ORIGINAL ARTICLE

Histopathological Findings in Brain Tissue Obtained during Epilepsy Surgery

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ABSTRACT

BACKGROUND

Detailed neuropathological information on the structural brain lesions underlying seizures is valuable for understanding drug-resistant focal epilepsy.

METHODS

We report the diagnoses made on the basis of resected brain specimens from 9523 patients who underwent epilepsy surgery for drug-resistant seizures in 36 centers from 12 European countries over 25 years. Histopathological diagnoses were determined through examination of the specimens in local hospitals (41%) or at the German Neuropathology Reference Center for Epilepsy Surgery (59%).

RESULTS

The onset of seizures occurred before 18 years of age in 75.9% of patients overall, and 72.5% of the patients underwent surgery as adults. The mean duration of epilepsy before surgical resection was 20.1 years among adults and 5.3 years among children. The temporal lobe was involved in 71.9% of operations. There were 36 histopathological diagnoses in seven major disease categories. The most common categories were hippocampal sclerosis, found in 36.4% of the patients (88.7% of cases were in adults), tumors (mainly ganglioglioma) in 23.6%, and malformations of cortical development in 19.8% (focal cortical dysplasia was the most common type, 52.7% of cases of which were in children). No histopathological diagnosis could be established for 7.7% of the patients.

CONCLUSIONS

In patients with drug-resistant focal epilepsy requiring surgery, hippocampal sclerosis was the most common histopathological diagnosis among adults, and focal cortical dysplasia was the most common diagnosis among children. Tumors were the second most common lesion in both groups. (Funded by the European Union and others.)

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*A complete list of members of the European Epilepsy Brain Bank (EEBB) Consortium is provided in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2017;377:1648-56.
DOI: 10.1056/NEJMoa1703784
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In 2015, the World Health Organization (WHO) recognized epilepsy as a serious public health concern. Approximately 50 million people worldwide currently have epilepsy,[1] and more than 30% of patients with epilepsy have inadequate seizure control with drug therapy.[2,3] Epilepsy surgery is appropriate for carefully selected patients with difficult-to-treat focal epilepsy,[4-6] and successful epilepsy surgery reduces mortality in this population.[7] Although the efficacy of epilepsy surgery has been established in retrospective series from tertiary epilepsy centers,[8-13] few of these studies have extensively explored the types of underlying pathologic brain lesions.

The European Epilepsy Brain Bank (EEBB) was established in 2006 under the direction of the Framework Program of the European Union to standardize histopathological reporting of specimens obtained during epilepsy surgery and to survey epileptogenic brain lesions. The EEBB collects a prespecified minimal data set of deidentified clinicopathological information for its database in accordance with this plan. The inception of the database also prompted the International League against Epilepsy (ILAE) to develop an international classification of clinicopathological subtypes of focal cortical dysplasia[14] and of subtypes of hippocampal sclerosis.[15] These standardized consensus classifications of specimens obtained during epilepsy surgery inform the study of epilepsy, which had previously relied on clinical series and small randomized trials for data on the underlying causes of seizures.[4-6] We present the histopathological diagnoses from the large EEBB database to complement existing information on drug-resistant epilepsy and epilepsy surgery.

Methods

Study Procedures

We examined specimens from the EEBB database, which includes 4944 men and 4579 women with surgically treated epilepsy who underwent surgery during the period from 1990 through 2014 in 36 specialized epilepsy surgery centers in Austria, the Czech Republic, France, Germany, Greece, Italy, the Netherlands, Portugal, Spain, Switzerland, Turkey, and the United Kingdom (Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Histopathological review of resected brain tissue was performed at local epilepsy centers and at the German Neuropathology Reference Center for Epilepsy Surgery in Erlangen, Germany. There was no systematic verification of diagnoses among centers, but the material was interpreted by experienced neuropathologists. For patients who underwent two or more resections, we used clinical data and histopathological diagnoses from the last surgical procedure. Before surgery, all patients had undergone a detailed clinical examination, electroencephalographic (EEG) investigation, and magnetic resonance imaging (MRI) of the head. Video EEG, neuropsychological and psychiatric testing, and functional imaging or invasive EEG were performed when clinically indicated and as was customary for each center.

The study was approved by the ethics review board of the University of Erlangen, and all procedures were conducted in accordance with the ethics requirements of the contributing centers. Written informed consent for the use of histopathological data was obtained from patients or their representative. Participating centers submitted the histopathological diagnosis of each specimen with a prespecified minimal clinical data set that included the patient's age at the onset of epilepsy, the patient's age at the time of surgery (with children defined as patients whose age was <18 years), duration of epilepsy before surgery (with dates rounded to whole year numbers), sex, side of lesion (left, right, or midline [i.e., hypothalamus]), location of the lesion (temporal, frontal, parietal, occipital, multilobar [including hemispheric], or midline [i.e., hypothalamus]), year of surgery, and histopathological diagnosis based on light-microscopic inspection of paraffin-embedded tissue stained with hematoxylin and eosin or additional histochemical staining and immunohistological methods when indicated.[16] Hippocampal sclerosis was defined histopathologically as segmental neuronal cell loss in anatomical sectors of the cornu ammonis of the hippocampus, as specified in the consensus classification of the ILAE.[15] Brain tumors were classified according to the WHO classification of tumors of the central nervous system.[17] Focal cortical dysplasia was defined according to the consensus classification system of the ILAE.[14]

A post hoc analysis of associations between histopathological diagnoses and the outcome of surgery was performed for a subset of the centers. We classified patients as seizure-free or not seizure-free on the basis of information obtained 12 months after surgery. Freedom from seizures corresponded to category IA in the Engel clas-

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Table 1. Demographic Characteristics of Children and Adults with Histopathological Analysis of Tissue Resected during Epilepsy Surgery.*

Characteristic	Female Patients	Male Patients	Overall
All patients (N=9523)			
Male sex (%)			51.9
Age at surgery (yr)	28.2±15.2	27.9±15.3	28.1±15.3
Age at seizure onset (yr)	11.6±11.2	12.1±11.7	11.9±11.4
Duration of epilepsy (yr)	16.4±12.6	15.6±12.5	16.0±12.6
Adults (N=6900)			
Male sex (%)			51.4
Age at surgery (yr)	35.1±11.3	35.2±11.2	35.2±11.2
Age at seizure onset (yr)	14.6±11.6	15.5±12.0	15.0±11.8
Duration of epilepsy (yr)	20.5±12.2	19.7±12.4	20.1±12.3
Children (N=2623)			
Male sex (%)			53.1
Age at surgery (yr)	9.3±5.2	9.2±5.2	9.3±5.2
Age at seizure onset (yr)	3.8±4.1	3.9±4.1	3.8±4.1
Duration of epilepsy (yr)	5.4±4.1	5.3±4.2	5.3±4.1

* Plus–minus values are means ±SD. Adults were defined as patients who were 18 years of age or older, and children were defined as patients who were younger than 18 years of age. The duration of epilepsy was disease duration from onset of seizures to epilepsy surgery.

sification (classes range from IA [completely seizure-free] to IVC [worsened seizures][18]) and was equivalent to category 1 in the ILAE classification system (scores range from 1 [completely seizure-free with no auras] to 6 [>100% increase in seizure days from baseline][19]).

STATISTICAL ANALYSIS

We analyzed differences among the seven histopathological categories in age at onset of seizures (<18 years vs. ≥18 years) and the side of the affected hemisphere, which resulted in 28 tests; we used Bonferroni adjustment with $P \leq 0.0017$ (i.e., $P < [0.05 \div 28]$) considered to indicate statistical significance.[20] Differences between groups were assessed with the use of an independent-sample t-test for continuous variables and a chi-square test for categorical data. Results that are not accompanied by statistical analyses are descriptive only of numerical differences between groups. Statistics were analyzed with the use of SPSS Statistics 23 (IBM).

RESULTS

PATIENTS AND SPECIMENS

Resected brain tissue for histopathological review was available for 3901 patients (41.0%) at local epilepsy centers and for 5622 patients (59.0%) at the German Neuropathology Reference Center for Epilepsy Surgery in Erlangen, Germany. A total of 367 patients (3.8%) underwent two or more resections; for these patients, we used clinical data and histopathological diagnoses from the last surgical procedure. The prespecified minimal clinical data set was 97.5% complete for the overall series, with 1936 data points missing, in most cases for side of surgery, year of surgery, or anatomical localization. Of the 36 centers, 20 reported seizure outcomes after surgery for 85.2 to 100.0% of their patients, and these data were used for the post hoc analysis of associations between histopathological diagnoses and the outcome of surgery. Information on seizure outcomes from these 20 centers was available for 5248 patients at 1 year after surgery and for an additional 1920 patients at 24 months; this sample represented 98.4% of the 7286 patients for whom any outcome data were available, or 75.3% of the total patients in the series. In the 20 centers from which information was used for post hoc analysis of surgical outcomes, antiepileptic drug treatment was continued after surgery in all adults and in more than 90% of children.

At the time of surgery, 6900 (72.5%) of the patients were adults and 2623 (27.5%) were children. A total of 51.9% of patients were male (Table 1). Seizure onset occurred in childhood (<18 years of age) in 75.9% of the patients, and seizures started earlier than 6 years of age in 36%. The region operated on was the temporal lobe in 71.9% of the patients. Surgical resection was performed on the left side of the brain in 49.1% of the patients, on the right side in 50.5%, and on midline structures in the remainder.

There were 36 histopathological diagnoses (Table 2, and Tables S2 through S4 in the Supplementary Appendix) that could be classified into seven major conventional categories (Table 3). The 10 most frequent histopathological diagnoses accounted for 86.7% of cases. Among the 7168 patients for whom reporting of postsurgical outcome was available, post hoc analysis indicated that 60.7% (66.4% of children and 58.6% of adults) were seizure-free 1 year after surgery (ILAE score of 1, Engel class IA).

HIPPOCAMPAL SCLEROSIS

Hippocampal sclerosis was the most common histopathological diagnosis; this condition was identified in 36.4% of all surgical specimens —

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Table 2. Summary of the 10 Most Common Histopathological Diagnoses among 9523 Patients Who Underwent Epilepsy Surgery.*

Diagnosis	Category	Patients with Condition (N=9523)	Age at Onset of Seizures	Duration of Epilepsy	Localization†	
		no. (%)	*years*		*lobe*	*%*
Hippocampal sclerosis	Hippocampal sclerosis	3463 (36.4)	11.3±10.1	22.5±12.7	Temporal	100.0
Ganglioglioma	Tumor	986 (10.4)	12.1±10.3	11.4±10.4	Temporal	82.5
Focal cortical dysplasia type II	Malformation of cortical development	859 (9.0)	5.6±6.9	14.0±11.7	Frontal	51.6
No lesion	No lesion	738 (7.7)	13.0±10.6	15.4±10.6	Temporal	67.7
Dysembryoplastic neuroepithelial tumor	Tumor	565 (5.9)	14.0±10.9	12.0±10.7	Temporal	68.1
Glial scar	Glial scar	461 (4.8)	10.7±10.3	14.8±11.1	Temporal	37.1
Cavernous angioma	Vascular malformation	431 (4.5)	25.4±13.0	12.3±11.2	Temporal	74.7
Mild malformation of cortical development	Malformation of cortical development	279 (2.9)	9.6±10.0	13.7±11.5	Temporal	49.1
Focal cortical dysplasia type I	Malformation of cortical development	268 (2.8)	7.4±9.6	9.3±8.1	Temporal	35.1
Focal cortical dysplasia not otherwise specified	Malformation of cortical development	206 (2.2)	8.0±8.0	13.4±11.5	Temporal	45.1
Total		8256 (86.7)	11.6±10.8	17±12.6	Temporal	71.9

* Plus–minus values are means ±SD. A full list of diagnoses is provided in Table S2 in the Supplementary Appendix.
† Data are the lobe in which surgery was most commonly performed for each condition and the percentage of cases in which surgery was performed in that lobe.

44.5% of those from adults and 15.0% of those from children (Table 3, and Tables S3 and S4 in the Supplementary Appendix). Hippocampal sclerosis was diagnosed in 54.4% of specimens obtained from the temporal lobe (Fig. 1A, 1B, and 1C).[15] A second histopathological diagnosis was made in 1.5% of specimens with hippocampal sclerosis, including ganglioglioma (25.2%), glial scars (23.7%), focal cortical dysplasia (8.6%), dysembryoplastic neuroepithelial tumors (8.6%), encephalitis (7.2%), and cavernous angioma (5.8%). The duration of epilepsy before surgery in patients with hippocampal sclerosis is shown in Table S5 in the Supplementary Appendix. The onset of epilepsy was slightly but significantly earlier among patients with left hippocampal sclerosis than among those with right hippocampal sclerosis (mean age [±SD], 10.7±9.8 vs. 11.9±10.2 years; P<0.001). A relationship between the age at the onset of seizures and the side of the affected hemisphere was not found for any other histopathological category. Overall, the rate of freedom from seizures 1 year after surgery was 61.4% among patients who had the diagnosis of hippocampal sclerosis.

TUMORS

Brain tumors were the second most common histopathological diagnosis, occurring in 23.6% of specimens, with ganglioglioma (Fig. 1D, 1E, and 1F) being the most frequent (found in 10.4% of all patients in the study population). A total of 82.5% of gangliogliomas were located in the temporal lobe. Dysembryoplastic neuroepithelial tumors were the second most frequent type of tumor (5.9% of patients); in 68.1% of cases, this tumor was located in the temporal lobe. Early seizure onset occurred in association with both types of tumor, with a mean age (±SD) at onset of 13.1±10.7 years. Other tumors associated with an onset of epilepsy that occurred mainly before 18 years of age were angiocentric glioma, gangliocytoma, isomorphic astrocytoma, pilocytic astrocytoma, neurocytoma, and pleomorphic xanthoastrocytoma, as well as low-grade neuroepithelial tumors, the detailed characteristics of which were not further specified by the neuropathologist. Most of these tumors were classified as low grade (WHO grade I), and together with gangliogliomas and dysembryoplastic neuroepithelial tumors they accounted for 79.2% of all tumors in this series. One year after surgery, 68.4% of patients with tumors (79.9% of children and 63.5% of adults) were seizure-free.

MALFORMATIONS OF CORTICAL DEVELOPMENT

Malformations of cortical development were found in 19.8% of specimens and were the third

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Table 3. Major Histopathological Disease Categories, Age at Onset of Seizures, and Duration of Epilepsy before Surgery among Adults and Children.*

Disease Category	Patients with Condition (N=9523)	Age at Onset of Seizures	Duration of Epilepsy
	no. (%)	*years*	
All patients			
Hippocampal sclerosis	3463 (36.4)	11.3±10.1	22.5±12.7
Tumor	2244 (23.6)	15.1±12.6	11.4±10.5
Cortical malformations	1888 (19.8)	6.2±8.0	12.2±11.1
No lesion	738 (7.7)	13.0±10.6	15.4±10.6
Vascular malformations	581 (6.1)	22.2±14.3	12.3±11.2
Glial scar†	464 (4.9)	10.6±10.3	14.8±11.1
Encephalitis	145 (1.5)	10.1±11.2	7.8±9.1
Total	9523	11.9±11.4	16.0±12.6
Adults‡			
Hippocampal sclerosis	3070 (44.5)	12.3±10.3	24.4±12.1
Tumor	1530 (22.2)	19.3±13.0	14.6±11.1
Cortical malformations	856 (12.4)	11.2±9.3	20.7±11.0
No lesion	577 (8.4)	15.4±10.6	17.9±10.5
Vascular malformations	497 (7.2)	25.2±13.0	13.7±11.4
Glial scar	311 (4.5)	14.4±10.4	19.1±10.8
Encephalitis	59 (0.9)	18.4±13.4	13.4±11.6
Total	6900 (72.5)	15.0±11.8	20.1±12.3
Children‡			
Cortical malformations	1032 (39.3)	2.2±2.9	5.1±4.1
Tumor	714 (27.2)	6.1±4.7	4.4±3.7
Hippocampal sclerosis	393 (15.0)	4.1±3.6	7.4±4.3
No lesion	161 (6.1)	4.4±4.0	6.5±4.0
Glial scar	153 (5.8)	2.9±3.4	6.0±4.3
Encephalitis	86 (3.3)	4.5±3.0	4.0±3.3
Vascular malformations	84 (3.2)	4.2±4.9	4.0±3.8
Total	2623 (27.5)	3.8±4.1	5.3±4.1

* Plus–minus values are means ±SD.
† Three additional patients who did not have a glial scar as their primary histopathological diagnosis but had a glial scar as a second histopathological condition are included in this major category: one with a diagnosis of encephalitis, one with a mild malformation of cortical development, and one with focal cortical dysplasia.
‡ The percentages shown are the percentages within the age category (adults or children), with the exception of that given in the total row, which is the percentage of the 9523 total patients in the series.

most frequent histopathological category; such malformations were identified in 39.3% of all specimens obtained from children. Subtypes of focal cortical dysplasia were the most common malformations of cortical development, accounting for 70.6% of cases. These malformations were characterized by architectural and cytoarchitectural abnormalities of the six layers of the cerebral cortex. The combination of dysmorphic neurons and balloon cells, which is characteristic of focal cortical dysplasia type II (Fig. 1G, 1H, and 1I), was the most common subtype of malformation (accounting for 45.3% of cases) and was present in 17.0% of all children in the series at the time of surgery (Table S4 in the Supplementary Appendix); this malformation was most often located in the frontal lobe (51.6%). The onset of epilepsy in patients with malformations of cortical development was earlier than that among patients with other disease categories (Table 3). Within this group, multilobar malformations were associated with the earliest onset of epilepsy; patients with hemimegalencephaly had a mean age (±SD) at onset of seizures of 0.1±0.7 years, patients with multilobar focal cortical dysplasia type II a mean age at onset of 2.3±4.3 years, and patients with polymicrogyria a mean age at onset of 3.3±5.5 years. Among the 367 patients who had two or more surgical resections, cortical malformations (32.2%) and tumors (26.4%) were the most common conditions. Overall, 57.6% of patients with malformations of cortical development (59.9% of children and 54.6% of adults) were seizure-free 1 year after surgery.

NO LESION

No specific lesion could be identified or characterized by means of microscopic inspection in 7.7% of patients (8.4% of adults and 6.1% of children). This included findings of nonspecific reactive gliosis as the only histopathologic abnormality in the neocortex, white matter, or hippocampus.[14-16] Freedom from seizures 1 year after surgery occurred in 50.2% of patients in this category (55.2% of children and 48.7% of adults).

VASCULAR LESIONS, GLIAL SCARS, AND ENCEPHALITIS

Vascular malformations were found in 6.1% of specimens, with cavernous angiomas in the temporal lobe being the most frequent type. Seizure onset among patients with vascular malformations occurred at a mean age of 22.2 years, the oldest age among the histopathological categories. Freedom from seizures 1 year after surgery occurred in 64.8% of patients with vascular malformations (73.0% of children and 63.4% of adults).

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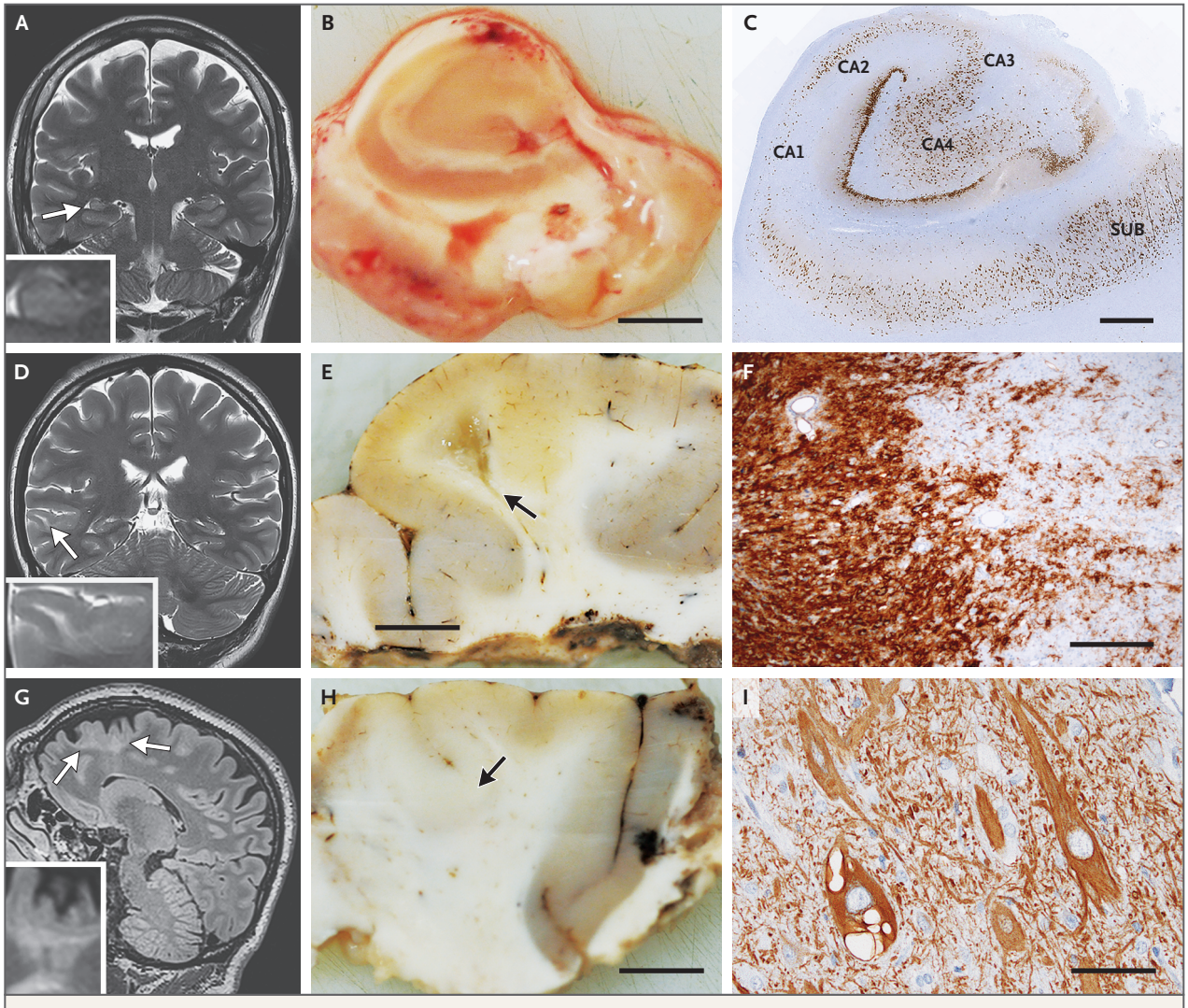

Figure 1. Findings from Three Patients with Conditions Commonly Diagnosed in the European Epilepsy Brain Bank.

Panel A shows a coronal T_2-weighted magnetic resonance imaging (MRI) scan of a 51-year-old male patient with hippocampal sclerosis who had had right temporal lobe epilepsy since 12 years of age. The atrophic right hippocampus (enlarged in the inset) is indicated by the arrow. Panel B shows a 5-mm slab of en bloc resected hippocampus from the same patient, cut perpendicular to the anterior–posterior axis at the level of the hippocampus body. The scale bar indicates 2 mm. Panel C shows NeuN immunohistochemical staining of the specimen obtained from this patient (brown color with hematoxylin counterstaining) indicating segmental neuronal cell loss in cornu ammonis area (CA) 1 — that is, hippocampal sclerosis type 2 (2013 International League against Epilepsy [ILAE] classification). SUB denotes subiculum. The scale bar indicates 1 mm. Panel D shows a coronal T_2-weighted MRI scan of a 13-year-old girl with ganglioglioma who had had right temporal lobe epilepsy since 8 years of age. The arrow points to a lesion at the right superior temporal gyrus (enlarged in the inset). Panel E shows a formalin-fixed en bloc resected specimen obtained from this patient, with partially cystic rarefaction of subcortical white matter indicated by the arrow. The scale bar indicates 4 mm. Panel F shows CD34 immunohistochemical staining of the specimen obtained from this patient (brown color with hematoxylin counterstaining), with diffuse tumor infiltration into adjacent cortex (on the right) characteristic of ganglioglioma World Health Organization (WHO) grade I (2016 WHO classification). The scale bar indicates 400 μm. Panel G shows a sagittal fluid-attenuated inversion recovery (FLAIR) image of a 32-year-old male patient with focal cortical dysplasia type II who had had left frontal lobe epilepsy since 10 years of age; the arrows point to focal cortical dysplasia with hyperintense transmantle sign toward the left ventricle (the enlargement in the inset was taken from an adjacent scanning level). Panel H shows an en bloc, formalin-fixed resected specimen obtained from this patient, with thickened and pale-colored neocortex (arrow) that is difficult to discriminate from white matter. The scale bar indicates 4 mm. Panel I shows immunohistochemical staining of the specimen obtained from this patient with monoclonal antibodies directed against nonphosphorylated neurofilament protein indicating intracytoplasmic neurofilament accumulation (brown color with hematoxylin counterstaining), which is a characteristic sign of dysmorphic neurons in focal cortical dysplasia type II. Histopathological detection of balloon cells (not shown) further classified this lesion as subtype IIb (2011 ILAE classification). The scale bar indicates 70 μm.

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Glial scars were found in 4.9% of specimens and were most often located in the temporal lobe or in multiple lobes (Table 3). The onset of seizures among patients with glial scars occurred at a mean age of 10.6 years, with a mean duration of epilepsy of 14.8 years before surgery. Glial scars occurred more often in men (61.0%) than in women (39.0%). The rate of postoperative freedom from seizures was numerically the lowest in this histopathological category (46.9%). A total of 1.5% of patients had a histopathological diagnosis of encephalitis, most commonly Rasmussen's encephalitis affecting multiple lobes. Seizure onset among patients with encephalitis occurred at a mean age of 10.1 years, and 50% of patients were seizure-free 1 year after surgery.

DISCUSSION

In this series of approximately 10,000 specimens of brain tissue obtained during epilepsy surgery, the 10 most frequent histopathological diagnoses accounted for 86.7% of cases of drug-resistant epilepsy. The detailed diagnoses could be categorized into seven broad categories. Hippocampal sclerosis was the most frequent lesion, a finding consistent with results of studies involving smaller series of patients who have undergone epilepsy surgery.[8,12,13] Pathological diagnosis was aided by identification of anatomical landmarks, best appreciated in gross anatomical specimens. An international consensus recommendation for the procurement of brain tissue from patients with epilepsy on the basis of the identification of anatomical landmarks has recently been proposed by the ILAE Commission on Diagnostic Methods.[16]

Among the patients with hippocampal sclerosis, 78.1% were younger than 18 years of age at disease onset; however, 88.7% of patients with this condition were adults at the time epilepsy surgery was performed, after a mean duration of epilepsy of 22.5 years. We suggested in a previous article that difficulties in identifying hippocampal sclerosis by means of routine MRI may contribute to this delay.[21] Our current analysis also suggests that patients with left hippocampal sclerosis had an earlier onset of epilepsy than did patients with right hippocampal sclerosis, but the differences were small and require confirmation.

Ganglioglioma and dysembryoplastic neuroepithelial tumors were the tumors most frequently found in our series, both in adults and in children. In contrast, infiltrating gliomas were uncommon, perhaps because patients with these tumors are usually not treated in specialized epilepsy surgery centers. Focal cortical dysplasias have been reported as being increasingly frequent in series of patients who have undergone epilepsy surgery.[8,10,11,13] Cognitive delay and early onset of seizures have been associated with these lesions, but the clinical implications vary according to subtype.[14] Among the subtypes, the histopathological diagnosis of focal cortical dysplasia type I is particularly challenging, and we used immunohistochemical staining for NeuN[22] and nonphosphorylated neurofilament protein to identify cortical-layer abnormalities. A new category of focal cortical dysplasia type III was introduced in the 2011 consensus classification system of the ILAE, but its pathogenic basis and histopathological definition have not been clarified,[14] and this subtype was not considered to be a separate entity in our analysis.

In children and adults, 6.1% and 8.4%, respectively, of tissue samples had astrogliosis only and could not be categorized as having any conventional lesion type. This does not imply that the tissue was functionally normal, since 50.2% of patients with drug-resistant seizures before epilepsy surgery and unclassifiable tissue samples were seizure-free 12 months after surgery, which implicates the resected tissue in the genesis of the seizures. It is also possible that a molecular alteration that can decrease seizure threshold but is not apparent as an abnormality on light microscopy was an element involved in the conditions in this group of patients.[23] Ambiguous histopathological findings may also result from the inconsistent nature of neurosurgical sampling. Newly characterized histopathological entities in patients with focal epilepsies, such as oligodendroglial hyperplasia in white matter and hyaline protoplasmic astrocytopathy, may reduce the number of histopathologically nonlesional diagnoses in samples obtained during epilepsy surgery in the future.[24,25]

The limitations of our study include the retrospective data analysis and biases that are inherent in selecting patients with epilepsy for surgical treatment. Furthermore, some of the surgical procedures during which tissue was obtained involved disconnection procedures that do not typically allow for the microscopic identification of a brain lesion. The data from this large series add to the information on microscopically de-

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fined pathologic conditions in specimens obtained from surgical resection in patients with drug-resistant focal epilepsy.[2,4]

This report describes independent research by the National Institute for Health Research (NIHR) Biomedical Research Centre Funding Scheme. The views expressed in this article are those of the authors and not necessarily those of the National Health Service, the NIHR, or the U.K. Department of Health.

Supported by the European Union (FP7 DESIRE GA grant 602531, to Drs. Blumcke, Spreafico, Haaker, Tassi, Guerrini, and Barba; FP7 EPITARGET GA grant 602102, to Drs. Becker, Aronica, Walker, and Sisodiya; FP7 EPISTOP grant 602391, to Dr. Aronica; and FP7 EpimiRNA GA grant 602130, to Drs. Hamer and Rosenow); EpiGENet (DFG Bl 421/3-1, to Dr. Blumcke); the Johannes and Frieda Marohn Foundation of the Friedrich-Alexander University Erlangen-Nuremberg (support to Dr. Blumcke); the Austrian Science Fund (FWF grant J3499, to Dr. Mühlebner and grants P21636, P24367, DK W 1233-G17, KLI543-B27, and KLI12-B00, to Dr. Trinka); the Italian Ministry of Health (grant RF-2011-02350578, to Drs. Spreafico, Tassi, and Guerrini, and grant RF-2010-2309954, to Dr. Barba), the National Institute for Health Research University College London Hospitals Biomedical Research Centre (support to Drs. Thom, Walker, Sisodiya, Duncan, and McEvoy); Great Ormond Street Hospital Children's Charity, the Brain Tumour Charity, Children with Cancer, Higher Education Funding Council for England, and the National Institute for Health Research (support to Dr. Jacques); the Anniversary Fund of the Central Bank of the Republic of Austria (grant ÖNB-12036, to Dr. Feucht); and Fundación Gmp (support to Dr. Gil-Nagel).

Dr. Kobow reports receiving lecture fees from Nutricia; Dr. Bien, receiving lecture fees, consulting fees, and travel support from Eisai, UCB, and Desitin, grant support and travel support from Griflos, grant support and lecture fees from Diamed and Fresenius Medical Care, lecture fees from Euroimmun, and consulting fees from Laboratory Krone; Dr. Elger, receiving honoraria and consulting fees from UCB, Desitin, Bial, and Eisai; Dr. Hamer, receiving advisory board fees and lecture fees from UCB, Desitin, Eisai, and Novartis, advisory board fees from Cerbomed, and lecture fees from Hexal and Boehringer Ingelheim; Dr. Stefan, receiving honoraria from Eisai, Elekta, Novartis, LivaNova, and Desitin; Dr. Walker, receiving grant support from Vitaflo, lecture fees and advisory board fees from Eisai and UCB Pharma, consulting fees from GlaxoSmithKline and Pfizer, lecture fees from Special Products, advisory board fees from Sanofi, holding a patent on "Therapeutic use of compounds" (WO 2012069790) licensed to Vitaflo, and holding a patent on "Combined use of a vector encoding a modified receptor and its exogenous agonist in the treatment of seizures" (WO 2015136247); Dr. Duncan, receiving grant support from Wellcome Trust; Dr. Schulze-Bonhage, receiving grant support from Bial, lecture fees and consulting fees from Eisai and UCB, and consulting fees from Precisis; Dr. Urbach, receiving lecture fees from Bayer, Bracco, Stryker, and UCB Pharma; Dr. Lerche, receiving consulting fees, lecture fees, and travel support from Bial, Eisai, and UCB Pharma, lecture fees and travel support from Desitin, and consulting fees from Biomarine; Dr. Jacques, serving as a director and holding equity in Neuropath, and serving as a director, company secretary, and holding equity in Repath; Dr. Cross, receiving grant support (paid to her department) from Zogenix, GW Pharma, and Vitaflo, lecture fees (paid to her department) from Shire and Nutricia, and advisory board fees (paid to her department) from Eisai and GlaxoSmithKline; Dr. Grunwald, receiving lecture fees from Desitin, Eisai, and UCB; Dr. Gil-Nagel, receiving grant support and lecture fees from Bial and UCB Pharma, lecture fees from Eisai, Sanofi, and Zogenix, and advisory fees from Esteve; Dr. Rosenow, receiving advisory board fees, lecture fees, and travel support from UCB Pharma, serving on an advisory board for Shire, Eisai, Desitin Arzneimittel, Bial, Cerbomed, and Sandoz, travel support from Novartis Japan, lecture fees from Bayer Vital and Verband der Forschender Arzneimittelhersteller, and grant support from the Detlev-Wrobel-Fonds for Epilepsy Research; Dr. von Oertzen, receiving advisory board fees and travel support from Eisai Pharma, grant support, travel support, and serving on an advisory board for UCB Pharma and Novartis, travel support from Medtronic, grant support from Grossegger and Drbal, serving on an advisory board for Roche, Biogen, and Sanofi-Genzyme, and serving as an expert witness for LivaNova. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

APPENDIX

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