is difficult to ascertain when studying patients with active epilepsy, and in fact all previous neuropsychological studies on temporal or occipital epilepsy were carried out on treated patients. The dissimilar patterns observed in patients with different epilepsy syndromes seem to suggest that the role of epilepsy type is more prominent in affecting neuropsychological functions than the possible role of AEDs. However, more extensive studies on patients on AED monotherapy and different epilepsy types are warranted in order to explore and understand the possible role of given AEDs in influencing neuropsychological testing.

In conclusion, our findings are in line with recent evidence suggesting that human epilepsy can be considered as a disorder of large cortical and subcortical networks, in which activity in any one part affects activity in all the others [48–51]. The structures underlying a specific patient's epilepsy are connected functionally and structurally; they are essential to development of seizures and to existence and maintenance of the epileptic disorder [48]. Our observation of impairment in frontal and parietal lobe functions in patients with nonsymptomatic OLE can be the result of epileptic activity spreading within a neural network involving structures far beyond the occipital lobe. Cooperative studies enrolling a larger number of cryptogenic and idiopathic OLE patients will help to comprehend whether nonsymptomatic OLE subtypes are related to different involvement of neural circuits, and to clarify the possible influence of clinical variables and drug treatment on cognitive and behavioral profile.

Conflicts of interest The authors declare that they have no conflict of interest.

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