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Cognitive dysfunctions in occipital lobe epilepsy compared to temporal lobe epilepsy

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Objective. To compare cognitive profiles of occipital lobe epilepsy (OLE) and temporal lobe epilepsy (TLE) and to investigate whether impairment of visuospatial functions is a specific deficit of OLE.

Method. Eighteen patients with OLE, 18 patients with TLE, and 18 controls underwent a neuropsychological battery assessing memory, visuospatial functions, and frontal/executive functions.

Results. Multivariate analysis evidenced poorer performance of patients with TLE and patients with OLE relative to controls on tasks assessing verbal and non-verbal long-term memory, frontal functions, and visuospatial functions. Patients with OLE had poorer performance than patients with TLE on visuospatial tasks, whereas patients with TLE performed worse than patients with OLE on verbal long-term memory test. Discriminant analysis identified two canonical discriminant functions: The first explained 53.3% of the variance, and the second explained 46.7% of the variance. The first function included verbal and non-verbal memory tests distinguishing controls from both OLE and TLE, whereas the second factor including a visuoconstructional test distinguished OLE from TLE and controls.

Conclusions. The results demonstrate that visuoconstructional dysfunction is related to OLE and support the idea that alterations of occipito-parietal stream may be specific to patients with OLE.

Cognitive impairment is one of the most frequent comorbidities in patients with epilepsy. Apart from the possible role of anti-epileptic treatment, several clinical features of the epileptic disorder do probably affect the cognitive profile of patients with epilepsy

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(Dodrill, 2004). Age at onset, type and frequency of seizures, aetiology, and topography of epileptogenic areas may all probably play a role. For this reason, it has been suggested that cognitive profiles in epilepsy are as heterogeneous as the epileptic syndromes themselves (Elger, Helmstaedter, & Kurthen, 2004).

Cognitive functions have been widely explored in patients with temporal lobe epilepsy (TLE). In comparison with healthy controls, the cognitive deficits most frequently observed in patients with TLE include memory dysfunctions, such as defects in learning and recall (Saling, 2009), and frontal dysfunctions, such as impairments of attentional control (Hudson, Flowers, & Walster, 2014), set-shifting, and working memory (Stretton & Thompson, 2012).

On the contrary, only few studies have assessed the cognitive profile related to occipital lobe epilepsy (OLE) in adults, perhaps due to the lower prevalence of OLE with respect to TLE. One study reported subtle difficulties in naming visually presented objects and identifying famous faces (Piazzini *et al.*, 2009), whereas the only systematic neuropsychological investigation revealed impairment in complex visuospatial skills, constructional abilities, and executive functions in adult patients with OLE compared with a sample of matched healthy controls (Bilo *et al.*, 2013). It is worth mentioning that impaired performance in visual–spatial tasks with high or low motor involvement has also been reported in children affected by benign epilepsy with occipital paroxysms (Germanò *et al.*, 2005). Such impairment of visuospatial or visuoconstructional functions might be specific to patients with OLE, but these cognitive abilities have been poorly explored in patients with TLE. One study revealed that patients with TLE performed as well as healthy control subjects on two low-level visual tasks, that is luminance and frequency discrimination with grey-scale stimuli, thus suggesting that occipital lobe function is not impaired in TLE (Grant *et al.*, 2008). However, Kimura (1963) reported impaired visual perception of nonsense abstract stimuli (but not of familiar stimuli, such as letters of objects) in epileptic patients with lesions of the right temporal lobe compared to patients with lesions of the left temporal lobe. Moreover, Hermann, Seidenberg, Schoenfeld, and Davies (1997) reported impaired visuoperceptual abilities on tasks such as judgment of line orientation and face recognition in patients with mesial TLE with hippocampal sclerosis compared to patients with mesial TLE without or with mild hippocampal sclerosis. In neither of these last studies, patients' performance was compared to that of control healthy subjects.

From brief overview, it appears evident that no studies on cognitive defects in adult epileptic patients compared neuropsychological performance of matched samples of patients affected by different epileptic syndromes with that of a matched group of healthy individuals. This procedure would also avoid considering possible non-specific consequences related to the disease state (e.g., psychological distress, necessity of chronic drug use, medicalization from early adolescence).

In this study, we performed a direct comparison of cognitive performance on a wide neuropsychological battery in two matched samples of patients with OLE and patients with TLE to identify possible different cognitive profiles between the two types of epilepsy. On the basis of the evidence briefly reviewed above, we expected that OLE is associated with impairments of visuospatial functions rather than with memory impairments, whereas TLE is associated with memory impairments rather than with visuospatial dysfunctions. Moreover, we did not expect to find significant differences between the two patient groups on frontal/executive functions.

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Method

Eligible subjects had to fulfil the following criteria: Active epilepsy, that is recurrent seizures within 5 years prior to the study (Cross, 2011); adult age (≥18 years) and educational level equal to or higher than elementary school; normal intelligence (age- and education-adjusted score ≥18.96 on Raven Coloured Progressive Matrices, RCPM (Carlesimo, Caltagirone, & Gainotti, 1996); absence of major depression according to DSM-IV criteria (American Psychiatric Association, 2000); and no medication but anti-epileptic drugs (AEDs). The specific diagnosis of OLE and of TLE was made according to criteria from ILAE classification of the epilepsies and epileptic syndromes (Commission on Classification and Terminology of the International League Against Epilepsy, 1989).

Among eligible subjects, to perform a case–control study specifically aimed at contrasting two samples of closely matched patients, we selected 18 patients with OLE (16 of whom participated in a previous neuropsychological study, Bilo *et al.*, 2013), and 18 patients with TLE paired for age and education.

The group of patients with OLE consisted of 11 women and seven men and included nine patients with idiopathic OLE (nine Gastaut type and one photosensitive type), seven patients with cryptogenic OLE, and two with symptomatic OLE (cortical dysplasia in both). Side of focus was left in eight patients, right in six, and bilateral in four. The TLE patient group consisted of 13 women and five men and included nine patients with cryptogenic mesial TLE, eight with symptomatic mesial TLE (hippocampal sclerosis in five, dysembryoplastic neuroepithelial tumour in one, cavernoma in one, and cortical dysplasia in one), and one with cryptogenic lateral TLE. Side of focus was left in 10 patients, right in three, and bilateral in five. Laterality of side of focus did not significantly differ in the two groups ($\chi^2 = 1.3, p = .5$). Patients' demographic and clinical details are reported in Table 1.

For each patient included in the study, we also enrolled an age- and education-matched healthy individual (11 women and seven men) not affected by any known neurological or psychiatric disorder, with general intelligence within normal range (age- and education-adjusted score ≥18.96 on RCPM Carlesimo *et al.*, 1996) and without major depression according to diagnostic criteria of DSM-IV (American Psychiatric Association, 2000).

Healthy controls were recruited among students and employees of the Second University of Naples. All data were collected from October 2010 to June 2012.

This study was reviewed and approved by the appropriate local ethics committee and has been performed in accordance with the ethical standards laid down in the 2013 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 provided their written informed consent, all participants underwent a battery of standardized neuropsychological tasks. An expert examiner, blinded to clinical and instrumental data, administered all the cognitive tests.

Neuropsychological assessment

All participants completed RCPM, and a neuropsychological battery including the following standardized and validated tests (references to Italian normative studies of the employed tests are reported in the Supporting Information): Benton Judgment of Line

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Table 1. Patients' demographic, clinical, and EEG data

Pt	Sex	Age	Syndrome	Age at onset (years)	Type of onset ictal symptom	Seizure frequency[a]	Interictal EEG: Side of paroxysmal activity[b]	AED treatment at study entry (mg/day)
Patients with OLE								
1	F	34	C	21	Elementary visual hallucinations	5	Left	LEV (3,000), CBZ (600), CNZ (1)
2	F	23	IP	16	Elementary visual hallucinations	0	Left	LTG (250)
3	F	41	C	15	Blindness	6	Left	OXC (1,050), TPM (200)
4	F	32	C	14	Elementary visual hallucinations	12	Right	LTG (450), CBZ (800)
5	F	22	IG	11	Elementary visual hallucinations;	5	Left	LEV (2,000)
6	M	50	C	18	Elementary visual hallucinations	0	Bilateral	OXC (1,500), LEV (3,000)
7	M	28	IG	13	Blindness	0	Right	CBZ (400)
8	F	24	IG	7	Elementary visual hallucinations	0	Bilateral	LEV (2,500)
9	F	27	IG	11	Elementary visual hallucinations	0	Right	PB (100)
10	F	30	C	9	Elementary visual hallucinations	20	Right	OXC (1,500), CNZ (3)
11	F	24	IG	18	Blindness	0	Bilateral	TPM (100)
12	M	26	IG	11	Elementary visual hallucinations	0	Left	CBZ (400)
13	M	25	IG	7	Elementary visual hallucinations	0	Left	LEV (1,500)
14	M	25	IG	7	Elementary visual hallucinations	0	Left	LEV (1,000)
15	M	50	C	12	Elementary visual hallucinations	0	Bilateral	OXC (1,800), LEV (3,000)
16	F	26	C	12	Elementary visual hallucinations	12	Right	LTG (250), VPA (1,100)
17	M	46	S	12	Elementary visual hallucinations	5	Right	CBZ (600), TGB (20)
18	F	39	S	29	Elementary visual hallucinations	35	Left	OXC (2,400), PGB 225
Patients with TLE								
1	F	39	MTLE-C	22	Rising epigastric sensation	18	Left	TPM (200), LEV (2,000)
2	F	20	MTLE-S	15	Fear/tachycardia	60	Left	LEV (1,500)
3	F	46	MTLE-S	4	Rising epigastric sensation, flushing of the face	18	Left	CBZ (1,200), LEV (3,000), PB (65)

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Table 1. (*Continued*)

Pt	Sex	Age	Syndrome	Age at onset (years)	Type of onset ictal symptom	Seizure frequency[a]	Interictal EEG: Side of paroxysmal activity[b]	AED treatment at study entry (mg/day)
4	M	37	MTLE-S	7	Rising epigastric sensation	200	Bilateral, asynchronous (Left > Right)	CBZ (1,600), LEV (3,000), PB (150)
5	F	20	LTLE-C	20	Annoying noise, vertiginous sensation	10	Left	LEV (3,000)
6	F	55	MTLE-C	33	Rising epigastric sensation	3	Bilateral, asynchronous (Left > Right)	OXC (1,650)
7	F	33	MTLE-C	21	Rising epigastric sensation, tachycardia, sialorrhea	1	Left	LEV (3,000), PB (100)
8	F	23	MTLE-C	12	Rising epigastric sensation	3	Right	CBZ (600), LEV (3,000)
9	F	32	MTLE-S	4	Fear/tachycardia	90	Bilateral, asynchronous (Left < Right)	CBZ (1,200), PHT (300), LCM (200)
10	F	35	MTLE-C	6	Rising epigastric sensation, tachycardia, fear	120	Right	PGB (300), PB (100)
11	M	25	MTLE-S	19	Rising epigastric, strong fear	0	Bilateral, asynchronous (Left > Right)	CBZ (1,200)
12	M	31	MTLE-S	5	Nausea, rising epigastric	15	Left	OXC (1,800), TPM (600), LTG (300), ZNS (300)
13	M	30	MTLE-S	28	Rising epigastric sensation	1	Left	OXC (1,500)
14	F	30	MTLE-C	25	Rising epigastric sensation	1	Left	PB (100)
15	F	55	MTLE-C	16	Rising epigastric sensation	0	Left	LTG (75)
16	F	31	MTLE-C	10	Nausea, tachycardia, Rising epigastric sensation	180	Right	OXC (1,200), LTG (400)

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Table 1. (*Continued*)

Pt	Sex	Age	Syndrome	Age at onset (years)	Type of onset ictal symptom	Seizure frequency[a]	Interictal EEG: Side of paroxysmal activity[b]	AED treatment at study entry (mg/day)
17	F	51	MTLE-S	32	Unpleasant smell	1	Bilateral, asynchronous (Left > Right)	CBZ (600)
18	M	44	MTLE-C	8	Joy/fear	2	Left	PB (100)

Note. OLE = occipital lobe epilepsy: C = cryptogenic; IP = idiopathic photosensitive type; S = symptomatic; IG = idiopathic Gastaut type; TLE = temporal lobe epilepsy: MTLE-S = mesial temporal lobe epilepsy – symptomatic; MTLE-C = mesial temporal lobe epilepsy – cryptogenic; LTLE-C = lateral temporal lobe epilepsy – cryptogenic.

[a]Seizure frequency refers to number of episodes occurred in the last year; EEG = electroencephalogram.

[b]That is, paroxysmal activity (as spikes, spike-wave or sharp-slow-wave complexes) detectable at least in one of available EEGs; AED = anti-epileptic drug (in parentheses dosage expressed as mg/die): VPA = valproic acid; LEV = levetiracetam; CBZ = carbamazepine; CNZ = clonazepam; LTG = lamotrigine; TGB = tiagabine; OXC = oxcarbazepine; TPM = topiramate; PB = phenobarbital; PGB = pregabalin; ZNS = zonisamide; PHT = phenytoin; LCS = lacosamide.

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Orientation Test (BJLOT), assessing visuospatial perception; Constructional Apraxia Test (CA), assessing visuoconstructional skills by copying of single geometrical figures; copying of the Rey-Osterrieth Complex Figure (ROCF), mainly assessing visuospatial planning abilities; Wisconsin Card Sorting Test (WCST), to assess cognitive flexibility; Stroop Color-Word Test, assessing inhibitory control; immediate and delayed recall of Rey's auditory 15 words, to assess verbal long-term memory; and delayed recall of ROCF, to assess non-verbal long-term memory.

Statistical analysis

To evaluate differences on demographic aspects (age, gender, and education) among the three groups (OLE group, TLE group, and control group), analysis of variance (ANOVA) and chi-square test were carried out, as appropriate. Group comparisons on continuous variables were made by means of multivariate analysis of variance, complemented by multivariate analysis of covariance (MANCOVA), and Bonferroni's *post-hoc* comparisons (with Bonferroni's correction for multiple comparisons: $p = .050/8 = .006$) were applied.

Stepwise discriminant function analysis (DFA) was run on all the neuropsychological scores included in this study, for identifying the cognitive measures most suitable to discriminate the three study groups.

Results

The three groups (patients with OLE, patients with TLE, and controls) did not differ on education, age, or gender (Table 2). TLE patients and OLE group significantly differed on seizures frequency (mean 40.2 ± 64.4 vs. 5.5 ± 9.3, $F = 5.096$, $p = .031$), whereas no significant difference was found between groups on age at onset and on number of AEDs (TLE vs. OLE: For age at onset, 15.9 ± 9.6 vs. 13.5 ± 5.5, $F = 0.878$, $p = .355$; number of AEDs, 1.8 ± 0.9 vs. 1.6 ± 0.6, $F = 0.701$ $p = .408$).

MANOVA showed significant differences among the three groups on cognitive tests (Wilks' lambda value = .161, $F = 7.125$, $p < .001$). Significant differences among groups were found on RCPM, and on immediate and delayed verbal recall, delayed recall of ROCF, interference task of the Stroop test, BJLOT, and CA (see Table 2).

Post-hoc analysis evidenced poorer performance of patients with TLE relative to controls on verbal immediate and delayed recall, delayed recall of ROCF, Stroop test, BJLOT, and CA. Patients with OLE showed poorer performance than controls on RCPM, and on immediate verbal recall, delayed recall of ROCF, Stroop test, CA, and BJLOT. The main finding of this study was that the comparison between OLE and TLE groups showed significant differences on RCPM, delayed verbal recall, and CA: Patients with OLE had poorer performance than patients with TLE on RCPM and CA, whereas patients with TLE performed worse than patients with OLE on delayed verbal recall. No significant difference between the two patient groups was found on immediate verbal recall, WCST, interference task of the Stroop test, BJLOT, copy and delayed recall of ROCF.

As patients with TLE and OLE group significantly differed on seizures frequency, we performed a MANCOVA in which seizures frequency was entered as covariate. Statistical analysis showed no effect of seizures frequency on cognitive performances (Wilks' lambda value = .809, $F = 0.657$, $p = .738$). MANCOVA confirmed the significant differences between TLE and OLE groups on RCPM, delayed verbal recall, and CA.

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Table 2. Demographic and cognitive comparisons among patients with OLE, patients with TLE, and healthy controls

	OLE (n = 18)	TLE (n = 18)	Controls (n = 18)	F	p
Gender (F/M)	11/7	13/5	11/7	0.663	.718
Age (years)	31.9 ± 9.2	35.3 ± 11.1	30.3 ± 10.4	1.323	.255
Education (years)	10.8 ± 3.8	11.1 ± 2.9	11.1 ± 4	0.050	.951
RCPM	27.5 ± 4.7[a]	28.1 ± 7.1	32.5 ± 2.8	8.565	.001
Memory domain					
Immediate recall	48.5 ± 8.6[a]	42.7 ± 10.4[a]	57.2 ± 9.1	8.813	.001
Delayed recall	11.4 ± 2.1[b]	8 ± 3.5[a]	13.3 ± 1.9	16.966	<.001
ROCF-delayed recall	12.6 ± 5.1[a]	7.9 ± 6.4[a]	20.3 ± 5.2	18.519	<.001
Frontal function domain					
Interference task of the Stroop test	18.7 ± 8.3[a]	21.4 ± 9.8[a]	31.8 ± 7.6	12.005	<.001
WCST	72.7 ± 31	68.9 ± 41.5	59.6 ± 34.1	1.030	.364
Copy ROCF	31.5 ± 4.6	29.8 ± 9	34.5 ± 3.2	2.587	.085
Visuospatial functions domain					
CA	11.4 ± 1.5[ab]	12.5 ± 1.3[a]	13.7 ± 0.6	15.180	<.001
BJLOT	19.1 ± 7.2[a]	21.7 ± 10.1[a]	27.1 ± 2.1	12.086	<.001

Note. F = females; M = males; WCST = Wisconsin Card Sorting Test; Copy ROCF = copying task of the Rey-Osterrieth Complex Figure Test (ROCF); RCPM = Raven's Coloured Progressive Matrices; CA = Constructional Apraxia test; BJLOT = Benton Judgment Lines Orientation Test; OLE = occipital lobe epilepsy; TLE = temporal lobe epilepsy.

[a]Significantly different from controls.

[b]Significantly different from TLE.

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Entering all single neuropsychological scores as variables, DFA showed that four cognitive variables were the most suitable to differentiate the three study groups: (1) delayed recall of ROCF (Wilk's lambda = .579; F = 18.519; df = 51; p < .001), (2) CA (Wilk's lambda = .400; F = 14.553; df = 100; p < .001), (3) delayed verbal recall (Wilk's lambda = .297; F = 13.655; df = 51; p < .001), and (4) immediate verbal recall (Wilk's lambda = .245; F = 12.242; df = 51; p < .001). Two canonical discriminant functions were produced: The first explained 53.3% of the variance, and the second explained 46.7% of the variance. The first function discriminated the control group (function at group centroid = 1.344) from OLE (function at group centroid = −0.241) and TLE (function at group centroid = −1.103). The second function discriminated OLE group (function at group centroid = −1.324) from TLE (function at group centroid = 0.857) and controls (function at group centroid = 0.466) (Figure 1).

The following tests were significantly correlated with the first function: Delayed recall of ROCF (r = .817), verbal delayed recall (r = .743), and verbal immediate recall (r = .563). Only CA was significantly correlated with the second function (r = .622). The classification results showed that 77.8% of the original group cases were correctly classified. Group membership was correctly predicted for 83.3% of the patients with OLE, 66.7% of the patients with TLE, and 83.3% of the controls.

Discussion

In the present study, we compared the cognitive profile of patients with OLE with that of patients with TLE to detect the specific cognitive deficits in these epileptic disorders. We found that both patient groups showed several cognitive impairments with respect to a sample of matched controls, but more interestingly, the discriminant analysis identified two functions: The first factor included verbal and non-verbal memory tests distinguishing

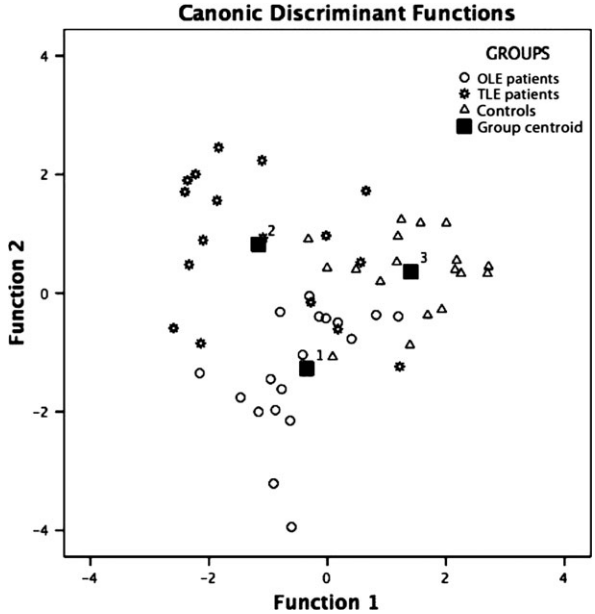

Figure 1. Scores of the two discriminant functions plotted by diagnosis of epilepsy.

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controls from both OLE and TLE, whereas the second function included a visuoconstructional test, which distinguished OLE from TLE and controls.

The second function identified by DFA underlined the specificity of visuoconstructive deficits, as assessed by copying of single geometrical figures, in OLE compared with TLE. These findings are in line with previous observations about subtle impairments in visuospatial processing such as object identification, mental manipulation of visuospatial stimuli, and visuoperceptual and visuoconstructional functions in both children (Brancati *et al.*, 2012; Chilosi, Brovedani, Moscatelli, Bonanni, & Guerrini, 2006; Germanò *et al.*, 2005) and adult (Bilo *et al.*, 2013; Piazzini *et al.*, 2009) patients with OLE. It is worth mentioning that our findings do not conflict with previous studies on TLE. Actually, our MANOVA demonstrated that TLE patients' performance on the visuoconstructive test was significantly lower than that obtained by healthy controls, in keeping with studies showing difficulties in specific visuospatial tests in such patients (Hermann *et al.*, 1997; Kimura, 1963). Nonetheless, our study demonstrated that very low scores on simple copying tests could distinguish patients with OLE from patients with TLE. It is also useful to underline that performance on a complex copying test (immediate reproduction of ROCF) did not discriminate between the two patient groups, as such test heavily relies on planning and executive functions that are likely impaired in both patient groups, as confirmed by the analysis of scores obtained on the tasks mainly evaluating cognitive flexibility and inhibitory control enclosed in the present study.

Recent neurofunctional studies demonstrated that constructional apraxia can be frequently associated with parieto-occipital lesions (Trojano & Conson, 2008); on this basis, the visuoconstructional deficits found in patients with OLE might be ascribed to an alteration of circuitries projecting from the occipital cortex towards the parietal and frontal cortexes. Surprisingly, we did not find significant differences between patients with OLE and patients with TLE on BJLOT, which is thought to be a good measure of visuospatial judgment mediated by the inferior parietal, occipito-parietal, and occipito-temporal regions of the right hemisphere (Tranel, Vianna, Manzel, Damasio, & Grabowski, 2009). However, recent functional imaging studies showed that performance on BJLOT activated both visuospatial areas (parietal and occipital areas) and dorsolateral prefrontal areas, likely because executive functions contribute to task performance (Kesler *et al.*, 2004). Therefore, the lack of significant differences between OLE and TLE groups might be ascribed to the poor performance on executive tests in both patient groups.

As for the first function identified by the discriminant analysis, verbal and non-verbal memory tests distinguished healthy controls from both OLE and TLE. The impairment of long-term memory occurring in both TLE and OLE, as compared to controls, is reinforced by the results of the multivariate analysis of variance. Memory deficits might be considered as a direct consequence of ictal and interictal epileptic paroxysmal activity involving the neural structures underpinning memory consolidation (hippocampus and related temporolimbic structures). In patients with TLE, this would be related to localization of epileptogenic foci in the medial temporal structures or to involvement of the medial temporal structures due to diffusion of paroxysmal activity originating in contiguous intratemporal foci. In our sample of patients with TLE, 15 of 16 had mesial TLE, with localization of the epileptogenic foci in the medial temporal areas. In the only patient with lateral TLE, the initial ictal auditory symptoms were quite often followed by oral automatisms, which suggest spreading of paroxysmal activity to the mesial temporal areas. This interpretation might find a support in case of material specific (verbal vs. non-verbal) memory defects in patients with unilateral paroxysmal activity (Blake, Wroe, Breen, & McCarthy, 2000; Hermann *et al.*, 1997), but we could not fully explore this issue

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because of the small number of patients with temporal paroxysmal activity localized only on the right side (3/18). In patients with OLE, it should be hypothesized that ictal and interictal epileptic paroxysmal activity arising in the occipital lobe tends to diffuse towards medial temporal structures (Salanova, Andermann, Olivier, Rasmussen, & Quesney, 1992). In fact, verbal memory impairment was recently found to be associated with left temporal lobe hypometabolism on [18F]-fluorodeoxyglucose positron emission tomography in patients with OLE (Knopman *et al.*, 2014), thus suggesting that cognitive dysfunctions in OLE patents are epiphenomena of epileptic seizures involving a wide cortical network, including occipital and extraoccipital regions. Within this context, the observation that patients with TLE had significantly poorer performances than patients with OLE in delayed verbal recall, as shown by the multivariate analysis of variance, might suggest that memory impairment is more specific and severe when the hippocampus is directly involved by the pathology. The absence of a correlation between frequency of seizures and memory deficits does not necessarily rule out the hypothesis that epileptic activity may play a role in memory impairment in these patients. For instance, interictal paroxysmal activity, not necessarily expressing as clinical seizures, might interfere with memory functioning (Mantoan *et al.*, 2009).

It is also possible to speculate that factors not specifically related to epileptic discharges might contribute to the memory impairments observed in both patients with TLE and patients with OLE with respect to controls. Both TLE and OLE are chronic conditions determining stress and have psychological and social consequences, which can be more debilitating than the seizures themselves (Living with Epilepsy Coping with Epilepsy, 2003; Sawyer & Escayg, 2010). The presence of a prolonged and chronic stressor condition might contribute to less efficient learning and memory (Hermann, Wyler, & Richey, 1988). We have no empirical evidence about this issue, as we did not collect information about the psychological status in our patients, but future studies might specifically test this possibility.

In the current study, the multivariate analysis of variance also showed significant impairment of inhibitory control in patients with TLE and in patients with OLE, as compared to controls. Such findings are in line with previous studies (Corcoran & Upton, 1993; Hermann, Seidenberg, Lee, Chan, & Rutecki, 2007; Horner, Flashman, Freides, Epstein, & Bakay, 1996; Kim, Lee, Yoo, Kang, & Lee, 2007) and indirectly support the idea that occurrence of executive dysfunction in both epileptic disorders might be due to a widespread cortical or subcortical involvement beyond the lobe from which the seizures arise (Dabbs, Jones, Seidenberg, & Hermann, 2009; Mueller *et al.*, 2009; Riley, Moore, Cramer, & Lin, 2011). However, the lack of any correlation of dysexecutive scores with the two factors identified by the discriminant analysis would suggest that these cognitive impairments are not specific of either TLE or OLE.

Several studies showed that cognitive impairment impacts on psychological functioning and quality of life in epileptic children (Caplan, 2013; Ferro *et al.*, 2013) and adult patients (Baker, Taylor, & Hermann, 2009; Baker *et al.*, 2008; Dodrill, 1992; International Bureau for Epilepsy, 2004). Cognitive dysfunction can affect day-to-day functioning, quality of life, and social relationships (Baker *et al.*, 2009), thus modifying employment status, interpersonal communication, and role within the family in epileptic patients (Baker *et al.*, 2008; International Bureau for Epilepsy, 2004). Therefore, neuropsychological assessment needs to become an integral aspect of the management of epilepsy (Baker *et al.*, 2009). Here, on the basis of our findings, we underline the utility to investigate visuoconstructional functions by specific cognitive tasks in patients with

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OLE in order to identify early these cognitive dysfunctions and to design optimal individualized cognitive rehabilitation.

Our study has several limitations. We did not assess low-level visual functions, such as visual acuity that might contribute to visuoconstructional disorders. However, we were mainly interested in use of widely known, standardized, and validated paper-and-pencil tests, which are easily employed in clinical settings. Analogously, it should be mentioned that defective processing of visuospatial material might lower performance on RCPM that have been used as a measure of intelligence in the present study. However, it is important to underline that the use of RCPM can allow to compare our findings with those of other studies on epileptic patients, in which general intelligence level has been evaluated by means of RCPM or of the Wechsler Adult Intelligence Scale, tapping executive functioning and visuospatial processing. Last, as already recalled above, we did not address the relationships between cognitive and psychological aspects of patients' life, which instead seem to be worth investigating.

In conclusion, the present study is the first to compare the cognitive profile of patients with OLE with that of patients with TLE in order to detect the specific cognitive deficits in these epileptic disorders. Although neuropsychological tests investigate more than one function and are not linked to specific brain regions, our results that visual constructive deficits appear significantly more impaired in patients with OLE in comparison with patients with TLE seem to support the idea that alterations of occipito-parietal stream may be specific in patients with OLE, whereas memory dysfunction distinguishes the cognitive profile of both patients with TLE and patients with OLE from healthy controls.

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Supporting Information

The following supporting information may be found in the online edition of the article:

Data S1. References to Italian normative studies of the employed tests.

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