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Selection of Candidates for Epilepsy Surgery, in Particular With a View Towards Selective Amygdalohippocampectomy

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Better knowledge of the electroclinical semiology of seizures, and in particular of the site of seizure initiation and spread, was gained from direct intracerebral recordings during presurgical evaluation of candidates for epilepsy surgery. These findings led us to classify focal epilepsies with complex partial seizures (CPS) into five subtypes: (a) mesiobasal limbic, (b) temporal polar-amygdalar, (c) temporal lateral (neocortical-posterior), (d) opercular-insular, and (e) frontobasal-cingulate[1]. By far the most frequent and therefore the most important subtype of focal epilepsies with CPS is the mesiobasal limbic one. In our series, 65 % of seizures classified as mesiobasal limbic originated simultaneously in the hippocampus and amygdala (Fig. 1), and about 10 % in the amygdala. Of those with amygdalar origin approximately two thirds invade the hippocampus within 3 to 5 s [2]

Based on these findings, we have argued that in patients with seizures of mesiobasal limbic origin, i.e. suffering from the syndrome of mesial temporal lobe epilepsy (MTLE), the "classical" anterior temporal lobe (TL) resection is too crude a surgical operation. The need for a more selective resection of the mesiobasal limbic structure was already proposed by Niemeyer as early as 1958[3] However, Niemeyer's transventricular approach was later on abandoned. The need to remove mesial TL structures without damaging lateral neocortical TL cortex was satisfied by M.G. Yasargil and resulted in the trans-sylvian selective amygdalohippocampectomy (AHE), performed in our hospital since 1975. At the end of June 1996, a total of 354 patients had undergone this operation in Zürich. At the second Palm Desert Conference on the Surgical Treatment of the Epilepsies[4] it was reported that worldwide a total of 548 AHEs were performed during the period 1986-1990. During the first years, the indication in Zürich for AHE was strictly confined to patients with focal seizure onset within the amygdala and hippocampal formation ("causal = curative AHE"). Satisfying early results[5] led us then to offer this type of surgery also to certain patients with a seizure origin in the lateral temporal cortex, in particular when located in the dominant hemisphere encroaching on indispensable language areas, but only if a secondary pacemaker role of the ipsilateral hippocampal formation could be proven ("palliative AHE"). Although the results of the palliative AHE were clearly less favorable compared with those obtained with a "causal indication", in general they were good enough to justify this approach. In turn, the sometimes unexpectedly good postoperative seizure control following palliative AHE led us to conceptualize the so-called amplifier role of the hippocampal formation, and in particular of the parahippocampal gyrus[1,6]

Although AHE is done today with a less restrictive indication than during the first decade of its use, it should be emphasized that in essence it remains a surgical treatment for drug-resistant MTLE with a well-defined, unilateral mesiobasal limbic seizure onset only[7]

The principal objective of this article is to review the results obtained with this operation. A short characterization of the MTLE-syndrome and a few remarks on the operative anatomy and surgical technique seem necessary, however. A more detailed description of the main surgical steps of this operation has been published elsewhere[5,8,9,10].

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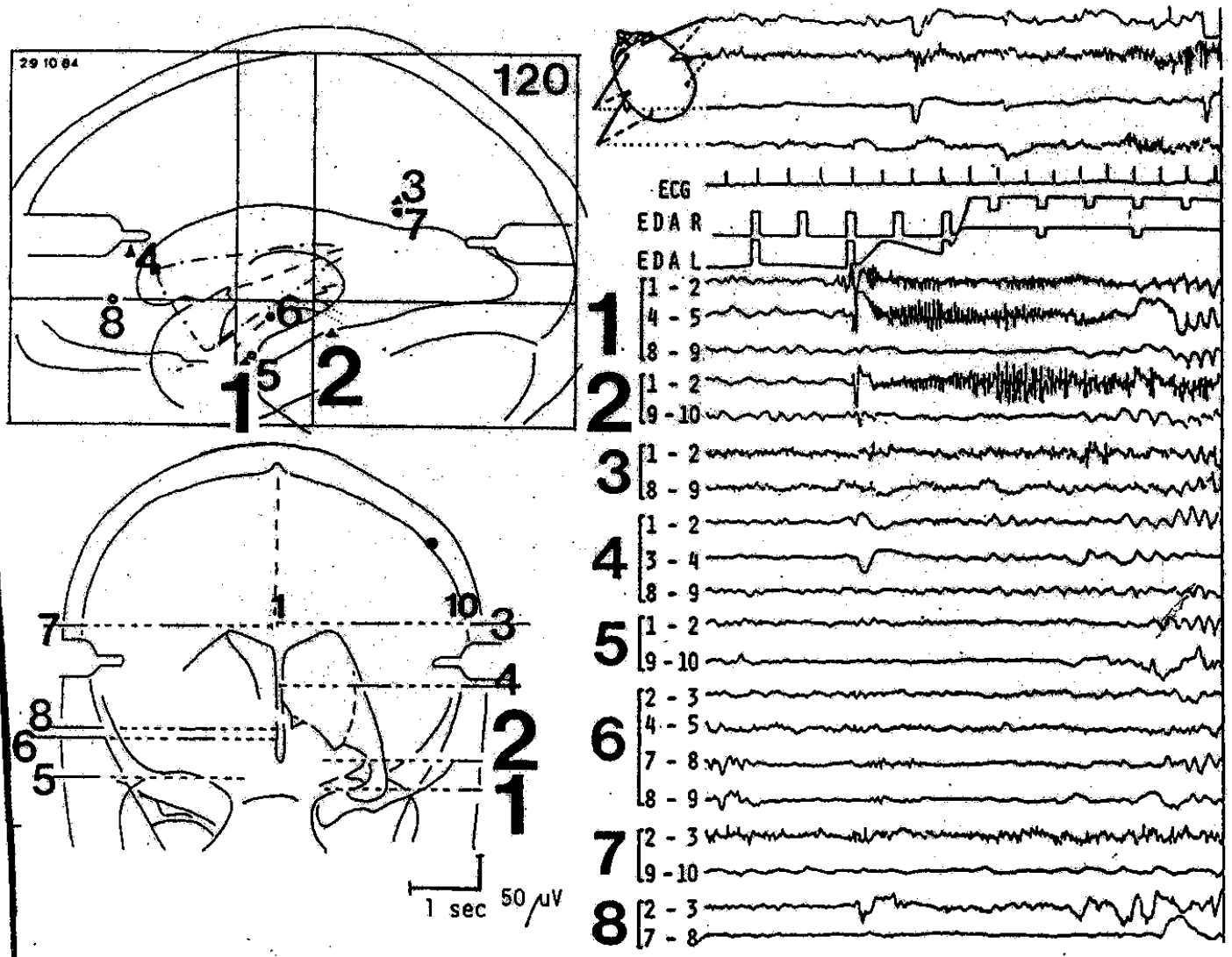

Figure 1: Combined scalp and sterotaxic depth (SEEG) recording at the beginning of a typical complex-partial seizure, showing the simultaneous seizure onset in the left amygdala (1/1-2 and 1/4-5) and hippocampus (2/1-2). There is a change in the electrodermal activity '(EDA) measured at the right (R) and left (L) hands. (ECG, electrocardiogram). The localization of the depth electrodes (*large bold numbers*) is indicated in the sterotaxic reference scheme. Each hollow- core electrode has 10 contacts (*small numbers*), with contact 1 located at the tip of the electrode.

The syndrome of mesial temporal lobe epilepsy (MTLE)

The syndrome of MTLE is a well accepted epilepsy syndrome that it is frequent, often drug-resistant, but amenable to successful surgical treatment [1,11,12,13]. It is widely recognized and has been elaborated fairly precisely in terms of clinical signs and symptoms including neuro-psychological and psychiatric aspects, electrophysiological characteristics, morphological and functional imaging findings, etiological and pathophysiological mechanisms, clinical course, and response to treatment, both to antiepileptic drugs (AEDs) and to surgery. The most characteristic feature is its unique pathophysiology, i.e. hippocampal sclerosis.

The key features of this syndrome are:

Epidemiology: Incidence and prevalence

Precise epidemiological information on MTLE is not available because this syndrome has only been

recently clearly defined, and only the medically refractory variant of this syndrome, which is referred to surgery, is usually identified.

About 40% to 50% of all newly diagnosed incidence cases and almost 60% of prevalence cases have partial seizures. Complex partial seizures (CPS) are the single most frequent class of partial seizures. However, not all patients with CPS have MTLE.

Overall, between 60% and 70% of patients with newly identified CPS have complete seizure control and in the majority the AEDs can be discontinued. However, between 5% and 10% of patients with newly identified CPS will have no seizure control and their epilepsy may actually progress. Response to AED treatment in the first few months correlates positively with a good outcome, whereas very young seizure onset (i.e. less than age 2), a high frequency of seizures, a known etiology, a history of status epilepticus, and a history of febrile seizures, represent factors associated with a lower likelihood of remission[14]

MTLE constitutes a subgroup of patients with CPS with a less favorable prognosis. Patients with MTLE experience a high rate of failure with AEDs. Associated with an aggravation of seizure problems, are often an accentuation of personality and behaviour problems, and a decline of memory.

Genetics and pathophysiology

Febrile seizures, in particular when complicated, i.e. prolonged, have been incriminated as one important factor for the development of MTLE associated with mesial temporal sclerosis (MTS) [15] although this issue remains controversial[16]. In surgical series the rate of febrile seizures ranges from 9% to 50%[17,18,1920]. In prospective cohort studies of children with febrile seizures the risk of developing epilepsy varied from 2% to 7%[12]. The prevalence of a positive family history of febrile convulsions is higher in patients with TLE treated surgically. It is assumed that the tendency for febrile seizures is to large extent genetically determined and inherited in a multifactorial way.

Hippocampal sclerosis (HS) with marked loss of neurons in the CA1 region , some loss in endfolium (CA3/CA4) but relative sparing of CA2 region is the most characteristic pathological substrate of MTLE. The subicular complex, entorhinal cortex, and the temporal gyri are relatively resistant to cell loss. The term HS has been used more or less synonymously with Ammon`s horn sclerosis and MTS, although these terms imply different degrees of anatomical involvement [21]. HS with hippocampal cell loss most pronounced in CA1 and hilar neurons and least in CA2 neurons, and associated with characteristic other features, such as mossy fiber sprouting [22] and selective loss of somatostatin and neuropeptide Y-containing neurons [23], is found in 70% of patients with medically refractory TLE undergoing surgery [24]. MTLE therefore seems to be the most common human epileptic syndrome, although it is currently impossible to give the exact percentage of patients with MTLE who are adequately controlled with AEDs and which then might bear relationships with the recently described syndrome of of benign familial temporal lobe epilepsy [25].

Clinical characteristics

Typically the clinical course of a patient with MTLE starts with onset of seizures at the end of the first decade. First attacks might present as complex partial or (secondary) generalized seizures. Initially seizures will respond well to AED, but will finally recur in adolescence or early adulthood and tend to become refractory to AEDs. A history of complicated febrile seizures can be found in approximately 30% of patients with MTLE with refractory seizures. In recent studies of surgically treated patients the rate of febrile seizures amounted to 40%. Other initial precipitating events are found in about 33 % [26,27,28].

Semiologically the seizures in MTLE typically are characterized by auras evolving into complex partial seizures with initial arrest (motionless stare), followed by oro-alimentary and other automatisms. Vegetative-autonomous signs and symptoms are marked. Auras occur frequently in isolation and typically consist of epigastric-rising sensations associated with olfactory, gustatory, and

psychic phenomena (fear, dreamy states, deja-vu, deja-vecu, deja entendu, other kinds of recollections) and alterations of self-perception (in time and space) as well as changes in the emotional and affective sphere [1,29,30,31,32]. Kotagal et al. (1989) have pointed out that posturing of one extremity can occur and is then a valid lateralizing sign pointing to contralateral ictal onset.[33] Automatisms may be ictal or postictal, de-novo or reactive. Ictal automatisms frequently consist of oro-alimentary symptoms, such as lip smacking and swallowing, and gestural, such as picking, fumbling and aimless movements. Consciousness typically is lost or at least clouded. Typical for the semiology of seizures in MTLE are varying degrees of postictal confusion with amnesia for the ictal event, and persisting postictal memory deficit. Postictal aphasia with left TL seizures, also is typical. Marked reactive automatisms might be seen in the postictal phase. Secondary generalization can occur, particularly in children, but is relatively infrequent in adults receiving standard AEDS.

Seizures typically occur at random with a frequency of a few seizures per month to a few per week. There is no marked circadian preponderance of seizure occurrence, but drowsiness and light sleep (Non-REM sleep stage I) as a rule, facilitate seizures. Sleep deprivation and all kinds of stress usually exacerbate seizures. In female patients with MTLE seizures might be exacerbated by certain phases of the menstrual cycle. However, catamenial epilepsy, i.e., seizures exclusively bound to the menstrual cycle, is rare.

Seizures associated with loss of consciousness are usually indicative for bilateral limbic involvement and a patient claiming that he/she lost his/her habitual aura might have developped a mirror focus in the contralateral TL and thus suffer from bilateral TL seizure foci.

Seizures with amygdalar onset exist but are rare and the discharges usually invade the ipsilateral hippocampal formation within 5 seconds [30]. Semiologically fear and autonomous signs and symptoms might be pronounced. The amygdala seizure subtype might show activation of epileptiform discharges, with concomittant focalization of the discharges, during REM-sleep [34].

Neurological, neuropsychological and psychiatric findings

The neurological examination is as a rule normal. Detailed neuropsychological examination, however, reveals various degrees of material-specific learning and memory deficits. Usually they are more pronounced with left MTLE and may be associated with subtle speech problems if the dominant hemisphere is predominantly involved. Patients considered at risk for an amnestic syndrome are usually subjected to amobarbital tests prior to surgery. In recent years selective TL amobarbital tests with toposelective inactivation of the mesial TL were developed [35,36,37] and are preferred to the classic intracarotid amobarbital test[38]. Endocrine functions remain usually normal, but some women may report on irregularities of the menstrual cycle or changes in the sexual sphere, in particular hyposexuality. Often, however, it is difficult to attribute these changes to the epileptic process per se and to differentiate from possible side effects of AEDs, in particular high dosed carbamazepine.

Patients with MTLE may be at greater risk to develop certain personality and behaviour peculariti-es. Waxman and Geschwind.[39] have described an "interictal behavioural and personality syndrome of TLE" explaining the irritabiliy, lower stress tolerance, "stickiness" and sometimes hypergraphia as well as changes of sexuality with altered self-perception as a kind of "sensory-limbic hyperconnection" syndrome[40,41] due to kindling-like mechanisms. Depression and psychosis-like states in the sense of schizophrenia-like psychosis[42] were also associated with MTLE, but this issue remains controversial[43,44]. In a more recent study no association between schizophrenia-like psychosis and MTS were found, but psychosis was associated with pinpoint perivascular white-matter softenings and with an increased rate of generalized seizures[45].

EEG

In MTLE rather characteristic and typical interictal and ictal EEG findings can be found. Interictally typically grouped blunt sharp-waves with or without slow waves recur with a frequency of about 1 per second and show a characteristic distribu-

tion with a maximum of their field in basal anterior electrodes (such as sphenoidal, or true temporal electrodes). They may be unilateral or bilateral dependent or independent[1,6,31]. Dipole analyses reveal a typical oblique dipole orientation in MTLE, whereas patients with straight laterally oriented dipoles show neocortical TL seizure onset [46,47,48].

Ictal scalp EEG findings typically consist of fairly regular theta-rhythms of about 5/sec with crescendo-like augmentation of the amplitude paralleled by a slowing of the discharge rhythms. Seizure onset might be characterized by regional or generalized attenuation of background EEG rhythms with disappearance of interictal "spikes". Direct recording from the hippocampal formation often show a so-called "hypersynchronous hippocampal discharge pattern"[49,32] followed by low-amplitude high-frequency recruiting rhythm of more than 20/sec[50,32]. Contralateral propagation usually occurs after 15 sec and is accompanied by loss of consciousness and the onset of symptoms characteristic of the complex partial ictal event. Localized hippocampal discharges might occur without any noticeable clinical accompaniments or consist of "minor" symptoms only. A regional but unilateral mesial TL involvement of the discharges usually is experienced as an aura by the patient[34]. In children with MTLE in the scalp EEG ictal seizure discharges might be more wide-spread and consist of irregular high-voltage spike-slow-wave patterns[51].

Tests for structural pathology and functional deficits

Nowadays high-resolution thin-section T1 weighted magnetic resonance imaging (MRI) can demonstrate hippocampal atrophy in a high percentage of patients with MTLE[52]. T2-weighted imaging techniques can visualize hippocampal sclerosis by increased signals. Quantitative MR volumetry is used to demonstrate asymmetries[53].

Cortical microdysgenesis and cortical dysplasia, i.e., alterations of neuronal migration[54] as well as hamartomas, small tumours and cavernomas can be round in addition to hippocampal sclerosis, a condition which has been referred to as "dual pathology"[55]

Magnetic resonance spectroscopy (MRS), in particular 1H-MRS has proven to be able to indicate hippocampal sclerosis by measuring reduced N-Acetyl-aspartat[56,57] and might become a valid clinical tool in the future.

Functional deficits in MTLE can be demonstrated in patients suffering from MTLE using 18F-fluorodesoxyglucose (FDG) positron emmission tomography (PET). Interictal hypometabolism is, as a rule, wide-spread and involves the ipsilateral lateral TL as well as ipsilateral thalamus and other subcortical structures[58,59,60]. Flumazenil-PET has demonstrated reduced benzodiazepine receptor binding[61] and Carfentanil-PET an up-regulation of mu-opiod receptor binding in mainly the ipsilateral TL[62,63].
Single photon emission tomography (SPECT) studies have shown reduced blood flow interictally in the TL ipsilateral to the epileptogenic mesial TL and ictal SPECT in MTLE temporal hyperperfusion during the seizures, mesial hyperperfusion and lateral TL hypoperfusion in the immediate postictal period, and hypoperfusion in the entire TL in later postictal seizure phase[64]. With ^{123}I - Iomazenil SPECT reduced benzodiazepine receptor binding in the area of the focus can be demonstrated[65].

Differential diagnosis, treatment and outcome

Both, benign childhood epilepsy with centrotemporal spikes and MTLE can begin in childhood with generalized seizures. However, the partial seizures of benign childhood epilepsy with centrotemporal spikes usually have sensory and/or motor lateralized symptoms localized around the mouth and/or the upper extremity. Interictal EEG spikes are also different in these two syndromes: The broad centrotemporal EEG spike is located more posteriorly and superiorly and has a characteristic transverse dipole, whereas in MTLE the spike or spike-wave discharges are located more anteriorly and basally with a characteristic oblique dipole direction. Differentiation from TLE due to other lesions in or close the mesial TL is usually easy by MRI. Clinical signs and symptoms might be similar, although in MTLE age of seizure onset is usually earlier, and there is a history of complicated

febrile seizures as well as an increased incidence of family members with seizures. Complex partial seizures of extratemporal origin often have an aura consisting of symptoms pointing more closely to the involved primary epileptogenic area.

Carbamazepine is considered the treatment of first choice in MTLE and response is usually satisfactory in the beginning. Later on, however, a substantial percentage obviously becomes refractory to available AEDs including classic first line AEDs, such as carbamazepine, phenytoin and primidon, and new AEDs, such as vigabatrin. Since the diagnosis of MTLE is rarely made until the patient becomes medically refractory, the percentage of patients of MTLE who respond satisfactorily to AED treatment is difficult to estimate[13].

Surgical therapy in medically refractory patients with MTLE is highly effective and renders about 80% of patients seizure-free. Most centers have modified TL surgery in MTLE with the goal to resect mesial TL structures more radically and to minimize lateral TL resection. Selective amygdalohippocampectomy[5,66], the so-called Spencer operation (resection of mesial temporal structures, of temporal pole and of only a small amount of anterior lateral temporal cortex) have been strongly advocated in MTLE[67]. There is evidence that sparing of the lateral TL cortex has advantages in terms of neuropsychological outcome[68] and that originally hypometabolic lateral TL structures show a trend for normalisation of their metabolism (Hajek et al.,1994). In well-chosen candidates for amygdalohippocampectomy, with an already present unilateral material-specific memory and learning deficit, postoperatively no significant additional deficits occur and the contralateral material-specific memory performance usually increases[38]. Patients without pre-existing memory deficits and in particularly those not becoming seizure-free following left TL resections, usually worsen in their memory. For a better prediction of the postoperative memory and learning in patients considered to be at risk, selective TL memory ambobarbital tests have been developed[37].

Without surgery the prognosis of medically refractory patients with MTLE is relatively poor. Both, severity and frequency of seizures may increase, and memory may decline, what may result in severe psychosocial disturbances. Early surgical intervention, i.e., relief of disabling seizures before the negative consequences of MTLE interfer critically with vocational and social development, results in best psychosocial outcome[69] and should be envisaged in this prototype of a surgically remediable epileptic syndrome. Several groups have reported good surgical results in children with temporal lobe epilepsy[70,71,72,73,74]. Today the diagnosis of MTLE can be often made without resorting to invasive methods. If lateralization is a problem "semi-invasive" foramen ovale electrodes may be very helpful and can be used even in very young children [75,76].

Principles of operative technique of selective amygdalohippocampectomy

The term *selective amygdalohippocampectomy* is not entirely correct, since it does not denote the removal of the parahippocampal gyrus, which is partly resected also. During 1975-1980, in Zürich the operative technique was slightly modified several times. Since then, however, the AHE has become a fairly standardized operation, as described by Yasargil et al.,[8,77]. Following a modified interfascial pterional craniotomy the trans-sylvian route - with a cortical incision of 1-2 cm lateral to the M-1 segment and anteromedial to the M-2 segment into the superior temporal gyrus - has been adapted to gain access to the tip of the temporal horn and to the amygdala. The amygdala is removed piecemeal both by rongeur (to provide histologic specimens) and by gentle suction. By use of the so-called keyhole technique, the hippocampus and the more anterior parts of the parahippocampal gyrus are then resected *en bloc*. The resected specimen measures approximately 3.5-4 cm in length, 1.5 cm in width, and 2 cm in depth. In the anteroposterior plane the posterior transection of the parahippocampal gyrus is at the level of the bifurcation of the P-2 segment to form the P-3 segments. This is at the level of the lateral geniculate body, where the fimbria ascends to the splenium to form the crus of the fornix. Figure 2 shows the extent of the resection in serial magnetic resonance imaging (MRI) scans.

Figure 2: Composition of serial MRI scans in all three planes showing the resection following a left selective AHE in a patient evaluated with the multipolar foramen ovale electrode recording technique. Coronal and sagittal images are T1-weighted, whereas the transverse images are T2-weighted (in order to improve visualization of suspected gliosis adjacent to the borders of the resection). The patient was operated on at age 11 years and remains seizure-free since the operation; postoperative follow-up was 9 years, and the patient has been off drugs since the end of the first postoperative year.

Relations between MR-imaged total amount of tissue removed, resection scores of specific mesiobasal limbic subcompartments, and clinical outcome following selective amygdalohippocampectomy

In a previously published study [78] we examined 30 patients in whom special preoperative and postoperative MRI was carried out and who had a follow-up of at least 1 year postoperatively. The mean total size of the resection was 7.2 cm^3 (range 2.1-17.7 cm^3). The extent of the removal with respect to anatomically defined specific limbic subcompartments [79] was rated by an estimation procedure involving three persons. The mean resection scores (in percentages) of the limbic subcompartments obtained from this study are amygdala 92%, pes hippocampi 92%, uncus 92%, hippocampus 46%, dentate gyrus 45%, parahippocampal gyrus 32%, and subiculum 40%. The main correlations with respect to the outcome are as follows: The seizure outcome tended to be the better the larger the resected volume. Since the resection scores of amygdala, pes hippocampi, and uncus are more or less the same in all outcome categories, the seizure outcome correlated most distinctly with the extent of the resection of the parahippocampal gyrus and in particular with that of its subicular part.

Neuropathologic findings

Table 1 shows the neuropathologic findings of the Zürich AHE series based on 354 patients. Tumors were classified according to the recommandations of the World Health Organization (WHO). In order to simplify further analyses, we grouped them into

benign, semibenign and malignant tumors. Arteriovenous malformations (AVM), cavernous angiomas, hamartomas and epidermoid cysts were classified together as dysontogenetic lesions (in all of these an abnormal ontogenesis is assumed). Hippocampal gliosis was differentiated into slight, moderate, and severe.
This grouping therefore resulted in seven histologic classes: benign (n=38), semibenign (n= 64), and malignant (n= 55) tumors; vascular (n=38); gliosis (n=112), "others" (n=13) and no microscopic pathology (n=34). This grouping was used for further analyses.

Table 1: Neuropathological Findings

benign tumorus*	38	(11 %)
semi-benign tumours	64	(18 %)
mailgnant tumours	55	(16 %)
vascular	38	(11 %)
gliosis	112	(32 %)
others*	13	(4%)
"normal"	34	(10 %)

includes dysontogenetic lesions, such as ganglioglioma, focal dysplasia, microdysgenesis, hamartoma and epidermoid

Clinical characteristics

In the Zürich AHE series (n=354), more males (56%) than females (44%) were operated on. The AHE was on the right in 51% and on the left in 49%.

The mean age at onset of epilepsy was 17.8 (SD 14.8) years. As might be expected, age at onset was the lowest in patients without a lesion or with gliosis compared with those with tumors. It is lower in patients with benign than in those with malignant tumors. Furthermore, there was a good correlation between age at first seizure and severity of gliosis: patients with severe gliosis had their first seizure earlier in life than those with slight gliosis. The main preoperative duration of seizure illness was 13.1 (SD 11.1) years. It was shorter in patients with malignant tumors than in patients with benign tumors; the more severe the gliosis, the longer the duration, and it was longer in patients without pathologic histologic findings compared with patients with tumors.

The mean age at surgery was 30.9 (SD 13.5) years. Patients with malignant tumors were older at surgery than patients with benign tumors.

Postoperative seizure outcome

The epileptologic outcome was classified into four categories according to Engel [80]: I = seizure-free, II = rare seizures (not more than two per year); III = worthwhile improvement ≥ 90% seizure reduction and significant improvement in quality of life); and IV = no worthwhile improvement. A follow-up of at least 1 year was required. With this requirement, outcome classification was possible in 283 patients at the end of 1995.
The year by year seizure outcome for the Zürich AHE series is given in Table 2.

Table 2: Year-by-Year Seizure Outcome

	1	2	3	4	5	10 (years)
n	283	235	205	181	153	76
I	67%	63%	60%	64%	66%	66%
II	8%	13%	12%	9%	8%	7%
III	12%	11%	13%	13%	12%	7%
IV	13%	13%	15%	14%	14%	21%

At the second Palm Desert Conference[4] outcome data were available for 413 patients worldwide who had AHE within the period 1986-1990. The folllowing numbers were reported: seizure-free 68.8%; "improved", 22.3%, and "not improved", 9.0%. Comparing the neuropathologic groups, three findings emerge: (a) in the tumoral groups the distribution between benign and semibenign in the seizure outcome categories is similar, (b) in patients with gliosis the operation was the more successful the more severe the gliosis; and (c) patients with a normal histology have a less favorable postsurgical seizure outcome than patients with tumors, dysontogenetic lesions, or gliosis.

Outcome with respect to "causal" versus "palliative" amygdalohippocampectomies ("nonlesional" cases)

One-hundred-thirty patients in the Zürich AHE series, who had either no histologic abnormality or only a gliosis, were separately analyzed with respect to their preoperative classification into "causal" (n=95) versus "palliative" (n = 35) operati-

ons. As can be seen fromTable 3, patients in whom the AHE was performed with a "causal" indication (i.e., who had seizure onset within the resected structures) did much better than those in whom the operation was performed with a "palliative" indication.

Table 3: Year-by-Year Seizure Outcome Curative = causal AHEs

	1	2	3	4	5	10 (years)
n	95	80	64	56	44	16
I	79%	73%	70%	75%	75%	81%
II	9%	15%	14%	9%	11%	19%
III	8%	9%	11%	13%	9%	0%
IV	3%	4%	5%	4%	5%	0%

Year-by-Year Seizure Outcome"Palliative" AHEs

	1	2	3	4	5	10 (years)
n	35	33	31	29	27	18
I	11%	6%	13%	17%	19%	17%
II	9%	12%	6%	3%	4%	6%
III	37%	30%	29%	34%	33%	28%
IV	43%	52%	52%	45%	44%	50%

Postoperative antiepileptic drug treatment in the Zürich AHE series

In order to rate the success or failure of the operation it is necessary to consider the changes in antiepileptic drug (AED) treatment. Whereas preoperatively all patients were drug-resistant and were taking, as a rule, high doses of AEDs in various combinations, postoperatively in many patients the AEDs could be withdrawn or dosages reduced.

The AEDs could be withdrawn postoperatively in 28 % of patients. The AEDs could be withdrawn in 42 % of patients with a follow-up 5 years and in 70 % of patients with a follow-up between 9 and 13 years. The mean postoperative period before withdrawal was 20.0 months (range: 1-78).

Neuropsychological data

It is of considerable interest to know whether and to what extent the unilateral, selective AHE influences postoperative neuropsychological performance. Earlier studies comparing the preoperative and postoperative neuropsychological performance showed that the neuropsychological postoperative results were better in AHE patients than in patients who underwent an anterior temporal lobectomy. In AHE patients the performance in postoperative learning and memory performance was the better, the better was the postoperative seizure outcome. Furthermore, it was found that the postoperative improvement was mainly due to the improvement of the nonoperated contralateral hemisphere, whereas the performance of the operated hemisphere remained more or less unchanged compared to the preoperative test performance[81,82,7]. In no case did we observe a severe memory deficit or an amnestic syndrome following AHE. Patients judged to be at risk for a worsening of their memory, however, were routinely submitted to a so-called selective temporal lobe amobarbital test [35,36,83].

Noninvasively, learning and memory where tested with three series of 15 items, each drawn or written in black ink on white cards (size 15x10 cm). The items of the first series were nonsense designs (in the following called "designs"). Drawings of common objects (called "drawings") were used in the second series. The third series consisted of concrete nouns (called "nouns"). The items were presented until the subjects were able to reproduce at least 12 items, but for a maximum of five trials. The reproduction of as many items as possible of each series (designs, drawings, nouns) after a distraction interval of 30 min. made up the memory performance. In order to avoid memory savings from preoperative to postoperative testing, parallel versions (A+B) of these tests were used. Half of the subjects were tested preoperatively with version A and postoperatively with version B, and *vice versa*.

This neuropsychological test[84]was performed in 43 patients (27 right-sided and 16 left-sided AHEs) before and in 67 patients (35 right-sided and 32 left-sided AHEs) after the operation.
The means of the memory performance for the four groups (preoperative and postoperative, right and left) are given in Table 4. These values suggest that the verbal memory improves slightly after a right-sided AHE, whereas it worsens slightly after a left-sided AHE. There is no significant change in the figural memory following a right or left AHE, but the pictoral memory seems slightly improved following a left AHE.

Table 4: AHE Series: Material Specific Preoperative and Postoperative Memory Performance as Measured by the Nadig Test

Time of Testing	Side of Operation	Number of Patients	Memory performance (x±SD) (Scores in Nadig Test Verbal	Figural	Pictorial
Preoperative	Right	27	7.8±2.3	11.0±2.0	8.8±1.9
Postoperative	Right	35	9.3±2.2	11.4±1.9	8.8±2.3
Preoperative	Left	16	7.2±2.0	10.7±2.5	6.9±2.9
Postoperative	Left	32	6.0±3.1	10.0±2.0	7.7±2.3

Psychosocial outcome

Together with Nadia Khan we have examined the psychosocial outcome of our AHE patients[85]. They were assessed for (a) psychosocial variables: emotional adjustment and coping abilities (depression, tension, fear, shame, disgust, guilt), interpersonal adjustment (social comfort, number of contacts and relationships), adjustment to seizures, and behavioral disturbances; (b) vocational and employment career; and (c) "family support".

The following results emerged: Postoperatively, psychosocial functioning improved in 72 % of AHE patients, remained unchanged in 15 %, and deteriorated in 13 %. All patients with a postoperative deterioration had persisting seizures, being classified in outcome categories III and IV. Probably, even more important is the fact that all of them had preoperatively marked personality and behavioral changes in line with the original description of Waxman & Geschwind [1975].[39]

With reference to the vocational and employment career, the preoperative-to-postoperative comparison revealed the following: *preoperatively* 61 % were employed and 39 % unemployed (including in the unemployed group are children, housewives, and students). *Postoperatively,* with a mean follow-up of 3.4 (standard deviation 2.6) years, 59 % were employed. One patient has lost his job because of the reappearance of a paranoid psychosis, and one claimed to have lost his job because of permanent headache associated with insomnia.

The employment status postoperatively was much better in 24 %, better in 45 %, unchanged in 23 %, slightly worse in 5 %, and markedly worse in 3 % of patients, compared to the preoperative state. There is a strong relationship between the scores of the "psychosocial variables", "employment status", "family support", and "seizure outcome". Patients with a good seizure outcome (categories I and II) improved postoperatively in all measured psychosocial variables and had significantly better family support. An improvement in the employment status, however, was observed nearly exclusively in only those patients who were completely seizure-free.

Concluding remarks

The selective AHE is technically difficult but an appealing operation for carefully selected patients suffering from the syndrome of mesial temporal lobe epilepsy.

In the hands of our Zürich neurosurgeons, the complication rate in terms of lasting morbidity of this operation is 0.3 %, that is, in only one patient an intraoperative spasm of the anterior choroidal artery resulted in a permanent slight hemiparesis. No visual field deficit was induced. There was no mortality related to AHE. No unexpected severe memory impairment and, in particular, no postoperative amnesia have been observed in our Zürich AHE series. It should, however, be emphasized that all candidates for AHE undergo exhaustive noninvasive neuropsychological examination and, if the patient is at risk, also invasive amobarbital (Amytal) testing. In order to better assess the possible risks in this regard, we have developed an use so-called selective TL amobarbital tests[35,36,37].
With the help of modern neurophysiology, including radiotelemetric long-term seizure monitoring and modern structural (MRI) and functional (single photon emission computed tomography, positron emission tomography) imaging methods, the majority of candidates for AHE can be assessed non-invasively or semi-invasively, with foramen ovale electrodes.

The operative technique in AHE should be such that it prevents any harm to the normal brain tissue during operation, in particular with respect to its vascular supply. Concerning the question as to the exact borders of the resection of potentially epileptogenic tissue, our results suggest that a certain critical mass of epileptic pacemaker neurons has to be resected in order to achieve good postoperative se-

izure control and that removal of the anterior parts of the parahippocampal gyrus, and particularly its subicular part, improves the results.

If careful presurgical evaluation and case selection are combined with an immaculate operative technique of a neurosurgeon thoroughly familiar with the operative anatomy of this region, the results of this selective TL surgery are very rewarding. Performed with a "causal" indication, complete or almost complete seizure control (outcome categories I and II) can be expected postoperatively in 80-90 % of patients according to our series. Associated with or as a consequence of postoperative seizure control, good to excellent neuropsychological and psychosocial outcome can be expected also. This, in turn, is linked with the early termination of, or at least considerable reduction in, antiepileptic drug treatment and the associated relief of the often severe side effects of high-dose AED treatment influencing neuropsychological and higher intellectual and emotional functions.

Since the syndrome of mesial temporal lobe epilepsy often is resistant to AED treatment but responds well to adequate surgical treatment, an indicated selective AHE should not be unnecessarily delayed. There is now ample evidence that at least this type of epilepsy should be viewed as a potentially ongoing process rather than a stable condition, and that the operative results are better with earlier seizure control.

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