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Object and proper name retrieval in temporal lobe epilepsy: A study of difficulties and latencies

Valérie Condret-Santi[a], Gladys Barragan-Jason[a], Luc Valton[a,b], Marie Denuelle[b], Jonathan Curot[a,b], Jean-Luc Nespoulous[c], Emmanuel J. Barbeau[a,*]

[a] *Centre de Recherche Cerveau et Cognition, CNRS et Université de Toulouse, UMR 5549, 31052 Toulouse Cedex, France*
[b] *Explorations Neurophysiologiques, Hôpital Pierre Paul Riquet, Centre Hospitalier de Toulouse, 31052 Toulouse Cedex, France*
[c] *Octogone, Université de Toulouse, EA 4156, 31052 Toulouse Cedex, France*

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Summary
Purpose: Retrieving a specific name is sometimes difficult and can be even harder when pathology affects the temporal lobes. Word finding difficulties have been well documented in temporal lobe epilepsy (TLE) but analyses have mostly concentrated on the study of accuracy. Our aim here was to go beyond simple accuracy and to provide both a quantitative and a qualitative assessment of naming difficulties and latencies in patients with TLE.
Methods: Thirty-two patients with temporal lobe epilepsy (16 with epilepsy affecting the cerebral hemisphere dominant for language (D-TLE) and 16 with epilepsy affecting the cerebral hemisphere non-dominant for language (ND-TLE)) and 34 healthy matched control subjects were included in the study. The experiment involved naming 70 photographs of objects and 70 photographs of celebrities as fast as possible. Accuracy and naming reaction times were recorded. Following each trial, a questionnaire was used to determine the specific nature of each subject's difficulty in retrieving the name (e.g., no difficulty, paraphasia, tip of the tongue, feeling of knowing the name, etc). Reaction times were analysed both across subjects and across trials.

Key findings D-TLE patients showed consistent and quasi-systematic impairment compared to matched control subjects on both object and famous people naming. This impairment was characterized not only by lower accuracy but also by more qualitative errors and tip of the

* Corresponding author. Tel.: +33 5 81 18 49 60.
E-mail address: emmanuel.barbeau@cerco.ups-tlse.fr (E.J. Barbeau).

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tongue phenomena. Furthermore, minimum reaction times were slowed down by about 70 ms for objects and 150 ms for famous people naming. In contrast, patients with ND-TLE were less impaired, and their impairment was limited to object naming.
Significance These results suggest that patients with TLE, in particular D-TLE, show a general impairment of lexical access. Furthermore, there was evidence of subtle difficulties (increased reaction times) in patients with TLE.

Introduction

Talking engages many processes, beginning with the thought of what we want to express and ending with the rapid articulation of sequences of words (Indefrey, 2011). This extraordinarily efficient and effortless ability (Alario et al., 2004) is underpinned by a widespread brain circuitry in which the temporal lobes play a central role (Hirsch et al., 2001). It is well established that people with temporal lobe epilepsy (TLE) have word finding difficulties following temporal lobe resection surgery (Drane et al., 2008). However, patients complain about word finding difficulties even before resection (Piazzini et al., 2001). Lomlomdjian et al. (2011) showed that almost one-third of patients with TLE reported frequent and severe word finding problems during spontaneous speech. These complaints are not systematically related with performance on testing (Thompson and Corcoran, 1992; Vermeulen et al., 1993; Giovagnoli et al., 1997), particularly when visual confrontation naming tasks are used (compared to auditory naming tasks, e.g. Hamberger and Tamny, 1999; Lomlomdjian et al., 2011). However, tests usually focus on accuracy and relate patients' failures to lexical loss, i.e. anomia (Laine and Martin, 2006). A recent study attempted to overcome this limitation using a detailed procedure. Drane et al. (2013) used the Iowa Famous Faces test to show that naming deficits are consistently observed in TLE patients both before and after resection surgery. They also noted that having additional time did not help these patients and that there were qualitative differences between left and right TLE patients.

Other difficulties could explain patients' problems. For example, even typical individuals occasionally experience difficulty retrieving a particular word, even if they know or ought to know the word. This complex cognitive phenomenon, which differs from lexical loss, is called ''word retrieval failure'' and has been investigated in linguistic and neuroimaging studies (Evrard, 2002; Burke and Shafto, 2004; Maril et al., 2005). There are two types of word retrieval failure. The first is the tip of the tongue phenomenon (TOT) which is defined by an incapacity to produce a specific word associated with a strong feeling that retrieval is imminent and usually combined with partial recall of some features of the word that is missing (phonological cues, word length, etc.). This phenomenon is thought to be due to the blocking of phonological representations (Brown and McNeill, 1966; Brown, 1991; Rastle and Burke, 1996; Burke and Shafto, 2004; Lindín et al., 2010). The second type of retrieval failure is the ''feeling of knowing the name'' phenomenon (FOKn), which is the feeling that one probably knows or has known the name but that it is too deeply buried in memory to be easily retrieved. As such, it is associated with an inability to access the lexical representation of the word. TOT and FOKn are both observed in healthy subjects (Evrard, 2002). Word retrieval failures can be solved after some time (the word one is searching for may come back to mind after a few seconds) or may remain unresolved, leading to the frustration so characteristic of these states.

Thus, a word retrieval failure is by definition characterized by abnormal latencies in name production. Studying naming latencies thus appears critical to investigating such language difficulties. However, this has seldom been carried out in previous studies of epileptic patients, a major problem since some anti-epileptic drugs are known to increase word finding difficulties. Gallegos and Tranel (2005) compared naming latencies for happy and neutral faces of celebrities in patients who had undergone left or right anterior temporal lobectomy and controls. They did not find any difference between groups, but they did not control for long latencies due to naming difficulties, such as Tip-of-the-Tongue States. Recently, Lomlomdjian et al. (2011) evaluated the time needed to correctly name pictures of the Boston Naming test in TLE patients and found no significant difference relative to controls. In contrast, mean response reaction times for famous face naming were found to be longer in both left and right pre-surgical TLE patients in Drane et al.'s (2013) study. However, the naming delays reported in these studies, as in some others (e.g., Bell et al., 2003), were longer than the expected delays reported in other studies (for a review, see Indefrey, 2011). This may be a problem since patients may use various sorts of compensatory strategies that could hide their difficulties if they are allowed unlimited time to answer. We therefore applied speed constraints in the present study to avoid this potential compensation.

Healthy subjects have more naming difficulties with proper names than common names (Evrard, 2002). In fact, the TOT phenomenon mostly affects the retrieval of proper names (Brédart, 1993). In certain cases, anomia may even be limited to proper names and spare common names (Semenza and Zettin, 1989; Semenza, 2006). Proper names are also more difficult to retrieve than other information about people (Cohen and Burke, 1994; Valentine et al., 1996). Left anterior temporal structures are known to be involved in proper name retrieval (Damasio et al., 1996; Tranel et al., 1997; Gorno-Tempini et al., 1998; Fukatsu et al., 1999; Grabowski et al., 2001; Glosser et al., 2003; Rotshtein et al., 2005; Trebuchon-Da Fonseca et al., 2009). For this reason, and because of their social importance, proper names are of special interest for people with TLE.

Table 1 *Demographic and neuropsychological data of the D-TLE, ND-TLE and control subjects (mean and standard deviation).* M = male, F = female; R = right, L = left; A = ambidextrous; educational level = number of years since first grade; WAIS = Wechsler adult intelligence scale-III (VIQ = verbal intellectual quotient, PIQ = performance IQ, FSIQ = full scale IQ); DO = dénomination orale.

	D-TLE (n = 16)	ND-TLE (n = 16)	Controls (n = 34)	p-Value
Demographic data				
Age at testing (years)	39.44 (12.36)	40.44 (10.33)	37.41 (13.26)	Ns
Gender (F/M)	13/3	6/10	19/15	<0.05[c]
Educational level (years)	11.67 (2.92)	12.31 (3.63)	12.53 (2.27)	Ns
Handedness (R/L/A)	16/0/0	12/2/2	31/1/2	Ns
Patients' characteristics				
Number of antiepileptic drugs	2.31 (.70)	2.50 (1.59)		Ns
Duration of epilepsy (years)	18.36 (12.54)	19.91 (17.82)		Ns
Age of seizure onset (years)	18.00 (9.78)	21.36 (15.39)		Ns
Current frequency of seizures (per month)	3.00 (2.52)	6.00 (4.41)		<0.05
Neuropsychological evaluation				
WAIS-III VIQ	86.56 (18.86)	93.77 (24.02)		Ns
WAIS-III PIQ	84.13 (16.13)	90.54 (23.92)		Ns
WAIS-III FSIQ	82.00 (17.34)	93.15 (23.06)		Ns
DO80 (naming task, max = 80)	76.50 (3.44)	78.58 (1.83)	79.13 (1.18)	<0.005[a,c]
Verbal fluency P (2mn)	18.50 (8.03)	19.08 (10.44)	24.23 (5.96)	<0.05[a,b]
Verbal fluency R (2mn)	16.92 (7.43)	16.14 (8.72)	22.49 (7.76)	<0.05[a,b]
Verbal fluency animals (2mn)	25.67 (7.16)	27.54 (10.29)	33.32 (6.44)	p < 0.05[a,b]
Verbal fluency fruits (2mn)	15.00 (3.51)	18.79 (5.51)	21.84 (4.12)	p < 0.001[a,b,c]
Pyramid and Palm tree test words	51.20 (1.03)	51.00 (1.66)	51.33 (0.96)	Ns
Pyramid and Palm tree test pictures	50.90 (1.45)	50.56 (2.79)	50.88 (1.27)	Ns

[a] Significant difference between D-TLE and control groups.
[b] Significant difference between ND-TLE and control groups.
[c] Significant difference between D-TLE and ND-TLE groups. Ns = non-significant.

In this study, we aimed to obtain an objective quantification and characterization of naming difficulties in patients with TLE. To address this issue, we analysed accuracy, latencies, and the type of word retrieval difficulty (TOT, FOKn, paraphasia ...) when participants named photographs of objects and famous people as fast as they could. Based on the available literature, we hypothesized that D-TLE (TLE affecting the cerebral hemisphere dominant for language) would lead to impaired naming accuracy and latency for both objects and celebrities while ND-TLE (TLE affecting the cerebral hemisphere non-dominant for language) would cause impaired accuracy and latency in naming celebrities but not objects.

Methods

Participants

Thirty-two patients with drug-refractory TLE and 34 control subjects matched for age, sex, handedness and education participated in this study (Table 1). Subjects were selected from a group of 315 patients with refractory epilepsy who had had a presurgical evaluation between 2007 and 2011. All patients underwent a comprehensive evaluation, including detailed history and neurological examination, neuropsychological testing, routine brain magnetic resonance imaging (MRI), and surface video-EEG recordings of seizures in order to identify the seizure onset localization (in two patients, intracranial video-EEG monitoring (stereo-EEG using depth electrodes) was also used). Ictal video-EEG recordings demonstrated unilateral temporal lobe seizure onset localized either in the hemisphere dominant (16 patients) or non-dominant (16 patients) for language. Hemispheric language dominance was determined by handedness assessment (Oldfield, 1971), or by a Wada Test in seven patients (Table 2). Postictal language difficulties were observed only in patients with TLE affecting the cerebral hemisphere dominant for language. Moreover, among the 23 patients who subsequently underwent an anterior temporal lobectomy, language difficulties were observed in all patients (n = 11) who had operations in the hemisphere dominant for language and never in those (n = 12) who had operations in the hemisphere non-dominant for language. Patients with ongoing psychiatric symptoms (as detected during the neurological consultation or neuropsychological testing) were not included in the present study.

Patients followed the protocol currently used in the Epileptology Unit at the Department of Neurology, Rangueil Hospital, University of Toulouse, France as part of their presurgical assessment.

Neuropsychological assessment

Each patient underwent a complete neuropsychological evaluation, including an assessment of IQ (Wechsler Adult Intelligence Scale-III (Wechsler, 1997), memory, language,

Table 2 *Description of patients*. Dominant hemisphere for language (D = dominant, ND = non dominant); manual laterality (L = left, R = right, A = ambidextrous); Oldfield test (11 items, R = right, L = left, B = both); Wada test (L = left, R = right); epilepsy side (L = left, R = right); age (years); sex (M = male, F = female); Operated patients (Y = yes, N = no, P = pending); education level (years since 1st grade); early childhood history (FC = febrile convulsion, M = meningo-encephalitis, ND = natal distress, T = toxoplasmosis); generalized seizure (Y = yes, N = no); seizure frequency (number of seizures per month, SM = several per month, SW = several per week); AED = antiepileptic drug (CBZ = carbamazepine, CLB = clobazam, CLN = clonazepam, GBP = gabapentine, LMT = lamotrigine, LVT = levetiracetam, OCZ = oxcarbazepine, PER = perampanel, PB = phenobarbital, PHT = phenytoine, PGB = pregabaline, TGB = tiagabine, TPM = topiramate, VPA = sodium valproate).

Patient	Dominant hemisphere	Manual Laterality	Oldfield test			Wada test	Operated Patient	Age	Sex	Education Level	Epilepsy side	Seizure onset	Early childhood history	Generalized seizures	Seizure frequency	AED		
			R	L	B													
1	D	R	11			L	Y	41	F	12	L	34		N	2.5	OCZ	LMT	
2	D	R	10		1		N	52	F	10	L			Y	2	CBZ	LVT	
3	D	R	11				N	24	F	9	L	14		N	1.5	LVT	CBZ	
4	D	R	11				Y	27	F	17	L	6	T	Y	4	LVT	OCZ	
5	D	R	11				Y	32	M	7	L	18	M	Y	2	LVT	CBZ	
6	D	R	6		5		N	17	M	11	L	17	FC	N	1	OCZ		
7	D	R	11				N	56	F	11	L	30	ND	Y	PM	PB	TGB	CLN
8	D	R	11				Y	46	F	10	L	24	M	Y	1.5	TPM	LVT	CLB
9	D	R	11				Y	38	F	16	L	15		N	6.5	CBZ	LMT	PER
10	D	R					Y	30	F	17	L	6	FC	Y	2	CBZ	PGB	
11	D	R	8		3		Y	53	F	9	L	3		N	6	CBZ	VPA	TPM
12	D	R					Y	59	M	10	L	8	FC	N	PM	GBP		
13	D	R	10		1	R	Y	27	F	11	R	17	FC	Y	7.5	OCZ	VPA	
14	D	R	10		1		N	45	F	13	L	34		N	7.5	LVT	LMT	
15	D	R	11				Y	38	F	10	L	7		N	5	CBZ	LVT	CLN
16	D	R					Y	45	F	11	L	30	FC	N	12	GBP	OCZ	
17	ND	R	11				Y	60	M	16	R	2	FC	Y	PM	LVT	CBZ	CLB
18	ND	R	10		1		Y	35	F	14	R	2	FC	N	4	LMT		
19	ND	R	11				Y	44	F	15	R	34	FC	N	0	VPA	TPM	
20	ND	L	11			L	Y	45	M	15	R	37		Y	8	LMT	CBZ	
21	ND	R					P	39	M	11	R	12	FC	Y	7	LMT	OCZ	TPM
22	ND	R	11				Y	43	M	16	R	27		Y	2.5	LVT	OCZ	
23	ND	R				L	Y	40	M	16	R	20	FC	N	12	CLN	LMT	TPM
24	ND	L				L	Y	21	M	14	R	17		N	3	LVT	OCZ	
25	ND	R	9		2	L	Y	18	F	11	R	11	FC	Y	2	LVT	LMT	
26	ND	R	11				Y	35	M	14	R	1	FC	N	5	CBZ	PB	PHT
27	ND	R	11				N	53	F	5	R	35		Y	PH	LVT	PGB	
28	ND	R	11				Y	46	M	11	R	31		Y	PH	CBZ	LVT	LMT
29	ND	A	4	1	6		Y	45	M	5	R	17	FC	N	PH	LVT	LMT	
30	ND	A	7	2	2		N	38	M	12	R	32	FC	N	0	PGB	CLB	
31	ND	R	11			L	Y	45	F	8	R	0	FC	Y	14	CBZ	TPM	CLB
32	ND	R					N	40	F	14	R	33	FC	N	7	PGB		

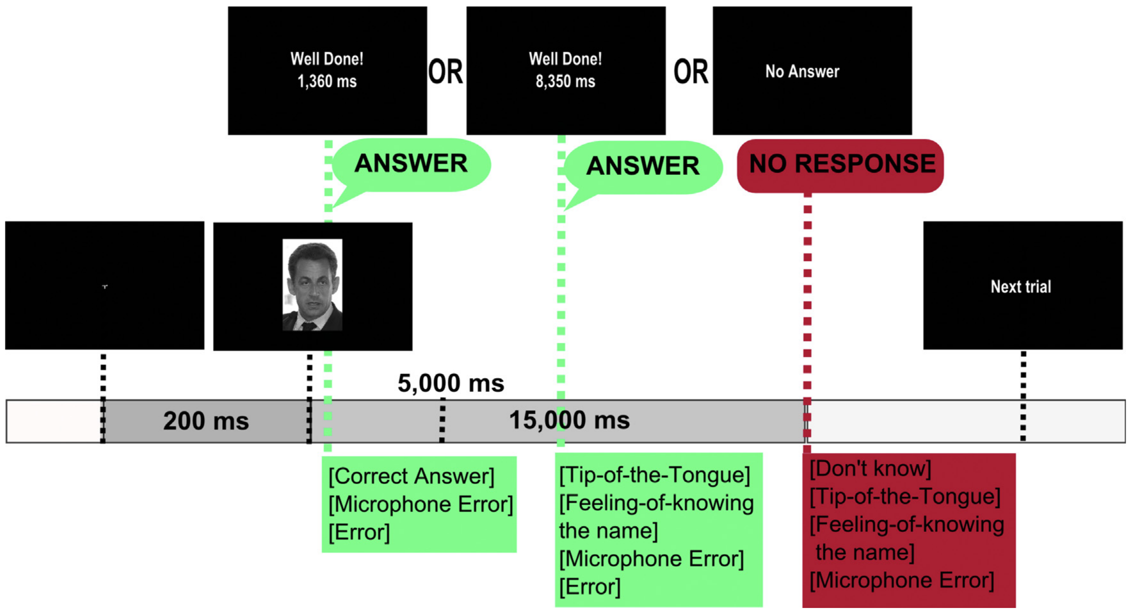

Fig. 1 Design of the experiment (©photo: European People's Party via @Flick'r).

and visual perception. Language skills were assessed using standard tasks such as the DO 80 (Deloche and Hannequin, 1997; a simple French confrontation naming test where subjects have to name 80 line-drawings of objects), the Pyramid and Palm Tree (Howard and Patterson, 1992) and word fluency tests (Horn, 1983) (Table 1).

Naming complaint

Each participant completed a complaint questionnaire in which they had to report how much a statement (e.g., ''The fact that I can't remember people's names has a negative impact on my daily life'') applied to them on a 4-point scale (1: never, 2: rarely, 3: sometimes, 4: always). Three statements related to object and people naming were analysed in the context of the present study.

Stimuli and materials

Stimuli were 70 photographs of famous people and 70 photographs of objects or animals. Famous people were well-known celebrities encompassing a broad spectrum of fields (politicians, comics, singers, movie actors, etc.) presented in natural scenes in grey shades. Background information was neutral and did not contain elements useful for recognizing the celebrity. Objects were presented in colour without any background (grey background). We selected objects that had a low oral frequency to avoid ceiling effects ($M = 4.24$, $SD = 2.70$ per million) from the ''lexique 3'' database, (www.lexique.org, New et al., 2004). The words were drawn from various categories (food: 9 items, tools: 28, animals: 21, furniture: 8, clothes: 4). No attempt was made to directly compare performance on objects and famous people naming since both class of stimuli and performance differed considerably.

Images were presented on a computer screen. The distance between the screen and the subject was ~70 cm, with stimuli subtending a visual angle of $\sim 7.2 \times 10.7$ degrees. Subjects held a microphone in their hand, which was used to record latencies. The microphone was linked to a dedicated response box allowing vocal key recording (Serial Response box from Psychology Software Tools, Inc, www.pstnet.com/eprime). Eprime software v2 (Psychology Software Tools, Inc. www.pstnet.com/eprime) was used to run the experiment and record all vocal and behavioural responses.

Procedure

The stimuli (objects and famous faces) were randomly presented one by one on a computer screen. First, participants saw a fixation cross during 200 ms followed by the target, which remained on screen until the participant responded or until 15 s had passed (Fig. 1). Subjects were instructed to name images as accurately and as quickly as they could. They were also instructed to directly provide the name of the object (without the articles that are used in French for objects, e.g., *la*, *le*, *les*.) or the surname of the person (without the first name). If subjects failed to follow these instructions (e.g., providing comments rather than the name) or if the microphone voice key was activated by noise unrelated to the experiment (e.g., lip smacking), the trial was discarded (''discarded trial''). If subjects could not correctly name the stimulus, for whatever reason, they were asked to continue their search and refrain from speaking until the end of the 15-s deadline. Feedback was displayed showing the reaction time for each trial after subjects had answered or at the end of the 15 s (Fig. 1). Subjects were asked to monitor this feedback so as to perform as fast as they could. All subjects were trained with the procedure before the experiment using a specific set of stimuli (four objects and four famous people) that were not repeated afterwards. The training could be repeated if the subject or the experimenter felt it was needed (this occurred only once in 66 subjects).

Depending on how subjects had answered and their latency, we rated their responses differently. If the subject answered correctly before an arbitrary delay of 5 s, then it was considered a ''correct response''. Concerning famous people, responses were judged correct when participants gave the first name and surname or surname only (even if they were asked to preferentially provide the surname to increase speed). A short interview was conducted to understand the nature of the error, and we differentiated ''Semantic errors'' (SE) (for example answering ''Gordon Brown'' for ''Tony Blair''), ''Phonological errors'' (PE) (answering ''bouche''—mouth instead of ''louche''—ladle) or ''visual errors'' (VE), when participants mistook the target (a rope for a rubber band for example). If the subject answered after a delay of 5 s but before the 15 s deadline, we interviewed him/her to determine if the problem was a TOT or a FOKn. This was classified as a resolved TOT or FOKn. A precise scoring method was developed to determine which recall state the subject was experiencing. Participants were asked to report their subjective feelings about the imminence of the word retrieval, the presence of phonological clues, etc. A trial was classified as a TOT if at least one of these subjective reports matched the subject's feeling and knowledge about the word: imminence, phonological clues, and numbers of letters. In the case when participants failed to answer before the 15 s deadline, we used the same questionnaire to determine whether this was due to a TOT or a FOKn, which were then classified as ''unresolved TOT'' and ''unresolved FOKn''. A last possibility could be that the stimulus was unknown to the subject, and thus classified as a ''Don't know'' answer (DK). In order to differentiate ''Don't know'' (DK) from FOKn answers, we asked the participants for semantic details about the person/object, we tried to prime the word using the first phoneme, and we proposed a multiple-choice questionnaire with the target word and two distractors, using a list of distractors matched to each target and prepared in advance (e.g., for the ''Sean Connery'' item, we asked if it was ''Roger Moore'', ''Sean Connery'' or ''Timothy Dalton''). After each response had been correctly characterized, the experimenter started the next trial.

Statistical analyses

We conducted ANOVAs on each dependent variable with the group (control subject, D-TLE, ND-TLE) as a fixed factor and using post-hoc analyses (Tukey's HSD) if necessary to compare differences in performance between groups. Gender (as a categorical variable) was analysed using a χ^2 test. Results on the complaint questionnaire did not follow a normal distribution, so a non-parametric Mann—Whitney test was used.

Reaction time (RT) latency analyses were performed across subjects and across trials. Across-trial analyses were performed by pooling all trials from all participants for a given group. Across-trial analyses have been used in previous studies (Rousselet et al., 2003; Barragan-Jason et al., 2012, 2013; Besson et al., 2012) and are like building a ''meta-participant,'' reflecting the performance over the entire population. To compare RT distributions across groups, trials were pooled in a sliding bin (width: 100 ms, step: 1 ms) for each group, and χ^2 tests were performed between groups on these bins. To avoid the problem of multiple comparisons, a bin was considered significant if the following 50 ms were also continuously significant (Liu et al., 2009).

To obtain an estimation of the minimal processing time required to recognize pictures (Rousselet et al., 2003; Barragan-Jason et al., 2012, 2013), the minimal behavioural reaction time was computed for each subject by identifying the shortest reaction time to correctly name stimuli in each condition (object or famous person); i.e. fastest correctly named object or famous face for each subject.

We looked at the impact of different linguistic characteristics on our main dependent variables using correlations (Pearson's r) and stepwise regression analyses to examine the contribution of each linguistic characteristic to naming latency independently. We ran ANOVAs for categorical variables (e.g., voiced vs. non-voiced first phoneme and living vs. non-living objects).

The statistically significant difference threshold was set at $p < 0.05$. All tests were two-tailed.

Results

Subject characteristics

Demographic data are presented in Table 1. Groups were homogenous for all characteristics except sex ratio, $\chi^2(2) = 7.67$, $p < 0.05$ as there were more females in the D-TLE group. Patients are described in Table 1 (group data) and Table 2 (individual data). The only difference between the two groups concerned the frequency of seizures. The neuropsychological assessments (Table 1) revealed differences between D-TLE and controls on a standard test of naming (DO80) as well as on fluency tests. ND-TLE differed from controls on the fluency tests.

Word finding complaint

D-TLE patients reported more difficulties than ND-TLE patients on the statement: ''The fact that I can't remember people's names has a negative impact on my daily life'' (D-TLE: $M = 1.88$, SD = 1.15; ND-TLE: $M = 1.31$, SD = 0.87; $U = 128$, $p < 0.05$). Likewise, they reported more difficulties than ND-TLE on the statement: ''I confuse names of objects'' (D-TLE: $M = 2.12$, SD = 0.96; ND-TLE: $M = 1.50$, SD = 0.73); $U = 704$, $p < 0.05$). No difference between D-TLE and controls was found, however.

In contrast, ND-TLE patients reported less difficulty than controls for the statements ''The fact that I can't remember people's names has a negative impact on my daily life'' (ND-TLE: $M = 1.31$, SD = 0.87; controls: $M = 1.74$, SD = 0.86; $U = 2312$, $p < 0.05$) and ''I have trouble remembering the names of objects I use in daily life (e.g., the names of tools)'' (ND-TLE: $M = 1.38$, SD = 0.89; controls: $M = 1.85$, SD = 0.82; $U = 2312$, $p < 0.05$).

Object naming

An ANOVA revealed an effect of the group on the number of discarded trials ($F(2,63) = 3.57$, $p < 0.05$) as D-TLE produced more discarded trials (3.88, SD = 4.67) than controls (1.65, SD = 1.87, $p < 0.05$) (Fig. 2). To suppress the bias induced by these discarded trials, we carried out our analyses on the proportion of correct responses corrected for the number

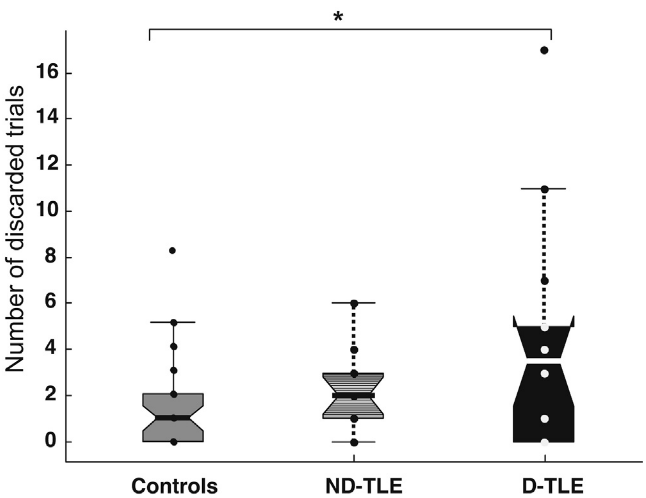

Fig. 2 Boxplot of the percentage of discarded trials for objects for each group. Boxes represent the 25th and 75th percentiles; the horizontal lines inside the boxes are the medians. Notches display the 95% confidence interval around medians. Lower and upper horizontal lines represent minimum and maximum performance. * $p < 0.05$.

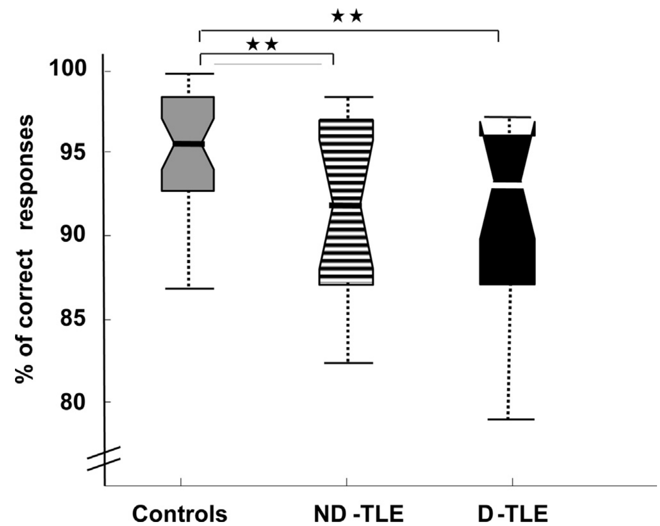

Fig. 3 Boxplot of the percentage of correctly named objects for each group. ** $p < 0.01$.

of discarded trials (number of responses/(total number of trials − number of discarded trials) × 100). Performance on the task is presented in Table 3 and Fig. 3. A between-factor ANOVA revealed a significant group difference for the number of correct responses ($F(2,63) = 125.58$, $p < 0.01$), D-TLE and ND-TLE being less accurate than controls (D-TLE: −4% of objects named, $p < 0.005$. ND-TLE: −3.5%, $p < 0.005$).

The total number of TOT was significantly different between groups ($F(2,63) = 4.707$, $p < 0.05$), with D-TLE experiencing 2.38% more TOT than controls ($p < 0.01$). However, the percentage of TOT compared to the total of answers provided was remarkably low overall (control subjects: 0.52%, ND-TLE: 1.67%, D-TLE: 2.90%). For this reason, no difference was found between resolved or unresolved TOT. Median latencies across subjects (Table 3) were different between groups ($F(2,63) = 6.21$, $p < 0.01$). D-TLE patients took 265 ms ($p < 0.01$) and ND-TLE patients 226 ms more time than controls ($p < 0.05$). Minimum latencies across subjects were also 70 ms longer in the D-TLE group ($p < 0.05$) and 80 ms longer in the ND-TLE ($p < 0.05$) than in the control group. No other differences were found between groups for any of the other measurements or types of errors.

RT distributions across trials are presented in Fig. 4 for each group. D-TLE and ND-TLE RT distributions were clearly shifted to the right, indicating overall longer RTs, with D-TLE patients slower than controls and ND-TLE patients in the 400—700 ms time-range.

Famous people naming

D-TLE patients ($M = 6.06$, SD = 4.57) showed a non-significant tendency to have a higher number of trials discarded than controls ($M = 3.32$, SD = 2.75, $p < 0.06$) (Fig. 5). A group effect was also found on the number of correct responses ($F(2,63) = 5.50$, $p < 0.01$) and total TOT ($F(2,63) = 6.25$, $p < 0.01$) and also resolved TOT ($F(2,63) = 3.78$, $p < 0.05$), D-TLE naming 20% less celebrities than controls ($p < 0.01$) (Fig. 6) and experiencing more total TOT (22.65%, SD = 14.90) than controls (12.19%, SD = 6.00, $p < 0.05$) and ND-TLE

Table 3 *Across-subjects results on the experimental naming task for the three groups.*

		Controls		D-TLE		ND-TLE	
		Mean	SD	Mean	SD	Mean	SD
Accuracy (%)	Objects	95.16[a,b]	3.89	90.87[a]	6.35	91.74[b]	5.60
	Celebrities	63.91[a]	18.64	43.64[a]	18.22	55.83	25.00
TOT (%)	Objects	0.52	0.88	2.90	4.61	1.67	2.12
	Celebrities	12.19[a,c]	3.00	22.65[a]	14.91	13.41[c]	10.81
Median RT (ms)	Objects	886[a,b]	178	1151[a]	299	1112[b]	425
	Celebrities	1645	370	1923	372	1699	473
Minimum RT (ms)	Objects	557[a,b]	112	627[a]	109	637[b]	182
	Celebrities	797[a]	196	936[a]	131	935	384

[a] Differences between controls and D-TLE.
[b] Differences between controls and ND-TLE.
[c] Differences between D-TLE and ND-TLE. For levels of significance, see Results.

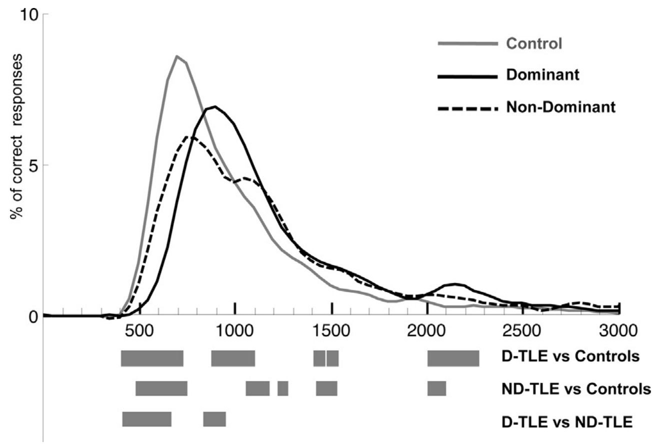

Fig. 4 Across-trials reaction time distributions (ms) for each group in the object naming condition. Grey rectangles under distributions represent significant differences between groups.

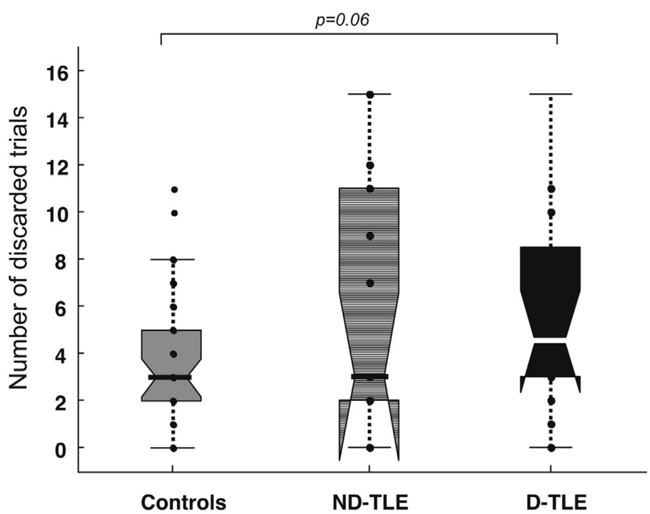

Fig. 5 Boxplot of the percentage of discarded trials for celebrities for each group.

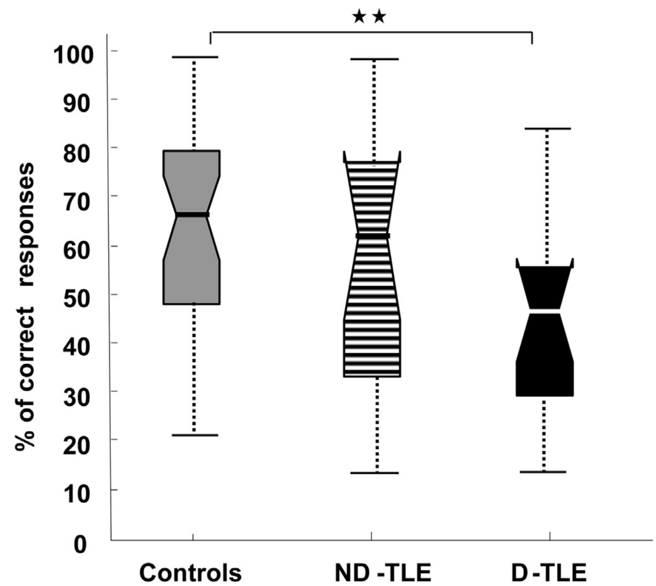

Fig. 6 Boxplot of the percentage of correctly named famous people for each group. ** $p < 0.01$.

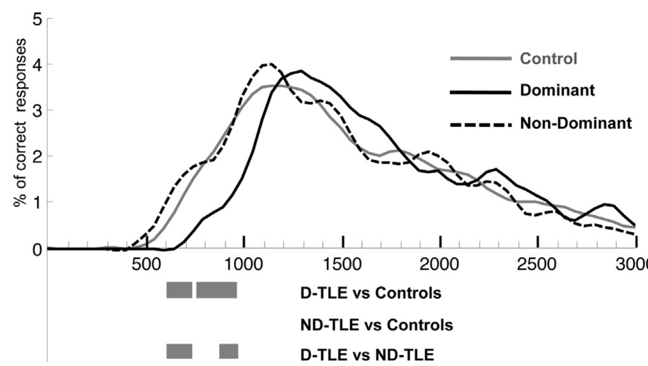

Fig. 7 Across trials reaction time distributions for each group in the famous people naming condition. Grey rectangles under distributions represent significant differences between groups.

(13.41%, SD = 10.81, $p < 0.005$), and more resolved TOT (10.51%, SD = 7.97) than controls (6.85%, SD = 3.42, $p < 0.05$). D-TLE minimum RTs (M = 936, SD = 131) were longer than controls' (M = 797, SD = 196; $p < 0.005$). No other differences were found between groups for any other variables or types of errors.

RT distributions across trials for the famous people naming condition are presented in Fig. 7 for each group. The D-TLE, but not ND-TLE, RT distribution was clearly shifted to the right, indicating overall longer RTs, with D-TLE patients slower than controls and ND-TLE patients in the 600—1000 ms range.

Correlations and predictions

Median reaction times, but not accuracy, of object and famous face naming were correlated in the D-TLE (Pearson correlation = 0.62, p = 0.01) and ND-TLE group (0.67, p = 0.005).

We then conducted different correlation analyses between (i) continuous neuropsychological data and demographic data and (ii) our dependent variables for each group of patients, D-TLE and ND-TLE. For categorical variables, we used Mann—Whitney or Kruskal—Wallis tests. Results are shown in Table 4 for D-TLE and Table 5 for ND-TLE.

We did not find any correlation between complaint and performance. Topiramate may induce word-finding difficulties, so we carried out a specific analysis to address this issue. Six patients were taking Topiramate (2 D-TLE, 4 ND-TLE) and these patients indeed showed more TOT for objects than controls did (4.79%, SD = 5.11 vs. 1.71%, SD = 2.98, U = 39.5, $p < 0.05$).

Linguistic characteristics

We also looked at the impact of different linguistic characteristics on latency in the group of patients (regardless of whether they were D- or ND-TLE). For the object naming condition, we analysed the relations between median RT and frequency, number of letters, and number of synonyms,

Table 4 *Significant relations among neuropsychological or demographic data and dependent variables for D-TLE patients*. CR: correct responses, RT: reaction times, DT: discarded trials, DK: don't know; TOT: tip-of-the-tongue, FOK: feeling-of-knowing, PP: phonological paraphasia, SP: semantic paraphasia, VE: visual error, NbAED: number of antiepileptic drugs.

	Objects										Celebrities									
	CR	Med RT	Min RT	DT	DK	TOT	FOKn	PP	SP	VE	CR	Med RT	Min RT	DT	DK	TOT	FOKn	PP	SP	VE
Age (years)						0.56*											−0.56*			
Education level (years)									−0.54*											
Sex (F/M)				U = 3.00 *																
Seizure onset (years)									0.68**											
Epilepsy Length (years)																0.66**				
Febril convulsion (yes/no)																				
Seizure frequency (per month)														0.58*	−0.61*		0.54*			
NbAED (1,2 or 3)																				
FS-IQ																				
V-IQ	0.68*																			
P-IQ																				
DO 80							−0.77**													−0.91**
Fluency P																				
Fluency R																				
Fluency animals												−0.62*								−0.68*
Fluency fruits												0.65*				−0.75**				
PPTT Images					−0.70*															−0.63*
PPTT Words																				

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

Table 5 *Significant relations among neuropsychological or demographic data and dependent variables for ND-TLE patients*. See legend of Table 4 for details.

	Objects										Celebrities									
	CR	Med RT	Min RT	DT	DK	TOT	FOKn	PP	SP	VE	CR	Med RT	Min RT	DT	DK	TOT	FOKn	PP	SP	VE
Age (years)			0.54*								−0.54*								0.54*	
Education level (years)															−0.58*					
Sex (F/M)																				
Seizure onset (years)	0.52*						−0.53*													
Epilepsy Length (years)	−0.57*	0.57*	0.67**				0.79**			0.60*					0.52*					
Febril convulsion (yes/no)								U = 16.50 *									U = 10.00 *			
Seizure frequency (per month)							0.63*													
NbAED (1,2 or 3)																				
FS-IQ	0.68*										0.66*				−0.59*					
V-IQ																				
P-IQ	0.85**								−0.60*		0.63*				−0.61*				−0.57*	
DO 80								−0.62*		−0.58*										
Fluency P											0.64*		−0.63*		−0.67*					
Fluency R	0.66**										0.54*				−0.60*					
Fluency animals	0.73**	−0.57*				−0.61*														
Fluency fruits	0.54*									−0.60*				−0.56*		−0.54*				
PPTT Images																				
PPTT Words																				

* $p<0.05$.

** $p<0.01$.

first phoneme acoustic characteristics (voiced/non-voiced), category, and if the object was a living or a non living entity. Frequency correlated with median RT ($R^2 = 0.07$, $F(1,69) = 4.95$, $p < 0.05$), and only this variable made a significant independent contribution to the variance ($\beta = 20.32$, $SE = 9.13$, $t = 24.69$; $p = 0.0001$). For the famous people condition, we looked at the relation between median reaction times and nationality (French vs. foreigners), number of letters, number of syllables, first phoneme for the first name and surname, and grammatical word gender (masculine vs. feminine). Nationality was related to median RT ($U = 324.5$, $p < 0.01$) and the stepwise regression revealed that it was the only predictor ($\beta = 320.26$, $SE = 80.57$, $t = 3.98$; $p = 0.0001$).

Discussion

Our aim in this study was to obtain an objective quantification and characterization of naming difficulties in patients with temporal lobe epilepsy. Beyond simple naming failures, we were interested in assessing naming latencies and related naming difficulties such as the tip of the tongue phenomenon. Our findings indicate that, compared to matched control subjects, patients with temporal lobe epilepsy affecting the cerebral hemisphere dominant for language (D-TLE) show a consistent and quasi-systematic impairment on many different variables in both object and famous people naming. In contrast, patients with temporal lobe epilepsy affecting the cerebral hemisphere non-dominant for language (ND-TLE) were less impaired, and their impairment was limited to object naming.

We asked all participants to name stimuli as fast as they could, and we displayed their reaction times after each trial so that they could monitor their performance. The rationale for this was that, if patients were allowed plenty of time to name stimuli, they would use various compensatory strategies that would mask their difficulties. Our group of control subjects had short reaction times (median RTs for object: 886 ms, for celebrities: 1645 ms). Clearly, 886 ms (for objects) is faster than the ~1—2 s usually reported in the literature.

It is worth noting that there may be other methodological reasons for the latency differences observed between our subjects and those of the literature. Because we used a voice-activated timing trigger, we discarded more trials than usual (e.g. those for which subjects made inappropriate initial sounds, such as lip smacking, or instances of self-correction). Only the last name of famous persons were requested, in contrast to other studies that required both first and last names (e.g. as in the Iowa Famous Faces test, Drane et al., 2013). Furthermore, the level of fame may have differed among studies, which would affect naming latencies. Lastly, any response taking over 5 s was considered as either TOT or FOKn. Such responses were thus not included in the minimum or median reaction times reported.

Indefrey (2011) has recently published a review in which he states that naming latencies range from 470 ms to 2000 ms. His schematic representation of the activation time course of brain areas involved in word production points to an utterance at around 600 ms (his Fig. 1). We thus expected to be in the lower range of these latencies if we used speed constraints and 886 ms appears reasonable in this context. Our lab has also published extensively on the subject of fast categorization (e.g., using human/non-human tasks) and the fastest behavioural latencies for such tasks are very short (around 260 ms, reviewed in Fabre-Thorpe, 2011). We have recently extended these results to familiar/unfamiliar tasks and have found that the fastest behavioural latencies are around 360 ms for either objects or celebrities (Besson et al., 2012; Barragan-Jason et al., 2013). These latencies appear compatible with the latencies reported by Indefrey. In our results, access to the name and its utterance could be expected to take more time than familiar/unfamiliar decisions, but not much more time, however. Hence, the speed constraints we used in the present study seem to have been efficient and they may have helped to increase differences between patients and controls. Because we used a rather different methodology, it is interesting to note that our results add weight to previous findings. It seems that, whether they are allowed plenty of time or not, patients with TLE show impaired naming latencies (Drane et al., 2013).

D-TLE had a higher number of ''discarded trials'' than controls. These were all trials that had to be excluded from further analyses because subjects triggered the microphone key with inappropriate sounds (lip smacking, heavy breathing, hesitations, etc.), despite training with the apparatus before the experiment. This result could be explained by impaired inhibitory processes in some patients. However, it seems difficult to explain why D-TLE rather than ND-TLE patients showed this pattern. A more likely explanation is therefore that these discarded trials reflected a more general qualitative language impairment in D-TLE, which was reflected in more hesitations, approximations, and circumlocutions.

D-TLE patients also named fewer objects and famous people than controls, an expected result in light of previous studies (Glosser et al., 2003). However, they were also slower overall. This was particularly clear in the reaction time distribution, which indicated a general slowing down of their naming latencies. This was particularly significant in the 400—1000 ms period after stimulus. This difference was also found between D-TLE and ND-TLE patients, indicating how specific to D-TLE these difficulties are. This indicates that, beyond the word retrieval failures that D-TLE patients may experience from time to time, their discourse may be characterized by increased latencies that may affect their well-being. Here, we did not find any relation between latency and complaint but our questions did not target this issue directly, and it will be interesting to assess whether patients specifically complain of increased latencies in future work.

D-TLE patients also experienced more TOT than control subjects (and ND-TLE patients concerning famous people naming), while no difference was found for ''Feeling of knowing the name'' responses. TOT is thought to be an incapacity to produce a specific word associated with a strong feeling that retrieval is imminent, usually combined with partial recall of some features of the word that is missing. This phenomenon is thought to be due to the blocking of phonological representations and is in accordance with the suggestion of Lomlomdjian et al. (2011) that naming deficits in patients with TLE are due to lexical access problems, rather than word loss, because patients were helped by phonemic cues. This is thought to be specifically related to left hemisphere TLE (Rohrer et al., 2008). Similarly, Trebuchon-Da Fonseca et al. (2009) suggested that naming problems in these patients arose because of problems at the lexical-phonemic stage. Overall, this pattern appears very consistent across studies despite the different methodologies used.

Overall, such difficulties appear to indicate a general impairment of lexical access in patients with TLE, resulting in blocking (TOT) or slowing down (RTs) rather than difficulties related to semantic memory. Indeed, D-TLE patients did not give more ''don't know'' answers (when the stimulus is unknown to the subject) than control subjects, which would have revealed a difficulty related to agnosia, nor did they show more semantic paraphasia. Likewise, they performed at the level of control subjects on the Pyramid and Palm Tree Test, a test requiring subjects to match pairs of stimuli that have a semantic relation.

In contrast to patients with D-TLE, patients with ND-TLE showed an impairment limited to object naming that concerned both correct naming and latency. Furthermore, their impairment tended to be less severe than that of D-TLE patients. They did not have a higher number of TOT or discarded trials than control subjects on any condition and actually had significantly fewer TOT trials than D-TLE patients. Our pattern of results tends to be consistent with the results of Lomlomdjian et al. (2011). Their patients (right and left) were impaired on both naming and latencies, and their right TLE patients obtained better scores than the left TLE (although the difference was non-significant). We did not assess recognition per se as in the Iowa Famous faces test. Consequently, it is difficult to ascertain whether the difficulty ND-TLE patients experienced with objects was related to language itself, or to an impairment of some preliminary processing phase that takes place before naming, e.g. recognition of objects. This could be improved in future studies. Furthermore, the impairment could be related to some baseline factor such as poor learning due to epilepsy or its treatment, rather than to retrieval difficulties as such.

In contrast, the fact that famous people naming was not impaired in ND-TLE appears surprising at first, given the known importance of the (right) non-dominant hemisphere for person processing (Joubert et al., 2004, 2006; Barbeau et al., 2008). However, the difficulties for ND-TLE concern recognition more than naming problems (Glosser et al., 2003; Drane et al., 2008, 2013). A left hemisphere superiority for famous faces has sometimes been reported, indicating at least that the left hemisphere can play a prominent role in the processing of such faces (Marzi and Berlucchi, 1977). In addition, famous face naming is not always impaired in ND-TLE patients relative to controls and face naming does not decline following non-dominant temporal lobe surgical resections to control seizures (Saykin et al., 1995). RT distributions between controls and ND-TLE patients were strikingly similar and, if anything, showed somewhat better RTs for patients (Fig. 5). The distribution of correct naming performance was also very similar, although rather more variability was observed in the ND-TLE group (Fig. 4). These patients actually tended to complain less than D-TLE, but also less than control subjects. Clearly, there is a need for further studies of the respective roles of the left and right temporal lobes in famous person naming and in TLE. In particular, confounding variables such as medication or interictal activities should be better analysed in future studies.

Previous studies analysing naming latencies have not shown differences between D and ND-TLE (Gallegos and Tranel, 2005; Lomlomdjian et al., 2011). A major difference in our protocol was that we tried to capture latencies related to naming only and discarded latencies from naming difficulties such as TOT or FOK. These latencies artificially increased naming RT and thus may have increased variability in previous studies. It is known that patients with temporal epilepsy show ipsi- and controlateral temporal lobe reorganization that may compensate for some difficulties (Guedj et al., 2011). In accordance with this idea, Yucus and Tranel (2007) showed the importance that age at seizure onset had on naming performance after left anterior temporal lobectomy. Similarly, object visual errors correlated with age at seizure onset in our group of D-TLE patients. These factors probably explain some of the heterogeneity observed across studies.

Predictors of picture naming latencies in healthy subjects were analysed by Alario et al. (2004). Using drawings of objects (as opposed to photos used in the current study) these authors found that visual complexity, image agreement, and name agreement were the major determinants of naming speed and that frequency and age of acquisition both made independent contributions. We also found an effect of frequency in agreement with this study and suggesting that epilepsy does not create new symptoms but rather increases difficulties for linguistic variables that are already predictive of lengthened RTs in healthy subjects.

Concerning celebrities, nationality predicted 19% of the variance of reaction times. Participants were more familiar with French celebrities and the names of foreign celebrities may have been more difficult to retrieve due to their atypical phonemic arrangement for a French speaker, but this issue needs to be investigated further. It would be interesting to investigate whether these patients with TLE have difficulties learning foreign languages compared to matched healthy controls.

Topiramate is known to induce naming difficulties (Mula et al., 2003; Kipervasser et al., 2004). In our study, Topiramate was related to increased TOT for objects, further implying a role of this treatment in phonological retrieval access. However, the number of patients taking Topiramate was very small overall ($n = 6$), implying that our results at the group level could not be explained solely by this substance.

Some other differences with previous studies should be noted and may help explain differences among studies. We used multiple choice questions to help differentiate a feeling of knowing from an unfamiliar (''don't know'') response. However, Drane et al. (2013) concluded that the multiple choice options change the nature of the task, allowing the subjects to reevaluate the picture while considering semantic and perceptual information triggered by the multiple choice options. Some potential limitations to our study should also be acknowledged. Language laterality was based on handedness assessment rather than on fMRI or Wada in most patients. Furthermore, a thorough inquiry into errors would be required to assess whether the substitution of a name is not a misrecognition, particularly in ND-TLE (Drane et al., 2013).

In conclusion, lexical access is impaired both qualitatively and quantitatively in D-TLE patients, with slower naming performance and more difficulties encountered.

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