Original article

Epileptic Disord 2020; 22 (1): 55-65

Clinical, semiological, electroencephalographic, and neuropsychological features of "pure" neocortical temporal lobe epilepsy

Hana Maizuliana [1,2], Naotaka Usui [1], Kiyohito Terada [1], Akihiko Kondo [1], Yushi Inoue [1]

[1] National Epilepsy Center, NHO Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan
[2] Universiti Sains Islam Malaysia, Kuala Lumpur, Malaysia

Received December 22, 2018; Accepted November 17, 2019

ABSTRACT – *Aims.* We examined the clinical, semiological, scalp EEG, and neuropsychological features of patients with "pure" neocortical temporal lobe epilepsy (NTLE) who were successfully treated by neocortical temporal resection sparing the mesial temporal structures.
Methods. This retrospective study included 17 patients with lesional NTLE who satisfied the following criteria: presence of a discrete structural lesion in the lateral temporal lobe on preoperative MRI; lateral temporal resection sparing the mesial temporal structures; follow-up for at least two years after surgery; and favourable postoperative seizure outcome (Engel Class I). The study included 10 females and seven males, and the age at surgery ranged from 15 to 48 years (mean: 30.7 years). Auras, video-recorded seizure semiology, interictal and ictal EEG, and pre- and post-operative neuropsychological data were reviewed. Twenty patients with mesial temporal lobe epilepsy (MTLE) with hippocampal sclerosis, who had a favourable postoperative seizure outcome (Engel Class I), were selected as a control group.
Results. Age at seizure onset was significantly greater in patients with NTLE than in controls. A history of febrile convulsion was significantly less frequent in NTLE patients. Epigastric ascending sensation (6% *versus* 40%; p=0.017), oral automatisms (29% *versus* 80%; p=0.003), gestural automatisms (47% *versus* 80%; p=0.047), and dystonic posturing (0% *versus* 40%; p=0.003) were significantly less frequent in NTLE than controls. Ictal unitemporal rhythmic theta activity was also significantly less frequent in NTLE than controls (35.3% *versus* 75%; p=0.015). Preoperative IQ score (range: 68 to 114; mean: 88.9) and preoperative memory quotient score (range: 56-122; mean: 98.1) were significantly higher in NTLE (p=0.003 and p=0.048, respectively).
Conclusion. There were notable differences in clinical, semiological, EEG, and neuropsychological features between "pure" NTLE and MTLE. These findings may be useful to identify the epileptogenic zone.

Key words: epileptic aura, dystonic posturing, neuropsychology, epilepsy surgery, neocortical TLE, mesial TLE

Correspondence:
Naotaka Usui
National Epilepsy Center,
NHO Shizuoka Institute of Epilepsy and Neurological Disorders,
Shizuoka, Japan
<usui-nsu@umin.ac.jp>

doi:10.1684/epd.2020.1132

Temporal lobe epilepsy (TLE) is the commonest type of focal epilepsy. Nearly two thirds of patients with intractable seizures are categorized in this group, for which definitive treatment is mainly surgical (Wiebe *et al.*, 2001; Schmidt and Stavem, 2009; Perry and Duchowny, 2013). Surgical treatment for TLE is superior to prolonged medical therapy (Wiebe *et al.*, 2001; Engel *et al.*, 2012). However, comprehensive pre-surgical evaluation, including video-EEG, is very important for identifying those patients who will be most likely to benefit from surgery (Rosenow and Lüders, 2001).

TLE is further subclassified into mesial TLE (MTLE) and neocortical TLE (NTLE) (ILAE, 1989). Mesial TLE accounts for the majority of TLE cases, as has been described extensively in the literature (Schulz *et al.*, 2000; Wieser, 2004; O'Dell *et al.*, 2012; Du *et al.*, 2015), whereas NTLE is found in only about 10% of cases (Schramm *et al.*, 2001). It is very important to distinguish NTLE from MTLE, because they differ in terms of surgical strategies and outcomes.

Many studies have compared the clinical and EEG characteristics of MTLE and NTLE (Burgerman *et al.*, 1995; Pacia *et al.*, 1996; Foldvary *et al.*, 1997; Pfander *et al.*, 2002; Lee *et al.*, 2006), with discordant results. However, few studies have examined patients with "pure" NTLE who became seizure-free after neocortical temporal resection, sparing the medial temporal structures. Our aim here was to clarify the clinical, semiological, EEG, and neuropsychological features of patients with "pure" NTLE who were successfully treated surgically.

Patients and methods

Demographic data

Between July 2006 and July 2014 at our centre, we performed temporal lobe resection on 323 patients, consisting of 94 lesional patients, 213 patients with hippocampal sclerosis (HS), and 16 patients with normal MRI. Patients with MTLE were included as controls for those with NTLE.

Patients with lesional NTLE who satisfied the following criteria were included: presence of a discrete structural lesion in the lateral temporal lobe on preoperative MRI; lateral temporal resection sparing the mesial temporal structures; follow-up for at least two years after surgery; and favourable postoperative seizure outcome (Engel Class I). Medical records were reviewed; the data collected included age at onset, duration of epilepsy, past medical history, family history of epilepsy and febrile convulsion, age at surgery, MRI findings, pathological findings, neuropsychological data, postoperative seizure outcomes, and duration of postoperative follow-up.

Seventeen patients fulfilled the inclusion criteria; 10 (58.8%) females and seven (41.2%) males, with age at surgery ranging from 15 to 48 years (mean: 30.7 ± 11.1 years). Mean age at seizure onset was 23.2 ± 9.3 years (range: 11 to 41 years), with a duration of epilepsy from two to 25 years (mean: 7.6 ± 5.8 years). There were eight right-sided and nine left-sided lesions. *Figure 1* shows the locations of the lesions in the 17 patients. Preoperative MRI revealed no hippocampal abnormality in 14 patients. In the remaining three, hippocampal atrophy ipsilateral to the lesion was observed. Fluorodeoxyglucose positron emission tomography (FDG-PET) was performed in eight patients. Hypometabolism in the ipsilateral mesial temporal region was observed in five of these eight patients. Four patients underwent intracranial EEG before resection surgery. Histopathological findings of the resected lesions revealed cavernoma (six patients), ganglioglioma (four patients), dysembryoplastic neuroepithelial tumour (two patients), oligodendroglioma (two patients), pleomorphic xanthoastrocytoma (two patients), and astrocytoma (one patient). The patients were followed for 2 to 10 years (mean: 3.65 ± 2.5 years) postoperatively. Postoperative seizure outcome was Engel Class Ia in 14 patients, Ib in two, and Id in the remaining patient. Characteristics of the 17 patients are shown in *table 1*.

Twenty patients with MTLE with hippocampal sclerosis who became seizure-free after surgery were chosen as controls. In the MTLE control group, there were 20 patients (seven males and 13 females). Age at surgery was 8 to 49 years (mean: 28.4 ± 11.4 years). Age at seizure onset was 3 to 45 years (mean: 10.9 ± 11.4 years), with an epilepsy duration of 4 to 36 years (mean: 17.6 ± 9.3 years). All patients underwent selective amygdalohippocampectomy, with the exception of one, who underwent standard anterior temporal lobectomy. Postoperative seizure outcome was Engel Class I in all 20 patients. None of the patients received intracranial EEG recording. Right-sided surgical resection was performed for eight patients and left-sided for 12 patients. A histological finding of hippocampal sclerosis was found in all patients. Postoperative follow-up duration was between six and seven years. FDG-PET studies were not performed in the control group.

All patients in both groups underwent preoperative long-term scalp video-EEG monitoring (EEG-1000, Nihon Kohden, Tokyo, Japan). The international 10-20 electrode system was used in all cases, with additional sphenoidal electrodes in 16 patients. Antiepileptic medications were usually reduced or stopped temporarily to facilitate the recording of seizures. At least one seizure episode was captured in each patient during the long-term video-EEG recording.

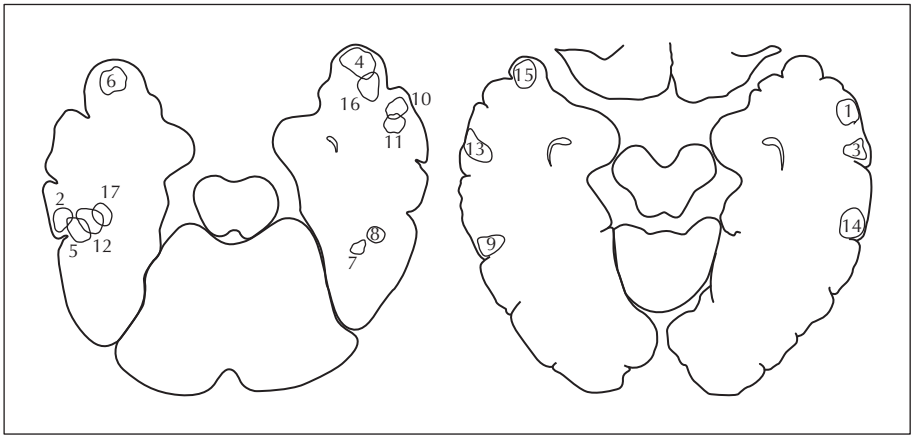

Figure 1. Locations of the lesions in the 17 patients with neocortical temporal lobe epilepsy. Numbers indicate patient numbers.

Semiology

Auras were investigated by reviewing the medical records of the patients. Video-recorded seizures were carefully reviewed, and the presence or absence of objective manifestations, including simple motor signs and complex behaviours, was determined. All recorded seizures were analysed, and if a symptom was present in at least one seizure it was defined as "present." If a symptom was never seen in the recorded seizures, the symptom was defined as "absent." The relative frequency of each symptom was compared between the two groups.

EEG

Interictal epileptiform abnormalities (sharp waves and spikes) were analysed. The anterior temporal region was represented by electrodes SP1/SP2 and F7/F8 and the lateral temporal region by T3/T4 and T5/T6. The other scalp electrodes were classified as extra-temporal electrodes. The laterality, frequency, and distribution of the ictal abnormalities at the onset and evolution of seizures were noted. EEG findings were compared between the two groups.

The video-recorded seizures and EEGs were reviewed by two epileptologists (HM and NU), separately at first. Later, the seizure videos and EEG were reviewed together to achieve consensus for the findings.

Neuropsychology

Sixteen NTLE patients underwent preoperative neuropsychological testing and all 17 had postoperative neuropsychological tests. Postoperative neuropsychological testing was performed two years after the surgery. The Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Japanese version) was used to evaluate intellectual function (the full-scale intelligence quotient [FSIQ]), whereas the Wechsler Memory Scale-Revised (WMS-R) (Japanese version) was used to determine memory components, including memory quotient (MQ) and verbal and visual memory scores.

In the MTLE control group, to evaluate FSIQ, the WAIS-R (Japanese version) was used in 17 adult patients, whereas the Wechsler Intelligence Scale for Children III was used in the three paediatric patients. The WMS-R (Japanese version) was used to determine memory components in the adult patients. A difference of more than 15 points between the pre- and post-operative scores was considered a significant change.

Statistical analysis

For the statistical analysis, two-sample *t*-tests and Fisher's exact tests were used to establish significance differences between the groups. A one sample *t*-test was used to compare the pre- and post-operative neuropsychological data. *P* values <0.05 were considered statistically significant.

Results

Demographic data

The NTLE and MTLE groups differed significantly in age at seizure onset, duration of seizures before surgery, and family history of epilepsy or febrile convulsion (*table 2*). In the NTLE group, a previous history of febrile convulsion was positive in one patient, negative in 15, and unclear in one. In the MTLE group; there was a previous history of febrile convulsions in 10 of 20 patients; this was significantly more frequent than in the NTLE group ($p<0.05$).

Table 1. Demographic and historical data on patients with neocortical temporal lobe epilepsy.

No.	Age at surgery (years) /Sex	FC	Family history of FC/epilepsy	Age at onset (years)	Seizure duration (years)	Seizure type	Lesion side	Surgical procedure	Seizure outcome	Pathology	Follow-up (years)
1	19/F	N	N	11	8	FIAS	L	LT lesionectomy	Ib	Oligodendroglioma	10
2	25/M	N	Y	19	6	FIAS	R	RT lesionectomy	Ia	DNT	9
3	24/F	N	N	15	9	FIAS	L	LT lesionectomy	Ia	DNT	5
4	19/F	N	N	17	2	FAS, FIAS, SGTC	L	LT lesionectomy	Ia	Pleomorphic xanthoastrocytoma	2
5	42/F	N	Y	32	10	FIAS	R	RT lesionectomy	Ia	Cavernoma	5
6	44/M	N	N	30	15	FIAS	R	RT lesionectomy	Ia	Cavernoma	5
7	48/F	N	N	23	25	FIAS, SGTC	L	LT lesionectomy	Ia	Cavernoma	2
8	34/F	N	N	21	13	FAS, FIAS, SGTC	L	LT lesionectomy	Ia	Ganglioglioma	2
9	16/M	Y	N	12	4	FIAS, SGTC	R	RT lesionectomy	Ia	Ganglioglioma	4
10	47/M	Unclear	N	42	5	FAS, FIAS, SGTC	L	LAT lesionectomy	Ia	Pleomorphic xanthoastrocytoma	2
11	27/M	N	Y	25	2	FAS, FIAS	L	LAT lesionectomy	Ib	Cavernoma	2
12	35/F	N	N	27	8	FAS, FIAS, SGTC	R	RT lesionectomy	Id	Cavernoma	2
13	15/F	N	Y	12	3	FAS, FIAS, SGTC	R	RT lesionectomy	Ia	Ganglioglioma	2
14	26/M	N	N	20	6	FIAS	L	LPT lesionectomy	Ia	Astrocytoma	3
15	25/F	N	N	19	6	FAS, FIAS	R	RT lesionectomy	Ia	Ganglioglioma	3
16	32/M	N	Y	28	4	FAS, FIAS, SGTC	L	LT lesionectomy	Ia	Cavernoma	2
17	44/F	N	Y	41	3	FAS, FIAS	R	RT lesionectomy	Ia	Oligodendroglioma	2

F: female; M: male; N: no; Y: yes; FC: febrile convulsion; FAS: focal aware seizures; FIAS: focal impaired awareness seizures; SGTC: secondary generalized tonic-clonic; L: left: R: right; LT: left temporal; RT: right temporal; LAT: left anterior temporal; LPT: left posterior temporal; DNT: dysembryoplastic neuroepithelial tumour. Seizure outcome is graded according to Engel's classification.

Table 2. Differences in demographic data between patients with NTLE and those with MTLE.

	NTLE *n*=17	MTLE *n*=20	*p* value
Gender (M/F)	7/10	7/13	NS
Age at onset of seizure: years, mean (range)	23.2 (11-41)	10.9 (3-45)	0.0011*
Duration of seizure: years, mean (range)	7.6 (2-25)	17.6 (8-49)	0.0005*
Age at surgery: years, mean (range)	30.7 (15-48)	28.4 (4-36)	NS
Side of lesion (R/L)	8/9	8/12	NS
Febrile convulsion (FC)	1	10	0.0039*
Family history of epilepsy or FC	6	10	NS
Surgical outcome (Engel's classification):			
Ia	14	13	NS
Ib	2	3	
Ic	0	4	
Id	1	0	

M: male; F: female; R: right; L: left; NTLE: neocortical temporal lobe epilepsy; MTLE: mesial temporal lobe epilepsy; FC: febrile conversion; NS: not significant. *p <0.05 signifies statistical significance.

Semiology

Thirteen patients (76.5%) in the NTLE group had auras (*table 3*). In MTLE group, 17 (85%) patients reported aura. Epigastric ascending aura was significantly less frequent in NTLE than in MTLE ($p<0.05$). No differences in frequency were observed for the other types of auras.

In the NTLE group, a total of 71 spontaneous seizures (mean: 4; range; 1 to 9 per patient) were recorded and analysed, whereas in the MTLE group, a total of 115 spontaneous seizures (mean: 6; range: 2 to 12 per patient) were analysed. Dystonic posturing was significantly less frequent in NTLE than in MTLE (0% *versus* 40%; $p=0.003$). Analysis of the data for other simple motor signs revealed no significant differences in the frequencies of clonic, tonic, and versive movements and secondary generalization among the two groups. In the NTLE group, gestural automatism was seen in eight of 17 patients (47.1%). Oral automatism was seen in five NTLE patients (29.4%). The frequencies of both oral and gestural automatisms were significantly lower in NTLE than in MTLE. The frequency of postictal confusion was significantly lower in NTLE (23.5%) than in MTLE (85%) ($p=0.001$).

Scalp EEG

There were no significant differences in the bilaterality of interictal epileptiform discharges between the two groups (*table 4*). Anterior temporal spikes were the type of interictal discharge seen most frequently in both groups. There were no significant differences in the distribution of interictal epileptiform discharges between the two groups.

Ictal unitemporal rhythmic theta activity was found in six NTLE patients and 15 MTLE patients; it was significantly less frequent in the NTLE group (35.3% *versus* 75%; $p=0.015$). Three NTLE patients had unitemporal delta activity and three had unitemporal theta-delta activity; one had unilateral posterior temporal discharges, one had lateralized-onset alpha-theta activity, one had contralateral temporal onset, and one had unifrontal delta activity. There was no significant difference in the frequency of contralateral propagation between the two groups (58.8% *versus* 85%). There was also no significant difference in the duration of EEG seizure between the two groups.

Neuropsychology

Pre-operatively, FSIQ in the 16 NTLE patients tested ranged from 68 to 114 (mean: 88.9 ± 15.2) (*table 5, figure 2*). In the MTLE controls, the preoperative FSIQ ranged from 52 to 100 (mean: 74.3 ±12.3). Pre-operative FSIQ was significantly higher in the NTLE group than in the MTLE controls ($p<0.003$). Preoperative MQ in the 16 tested NTLE patients ranged from 56 to 122 (mean:

Table 3. Seizure semiology in NTLE and MTLE patients.

Seizure semiology	NTLE *n*=17 (%)	MTLE *n*=20 (%)	*p* value
Aura			
Any aura	13 (76.5)	17 (85)	NS
Autonomic	4 (23.4)	4 (20)	NS
Cephalic	2 (11.8)	0	NS
Somatosensory	1 (5.9)	0	NS
Epigastric ascending sensation	1 (5.9)	8 (40)	0.017*
Auditory (melody)	1 (5.9)	0 (0)	NS
Visual	0	1 (5)	NS
Psychic	1 (5.9)	4 (20)	NS
Unclassifiable	4 (23.5)	3 (15)	NS
Autonomic signs			
Drooling	1 (5.9)	4 (20)	NS
Hyperventilation	2 (11.8)	2 (10)	NS
Simple motor signs			
Face clonic	2 (11.8)	3(15)	NS
Dystonic	0	8 (40)	0.003*
Tonic	0	4 (20)	NS
Versive	0	0	NS
Complex behaviours and other seizures			
Oral automatism	5 (29.4)	16 (80)	0.003*
Gestural automatism	8 (47.1)	16 (80)	0.047*
Ictal speech	1 (5.9)	3 (15)	NS
Automatisms with preserved responsiveness	0	0	NS
Hypermotor behaviours	0	0	NS
Postictal confusion	5 (23.5)	17 (85)	0.001*
Postictal aphasia	1 (5.9)	0	NS
Nose wiping	2 (11.8)	6 (30)	NS
SGTC	3 (17.6)	2 (10)	NS

SGTC: secondarily generalized tonic-clonic; NTLE: neocortical temporal lobe epilepsy; MTLE: mesial temporal lobe epilepsy; NS: not significant. *p <0.05 signifies statistical significance.

98.1 ± 19.1). In the 17 adult MTLE controls, preoperative MQ ranged from 55 to 116 (mean: 84.9 ± 17.7). Preoperative MQ was also significantly higher in the NTLE group than in the MTLE controls (p=0.048). Postoperative FSIQ in the 16 tested NTLE patients ranged from 68 to 116 (mean: 88.8 ±15.0), and declined relative to the preoperative values in two of the patients. In the NTLE group, postoperative MQ ranged from 81 to 126 (mean: 106.2 ± 14.7), and improved in four of the patients. Postoperative verbal memory in the NTLE patients ranged from 78 to 127 (mean: 105.4 ± 16.0), and increased in four patients. The postoperative MQ and verbal memory scores were significantly better than preoperative results (p<0.05). The postoperative visual memory score increased in one patient and decreased in another.

Discussion

The strength of our study is that only patients with "pure" NTLE who had undergone neocortical temporal resection sparing the mesial temporal structures and had achieved excellent postoperative seizure outcomes were included. We could therefore be certain that in our group, the seizures were of lateral temporal lobe origin only. Although the number of patients was small, our study was able to reveal significant clinical, semiological, EEG, and neuropsychological differences between NTLE and MTLE.

It has been proposed that the distinction between MTLE and NTLE is an oversimplification. Medial and lateral subtypes were proposed by Bartolomei *et al*. (1999) and Maillard *et al*. (2004) by analysing

Table 4. Interictal scalp EEG features in NTLE and MTLE patients.

		NTLE (*n*=17)	MTLE (*n*=20)	*p* value
Lateralization	Unilateral	12	16	NS
	Bilateral	5	4	
Distribution	AT	9	16	NS
	AT and LT	6	3	
	AT + LT + ET	1	1	
	No IID	1	0	
Ictal EEG	Unitemporal θ	6	15	0.015*
	Contralateral propagation	10	17	NS
	EEG seizure duration (seconds)	48∓22	54∓11	NS

AT: anterior temporal; LT: lateral temporal; NTLE: neocortical temporal lobe epilepsy; MTLE: mesial temporal lobe epilepsy; ET: extratemporal; NS: not significant. *p <0.05 signifies statistical significance.

Table 5. Pre-operative neuropsychological test scores in NTLE and MTLE patients.

	NTLE Mean (SD) (*n*=16)	MTLE Mean (SD) (*n*=17)	*p* value
FSIQ	88.9 (15.2)	74.3 (12.3)	0.003*
MQ	98.1 (19.1)	84.9 (17.7)	0.048*
Verbal memory	97.2 (19.3)	82.9 (19.6)	0.043*
Visual memory	102.6 (14.3)	93.1 (18.6)	NS

SD: standard deviation; NTLE: neocortical temporal lobe epilepsy; MTLE: mesial temporal lobe epilepsy; FSIQ: full-scale intelligence quotient; MQ: memory quotient; NS: not significant. *p <0.05 signifies statistical significance.

seizures recorded by using stereoelectroencephalography. Even for TLE with hippocampal sclerosis, Kahane and Bartolomei (2010) suggested temporopolar, mesiolateral, lateral, and temporal "plus" subtypes. Nonetheless, differentiating these subtypes has remained a challenge both clinically and electrophysiologically.

Demographic data

Our NTLE patients were significantly older at seizure onset than those with MTLE. This finding is similar to those of previous studies (Burgerman *et al*., 1995; Foldvary *et al*., 1997). Foldvary *et al*. (1997) found that only one of their eight patients with NTLE was aged less than 16 years at seizure onset; in contrast, 90% of their MTLE patients were aged less than 16 at seizure onset. The frequency of previous febrile convulsions in our patients was significantly higher in MTLE than in NTLE; this result is consistent with those of previous studies (Foldvary *et al*., 1997). The importance of the initial precipitating injury in MTLE has been reported (French *et al*., 1993).

Semiology

Epigastric ascending aura was significantly more frequent in MTLE than in NTLE. Epigastric ascending sensation is considered a typical subjective symptom of MTLE (Pfander *et al*., 2002, Maillard *et al*., 2004). Gil-nagel and Risinger (1997) reported that epigastric aura preceded seizures in five of 16 patients with hippocampal temporal lobe seizures (31.3%) and none with extrahippocampal temporal lobe seizures.

The frequency of psychic aura did not differ significantly between NTLE and MTLE in our study. However, experiential phenomena, including *déjà vu*, *jamais vu*, and depersonalization, were the auras reported most frequently in 10 of 21 NTLE patients in a previous study (Pacia *et al*., 1996). Psychic auras, such as a dreamy state,

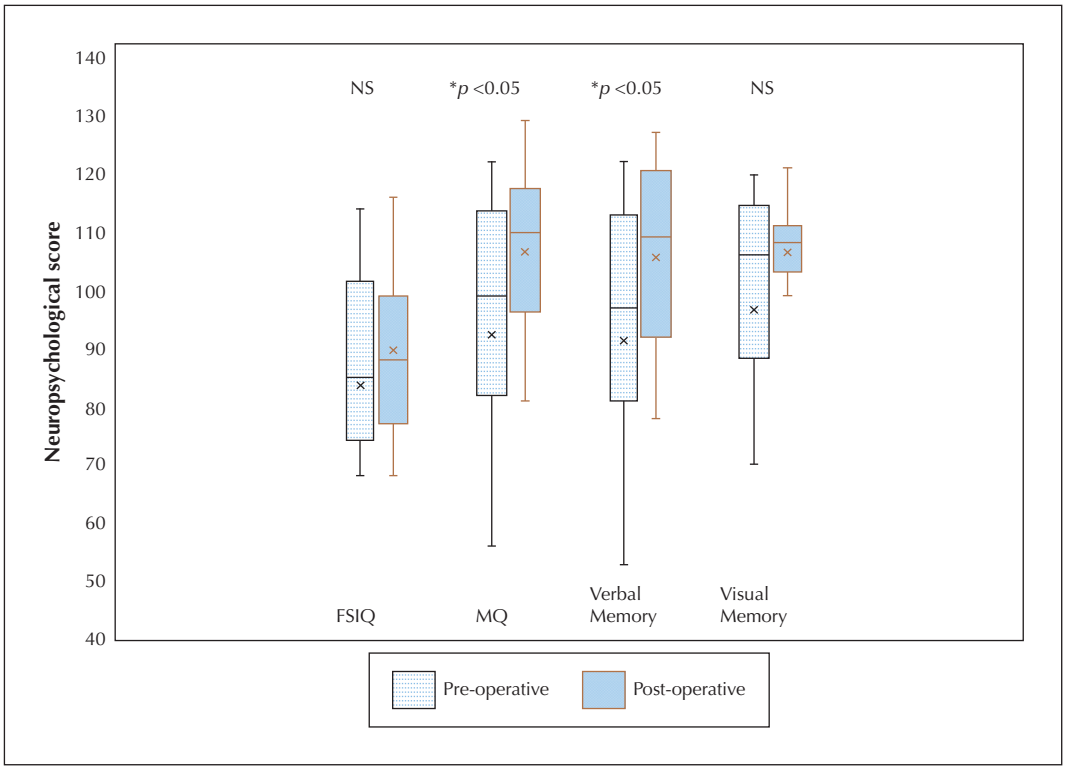

Figure 2. Pre-and postoperative neuropsychological scores in patients with neocortical temporal lobe epilepsy. FSIQ: full-scale intelligence quotient; MQ: memory quotient.

are considered to be generated by activation of both the mesial and lateral temporal lobe (Bancaud *et al.*, 1994). In our patients with strictly NTLE, mesial temporal involvement during the aura phase may have been more limited than in patients with NTLE in previous studies.

Our NTLE patients had significantly lower frequencies of gestural automatism, dystonic posturing, and oral automatism than MTLE patients. Dystonic posturing was not seen, and this finding is consistent with previous reports (O'Brien *et al.*, 1996; Foldvary *et al.*, 1997; Pfander *et al.*, 2002). The symptomatogenic zone for dystonic posturing is considered to be in the basal ganglia, ipsilateral to the epileptogenic zone. O'Brien *et al.* (1996) found that ictal dystonic posturing occurred in 52% of their patients with mesial temporal sclerosis, *versus* 26% in NTLE; as they noted, seizures of mesial temporal origin are more likely to propagate to the basal ganglia than seizures of neocortical temporal origin.

Oral automatisms are considered to be related to activation of the amygdala. In one study, early oral automatisms were present in 11 of 16 patients with hippocampal temporal lobe seizures (68.8%) but in only two of 19 patients with extrahippocampal temporal lobe seizures (10.5%) (Gil-nagel and Risinger, 1997).

Duchowny *et al.* (1994) studied 14 patients with posterior temporal epilepsy treated surgically. Automatisms were seen in seven patients, but they were never the first signs. In most of the patients, automatisms occurred late in the ictal sequence. In our study population, the frequency of typical gestural automatism was less frequent in NTLE. This finding is also similar to those in previous reports (Foldvary *et al.*, 1997; Pfander *et al.*, 2002). The absence of automatisms may be a key to the diagnosis of NTLE.

Postictal confusion was seen less frequently in NTLE than in the MTLE group. The postictal phase is a form of functional deficit and could be helpful in localizing the seizure focus (Jan and Girvin, 2008; Krauss and Theodore, 2010; Rémi and Noachtar, 2010). No previous studies have compared the occurrence of postictal confusion between NTLE and MTLE. Postictal dysfunction occurs frequently after seizures of mesial temporal origin and is thought to originate in the limbic area; it is characterized by cognitive impairment, memory deficits, mood changes, and language deficits (Wieser, 2004). The degree of limbic structure involvement may be less prominent in seizures originating in the lateral temporal lobe than in those originating in the mesial temporal lobe.

Selecting seizure-free patients after resection surgery is essential for verifying the site of seizure onset. However, several previous studies have included both seizure-free and non-seizure-free patients postoperatively (Burgerman *et al*., 1995; Pacia *et al*., 1996; Pfander *et al*., 2002). Some studies (Tao *et al*., 2011; Ochoa *et al*., 2017) have included patients who have undergone resection of both lateral temporal lesions and mesial temporal structures, and the results have been discordant. In contrast, our study included only "pure" NTLE patients who had undergone lateral temporal resection sparing the mesial temporal structures and had achieved favourable postoperative seizure outcomes. Therefore, we consider that these results reflect the true differences between NTLE and MTLE.

EEG

There were no significant differences in the distribution of spikes between the two groups. Other authors have obtained similar findings (Burgerman *et al*., 1995; O'Brien *et al*., 1996). In contrast, Pfander *et al*. (2002) reported that the interictal epileptiform discharges in MTLE occurred predominantly (>67%) over the ipsilateral mesial temporal regions (MTLE 65% vs. NTLE 33%). They did not perform surgical resection in all patients, and data on postoperative seizure outcome were not provided. Differences in patient inclusion criteria may have been the cause of the discrepancy relative to our study.

The ictal EEG findings in our NTLE patients were variable. Unilateral temporal theta activity was significantly less frequent in NTLE than in MTLE. The relationship between MTLE and unitemporal rhythmic theta activity on ictal EEG was concordant with previous reports.

Foldvary *et al*. (1997) compared the clinical and EEG features of NTLE and MTLE. The NTLE ictal EEGs demonstrated a lower mean frequency of lateralized rhythmic activity, which frequently had a hemispheric distribution, whereas in MTLE, lateralized rhythmic activity peaked over the ipsilateral temporal region. Ebersole and Pacia (1996) found that a regular 5- to 9-Hz rhythm localized to the temporal region was associated with MTLE, whereas the EEG in NTLE was more often characterized by irregular, polymorphic 2- to 5-Hz lateralized activity or non-lateralized ictal patterns. The ictal EEG patterns in NTLE were more variable than those in MTLE in our study. One study observed bilateral ictal EEG activity more frequently in NTLE patients (O'Brien *et al*., 1996). The authors considered that this finding may have reflected early seizure spread to the contralateral temporal neocortex. In our study, the frequency of contralateral propagation did not differ significantly between MTLE and NTLE.

Previous studies have shown longer seizure duration in MTLE patients than in NTLE (Foldvary *et al*., 1997; Maillard *et al*., 2004). However, this was not seen in our study. This discordance may have been due to the small number of patients in our study.

Neuropsychology

Helmstaedter *et al*. (1997) revealed that patients with hippocampal sclerosis had significantly poorer performance in delayed recall than patients with lateral temporal pathology. We found significantly higher preoperative IQ and memory scores in NTLE than in MTLE. Hippocampal atrophy was not seen in most of our patients with NTLE. This may explain the higher memory scores in NTLE than MTLE. The hippocampus is thought to be involved in the functional connectivity required to maintain and execute working memory function (Zhao *et al*., 2014). The lower baseline IQ scores in MTLE may reflect the wider epileptogenic network, extending beyond the hippocampus in MTLE (Karunakaran *et al*., 2018). Furthermore, our MTLE patients had significantly longer disease duration than in NTLE patients. Many studies have found an association between chronic epilepsy and relatively low baseline IQ due to neuronal damage from repeated or prolonged seizures (Elger *et al*., 2004; Wieser, 2004; Black *et al*., 2010; Oyegbile *et al*., 2011; Zhao *et al*., 2014). There is a known risk of decline in cognitive function among patients who undergo epilepsy surgery for TLE (Baxendale, 2008; Bell *et al*., 2011). Reports of neuropsychological testing after surgery for TLE have shown various outcomes, depending on the approach and extent of the surgical removal (Jones-Gotman *et al*., 1997; Clusmann *et al*., 2002; Bell *et al*., 2011; Boucher *et al*., 2015; Helmstaedter, 2016; Foged *et al*., 2018). However, there have been very few studies on these outcomes after lateral temporal resection for NTLE (Helmstaedter *et al*., 1997; Helmstaedter, 2016). In our cohort, we found postoperative improvements in general and verbal memory function. The memory improvement in our patients may have been due to postoperative freedom from seizures, along with the preservation of mesial temporal structures. Helmstaedter *et al*. (1997) studied pre- and postoperative verbal memory performance in 47 patients with left temporal lobe epilepsy who underwent lateral lesionectomy, anterior temporal lobectomy, or selective amygdalo-hippocampectomy. The authors found more favourable memory outcomes associated with lateral lesionectomy than with the other two procedures. On the contrary, Jones-Gotman *et al*. (1997) reported similar verbal learning and memory outcomes after left temporal resection, irrespective of whether the medio-basal structures were spared or the temporal neocortex was spared. However, in their patients with lateral temporal resection, considerable amounts of the medial temporal structures were in

fact resected. In lesional NTLE, lesionectomy is usually sufficient for postoperative seizure freedom and also favours the preservation of memory function (Clusmann *et al*., 2002).

Limitations of this study

The main limitation of this study is the small sample size. However, the strength of our study is the inclusion of only those patients with a pure neocortical temporal epileptogenic zone. Although there have been several previous studies of NTLE, only one study (Foldvary *et al*. (1997) included patients with a strictly neocortical temporal epileptogenic zone.

Conclusion

In conclusion, we identified significant differences between pure NTLE and MTLE in terms of clinical presentation, semiology, EEG findings, and neuropsychology. These features may be useful for differentiating between NTLE and MTLE and helping to determine the type of surgery needed. □

Supplementary data.
Summary didactic slides are available on the www.epilepticdisorders.com website.

Acknowledgements and disclosures.
We thank the doctors and nurses of the National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan, who helped to care for the patients.
None of the authors have any conflict of interest to declare.

References

Bancaud J, Brunet-Bourgin F, Chauvel P, *et al*. Anatomical origin of déjà vu and vivid 'memories' in human temporal lobe epilepsy. *Brain* 1994; 117(1): 71-90.

Bartolomei F, Wendling F, Jean-Pierre V, *et al*. Seizures of temporal lobe epilepsy: identification of subtypes by coherence analysis using stereo-electro-encephalography. *Clin Neurophysiol* 1999; 110(10): 1741-54.

Baxendale S. The impact of epilepsy surgery on cognition and behavior. *Epilepsy Behav* 2008; 12(4): 592-9.

Bell B, Lin JJ, Seidenberg M, *et al*. The neurobiology of cognitive disorders in temporal lobe epilepsy. *Nat Rev Neurol* 2011; 7(3): 154-64.

Black LC, Schefft BK, Howe SR, *et al*. The effect of seizures on working memory and executive functioning performance. *Epilepsy Behav* 2010; 17(3): 412-9.

Boucher O, Dagenais E, Bouthillier A, *et al*. Different effects of anterior temporal lobectomy and selective amygdalohippocampectomy on verbal memory performance of patients with epilepsy. *Epilepsy Behav* 2015; 52: 230-5.

Burgerman RS, Sperling MR, French JA, *et al*. Comparison of mesial *versus* neocortical onset temporal lobe seizures: neurodiagnostic findings and surgical outcome. *Epilepsia* 1995; 36(7): 662-70.

Clusmann H, Schramm J, Kral T, *et al*. Prognostic factors and outcome after different types of resection for temporal lobe epilepsy. *J Neurosurg* 2002; 97(5): 1131-41.

Du XP, Usui N, Terada K, *et al*. Semiological and electroencephalographic features of epilepsy with amygdalar lesion. *Epilepsy Res* 2015; 111: 45-53.

Duchowny M, Jayakar P, Resnick T, *et al*. Posterior temporal epilepsy: electroclinical features. *Ann Neurol* 1994; 35(4): 427-31.

Ebersole JS, Pacia SV. Localization of temporal lobe foci by ictal EEG patterns. *Epilepsia* 1996; 37(4): 386-99.

Elger CE, Helmstaedter C, Kurthen M. Chronic epilepsy and cognition. *Lancet Neurol* 2004; 3(11): 663-72.

Engel J, McDermott M, Wiebe S, *et al*. Early surgical therapy for drug-resistant temporal lobe epilepsy. *J Am Vet Med Assoc* 2012; 307(9): 922-30.

Foged MT, Vinter K, Stauning L, *et al*. Verbal learning and memory outcome in selective amygdalohippocampectomy *versus* temporal lobe resection in patients with hippocampal sclerosis. *Epilepsy Behav* 2018; 79: 180-7.

Foldvary N, Lee N, Thwaites G, *et al*. Clinical and electrographic manifestations of lesional neocortical temporal lobe epilepsy. *Neurology* 1997; 49(3): 757-64.

French JA, Williamson PD, Thadani VM, *et al*. Characteristics of medial temporal lobe epilepsy: I. Results of history and physical examination. *Ann Neuro* 1993; 34(6): 774-80.

Gil-nagel A, Risinger MW. Ictal semiology in hippocampal *versus* extrahippocampal temporal lobe epilepsy. *Brain* 1997; 120: 183-92.

Helmstaedter C. Cognitive outcomes of different surgical approaches in temporal lobe epilepsy. *Epileptic Disord* 2016; 33: 21-37.

Helmstaedter C, Grunwald T, Lehnertz K, *et al*. Differential involvement of left temporolateral and temporomesial structures in verbal declarative learning and memory: evidence from temporal lobe epilepsy. *Brain Cogn* 1997; 35(1): 110-31.

ILAE (International League Against Epilepsy) Commission on Classification and Terminology. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989; 30(4): 389-99.

Jan MM, Girvin JP. Seizure semiology: value in identifying seizure origin. *Can J Neurol Sci* 2008; 35(1): 22-30.

Jones-Gotman M, Zatorre RJ, Olivier A, *et al*. Learning and retention of wards and designs following excision from medial or lateral temporal-lobe structures. *Neuropsychologia* 1997; 35(7): 963-73.

Kahane P, Bartolomei F. Temporal lobe epilepsy and hippocampal sclerosis: lessons from depth EEG recordings. *Epilepsia* 2010; (1): 59-62.

Karunakaran S, Rollo MJ, Kim K, *et al*. The interictal mesial temporal lobe epilepsy network. *Epilepsia* 2018; 59(1): 244-58.

Krauss G, Theodore WH. Treatment strategies in the postictal state. *Epilepsy Behav* 2010; 19(2): 188-90.

Lee SY, Lee SK, Yun CH, *et al*. Clinico-electrical characteristics of lateral temporal lobe epilepsy ; anterior and posterior lateral temporal lobe epilepsy. *J Clin Neurol* 2006; 2: 118-25.

Maillard L, Vignal J, Gavaret M, *et al*. Semiologic and electrophysiologic correlations in temporal lobe seizure subtypes. *Epilepsia* 2004; 45(12): 1590-9.

O'Brien TJ, Kilpatrick C, Murrie V, *et al*. Temporal lobe epilepsy caused by mesial temporal sclerosis and temporal neocortical lesions: a clinical and electroencephalographic study of 46 pathologically proven cases. *Brain* 1996; 2(119): 2133-41.

O'Dell CM, Das A, Wallace G, *et al*. Understanding the basic mechanisms underlying seizures in mesial temporal lobe epilepsy and possible therapeutic targets: a review. *J Neurosci Res* 2012; 90(5): 913-24.

Ochoa JG, Hentgarden D, Paulzak A, *et al*. Subtle pathological changes in neocortical temporal lobe epilepsy. *Epilepsy Behav* 2017; 71: 17-22.

Oyegbile T, Dabbs K, Jones J, *et al*. The nature and extent of cerebellar atrophy in chronic temporal lobe epilepsy. *Epilepsia* 2011; 52(4): 698-706.

Pacia SV, Devinsky O, Perrine K, *et al*. Clinical features of neocortical temporal lobe epilepsy. *Ann Neurol* 1996; 40: 724-30.

Perry MS, Duchowny M. Surgical *versus* medical treatment for refractory epilepsy: outcomes beyond seizure control. *Epilepsia* 2013; 54(12): 2060-70.

Pfander M, Arnold S, Henkel A, *et al*. Clinical features and EEG findings differentiating mesial from neocortical temporal lobe epilepsy. *Epileptic Disord* 2002; 4(3): 189-95.

Rémi J, Noachtar S. Clinical features of the postictal state: correlation with seizure variables. *Epilepsy Behav* 2010; 19(2): 114-7.

Rosenow F, Lüders H. Presurgical evaluation of epilepsy. *Brain* 2001; 124: 1683-700.

Schmidt D, Stavem K. Long-term seizure outcome of surgery *versus* no surgery for drug-resistant partial epilepsy: a review of controlled studies. *Epilepsia* 2009; 50(6): 1301-9.

Schramm J, Kral T, Grunwald T, *et al*. Surgical treatment for neocortical temporal lobe epilepsy: clinical and surgical aspects and seizure outcome. *J Neurosurg* 2001; 94(1): 33-42.

Schulz R, Lüders HO, Hoppe M, *et al*. Interictal EEG and ictal scalp EEG propagation are highly predictive of surgical outcome in mesial temporal lobe epilepsy. *Epilepsia* 2000; 41(5): 564-70.

Tao JX, Chen X, Baldwin M, *et al*. Interictal regional delta slowing is an EEG marker of epileptic network in temporal lobe epilepsy. *Epilepsia* 2011; 52(3): 467-76.

Wiebe S, Blume WT, Girvin JP, *et al*. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *N Engl J Med* 2001; 345(5): 311-8.

Wieser HG. Mesial temporal lobe epilepsy with hippocampal sclerosis. *Epilepsia* 2004; 45(6): 695-714.

Zhao F, Kang H, You Li H, *et al*. Neuropsychological deficits in temporal lobe epilepsy: a comprehensive review. *Ann Indian Acad Neurol* 2014; 17(4): 374-82.

TEST YOURSELF

(1) What are the semiological features in NTLE that differ from MTLE?

(2) What are the differences in ictal EEG findings between NTLE and MTLE?

(3) Which subtype of TLE is associated with a significantly higher preoperative IQ?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".