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Acute hippocampal recording and pathology at temporal lobe resection and amygdalo-hippocampectomy for epilepsy

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SUMMARY An electrocorticographic (ECoG) study is reported of patients undergoing surgery for epilepsy of temporal lobe origin. During 22 en bloc resections and six out of a total of 18 amygdalo-hippocampectomies, the activity of the hippocampus was also recorded by a multipolar strip electrode placed along its axis on the ventricular surface.

Patients with mesial temporal pathology, chiefly mesial temporal sclerosis, made up the majority of those selected for amygdalo-hippocampectomy. They showed a characteristic ECoG pattern, with spikes localised to the mid part of the second and third convolutions and inferior aspect of the temporal lobe. Typically, this was associated with hippocampal discharges showing an anterior maximum. Pathology involving lateral temporal neocortex and non-specific findings were associated with more widespread temporal spikes and a maximum discharge amplitude over the mid and posterior parts of the hippocampus. It is suggested that intraoperative recording of the ECoG and hippocampal activity may provide a guide to the choice between en bloc resection and amygdalo-hippocampectomy.

The surgical treatment of temporal lobe epilepsy has always had an empirical basis. The role of neurophysiological studies has waxed and waned, but every programme selecting patients for epilepsy surgery has to include neurophysiological investigation of various degrees of complexity.

One of the most difficult problems has been the relationship between pathology and abnormal neurophysiology, especially in the management of mesial temporal or hippocampal sclerosis, found in up to 50% of temporal lobe operations (the term 'MTS' will be used here to include both pathologies). Even if this lesion can be predicted before operation, it is impossible to estimate its extent. Other lesions such as indolent tumours, arteriovenous malformations, and hamartomata can be demonstrated either by high quality CT scans with appropriate tilting of the gantry, or by MRI scans, in 95% or more of patients.[1,2] However, scarring of the temporal structures is more difficult to demonstrate radiologically. In CT scans it can only be inferred, that is by an enlarged CSF space such as the temporal horn or basal cistern, or atrophy of normal brain tissue, but not by alteration of tissue density. It would be expected that MRI scanning would reveal differences in tissue density but at present this is a controversial topic. Some authors report significant changes before operation in patients subsequently proven to have MTS, whereas others find normal scans.[3,4] The current methods of functional brain imaging such as PET and SPECT do not have sufficient resolution to show fine detail in the temporal lobes.[5] Nevertheless it has been shown by Babb and Jann-Brown[6] that in MTS there is a clear relationship between the site of the seizure activity in the hippocampus, the extent of the cell loss in the specimen and the outcome of the operation.

If brain imaging cannot give an accurate picture of the extent of subtle hippocampal pathology then can that be obtained from neurophysiological studies? Apart from extensive chronic depth recording which is required to determine the site of seizure onset in only a minority of patients,[7] pre-operative neurophysiological techniques do not supply this information.

The investigations we have reported involved recordings using strip electrodes from the ventricular surface of the hippocampus exposed at operation in two groups of patients. In the first group receiving a

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standard *en bloc* temporal lobectomy,[8] the object was to correlate the findings from the hippocampal strip recording with those of conventional, acute corticography from the surface of the temporal lobe and adjacent brain, with the pathology shown in the resected hippocampus and eventually with the surgical results.

The second group were patients submitted to the procedure of selective amygdalo-hippocampectomy as described by Wieser, Yasargil *et al.*[9 10] This operation is applicable to patients with temporal lobe disease who would suffer intellectual impairment as a result of an *en bloc* lobectomy. The operation is very successful in patients with indolent tumours, hamartomata and similar pathology who form the majority of their series.[9] It is less successful in patients with MTS or non-specific findings in the resected specimen, who comprise the majority of those undergoing temporal lobe surgery operation at the Maudsley Hospital. Moreover, 'palliative' amygdalo-hippocampectomy, for seizures not arising in mesial structures, gives results inferior to those of 'causal' operations, directed at mesial temporal foci.[9]

We performed acute corticography in these patients as well as hippocampal strip recording in some. These studies may give some guidance to the surgeon who has to make a choice between the various procedures now available for treating epilepsy of temporal origin, especially in MTS.

Material and methods

Two overlapping sets of patients were investigated: (a) a consecutive series of 28 patients in whom corticography during temporal lobe surgery was supplemented by the insertion of hippocampal strip electrodes; (b) 18 consecutive patients undergoing selective amygdalo-hippocampectomy. Six subjects were common to both groups.

All procedures were performed under general anaesthesia,[11] with intermittent positive pressure ventilation to produce normocapnia or mild hypocapnia (end tidal carbon dioxide concentration around 4%). Muscle relaxation was obtained with atrocurium bolus and infusion, and anaesthesia with nitrous oxide supplemented with a volatile agent (usually isoflurane). Both the preliminary ECoG and the hippocampal strip recording were activated by intravenous thiopentone. .This was given at a rate of 25 mg every 30 seconds up to a total dose of around 3 mg/kg body weight, that is, typically 200 mg in adult patients.

An extensive temporal craniotomy was performed and electrocorticography carried out using an array of 16 independently positioned Montreal type ECoG electrodes.[12] Five monopolar flexible electrodes were inserted around the margins of the craniotomy and included one orbital frontal, three sub-temporal, and one parietal placement. The ECoGs were recorded using a 21-channel Nihon Kohden electroencephalograph at a high frequency setting of 70 Hz (3db point) and typically a time constant of 0·3 seconds. This last was sometimes shortened to reduce slow artefacts, for instance from respiration or pulse. Common reference derivation was employed in all patients, exclusively in the majority. The chosen reference was determined by the ECoG

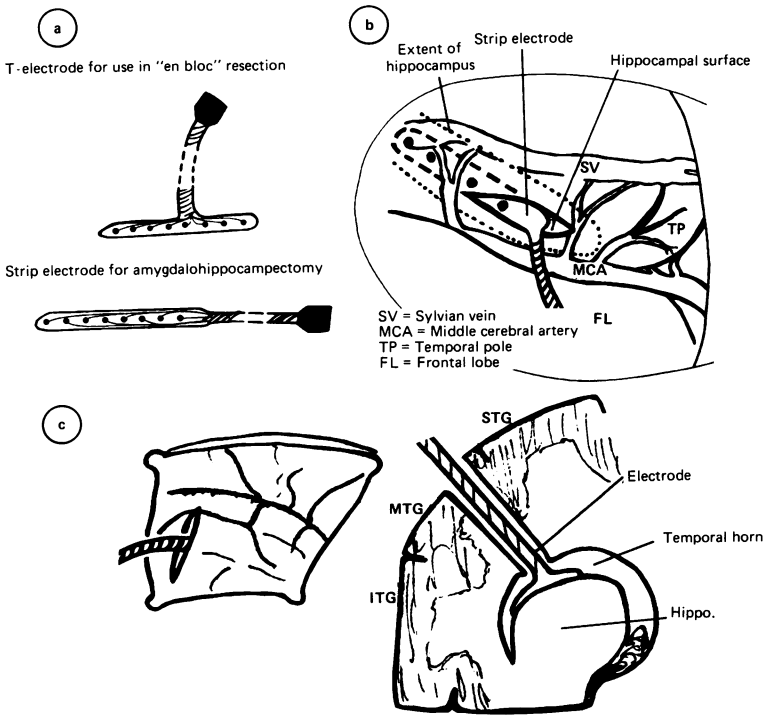


Fig 1 *Hippocampal strip electrodes. (a) Electrodes for use during en bloc resection (above) and amygdalo-hippocampectomy (below). (b) Electrode in place during amygdalo-hippocampectomy. (c) Electrode placement for en bloc resection (Key: STG, MTG, ITG = superior, mid, and inferior temporal gyri).*

findings but was typically a post-central ECoG electrode, but common average reference was also used if there were widespread potential fields extending from the temporal to parietal regions.

Surgical Techniques:
Because all patients undergoing temporal lobe surgery had acute electrocorticography the initial exposure was the same for both *en bloc* lobectomy and selective amygdalo-hippocampectomy. In the case of the latter the head was positioned as described by Yasargil,[10] otherwise access to the Sylvian fissure is impossible. A five or six point osteoplastic bone flap was turned and again when selective amygdalo-hippocampectomy was considered the sphenoid wing was drilled away. The dura was hitched up and opened and then acute corticography undertaken as already described.

Following a preliminary ECoG recording, hippocampal strip electrodes (where used) were inserted as follows. When the operation was to be an *en bloc* temporal lobectomy then a transverse incision was made across the middle temporal gyrus usually between 5·5 cm and 6·5 cm from the pole. The incision was deepened until the temporal horn was entered and extended a little laterally at the level of the roof of the temporal horn to expose the surface of the hippocampus. The T-shaped electrode (figure 1) was then introduced into the temporal horn, the anterior, usually longer limb first, and then the posterior limb. The centre of the T usually was about 2 cm from the tip of the hippocampus. A cottonoid patty was placed in the incision. The corticography apparatus was replaced and the other electrodes positioned and the recording then made. The hippocampal electrode was left in place until the stage in the *en bloc* resection when the temporal horn was exposed from the posterior aspect, so that its position was confirmed visually; it was then removed.

When the operation was a selective amygdalo-hippocampectomy then, under the operating microscope, the Sylvian fissure was opened up and the internal carotid and middle cerebral arteries and their branches displayed. The place for the cortical incision in the anterior temporal region was then identified. The incision was then made and deepened to find the temporal horn. Sometimes this was impossible without risking damage to the mesial temporal structures, in which case the recording was abandoned. If, however, the temporal horn and the ventricular surface of the hippocampus was easily identified we then slid the strip electrode into the incision and into the ventricle so that it lay along the axis of the hippocampus with the cable exit at the cortical incision. This probably provided contact with all of the hippocampus except the anterior extremity. The microscope was removed, the corticography apparatus and other electrodes replaced and the recording made. The strip electrode was then withdrawn and the resection continued.

Activation of the ECoG was carried out both before and after insertion of strip electrodes, using intravenous sodium thiopentone. This drug was given until either considerable activation of ECoG epileptiform phenomena appeared or until early signs of burst suppression were seen. The rate of administration was 50 mg per minute, and the dose typically 150–225 mg. Following the operative procedure a check electrocorticogram was obtained, using in the case of *en bloc* resection a reduced electrode array, but generally including a flexible lead placed over the trigone.

The neuropathological examination included inspection, weighing and macroscopic description of all the specimens, and photographing all the *en bloc* ones after, and some before, coronal slicing. All the material from the amygdalo-hippocampectomies was sectioned, stained with haematoxylin and eosin, Luxol fast blue/Nissl and glial fibrillary acidic protein. From the 22 *en bloc* resections, only selected blocks were examined histologically. The staining techniques were as in the amygdalo-hippocampectomies. In both groups other techniques including electron microscopy were employed as necessary.

Results

ECoG
The ECoG findings fell into four distinct patterns (figure 2) which were to some extent predictive of the presence or absence of hippocampal pathology.

Pattern 1, seen most typically in patients with MTS, comprised sharply localised spikes over the mid-parts of the second and third temporal convolutions often extending onto the adjacent inferior aspect of the temporal lobe. Following barbiturate activation, the discharges often became more widespread but the location of the maximum epileptiform activity remained as before. Patterns 2 and 3 comprised increasingly widespread temporal discharges involving also the anterior temporal area (Pattern 2) and both anterior and posterior temporal regions (Pattern 3). A fourth pattern was seen in only one patient, namely more widespread epileptiform discharge prior to activation involving orbital frontal and pre-central contacts in addition to those over the temporal lobe.

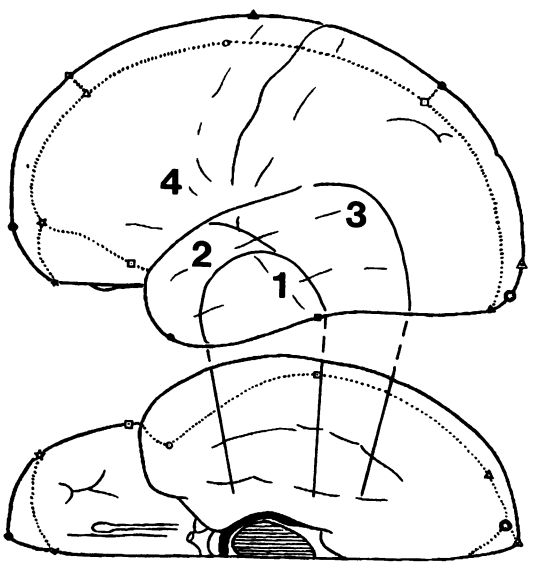


Fig 2 *Topographic patterns of electrocorticographic discharges.*

Table 1 *Distribution of discharges in ECoG and hippocampal strip recordings*

		Patterns in ECoG and strip recordings			
		Hippocampal discharges			
ECoG		*Anterior*	*Mid-post*	*Normal*	*Other*
1	Mid to antero-inferior temporal spikes 21:	10	1	0	1
2	Spikes anterior half temporal lobe 10:	2	5	0	0
3	Widespread temporal spikes 8:	4	3	1	0
4	Fronto-temporal spikes 1:	0	1	0	0
	Totals (Hippocampal recordings only, n = 28)	16	10	1	1

Hippocampal strip recordings

Spikes and/or sharp waves were recorded in all but two patients. Two patterns of distribution predominated. In some subjects the discharges were confined to the anterior 2 or 3 hippocampal contacts, possibly spreading with much reduced amplitude to the 4th and 5th contacts (anterior pattern A in table 1). In other subjects there was a mid or posterior maximum of discharge amplitude, the anterior part of the hippocampus often being little involved (Pattern M). Nine out of 16 patients showing the anterior pattern had discrete hippocampal pathology whereas five out of 10 with the mid to posterior pattern had normal hippocampi (N) (table 2). One showed another pattern (O), not classifiable as above, with diffuse slow activity.

Typically the type 1 electrocorticographic pattern was accompanied by anterior hippocampal discharges (10 out of 12 instances), both being associated with hippocampal pathology. Conversely of the 10 subjects investigated with hippocampal strips who showed ECoG pattern 2, five had mid-hippocampal discharges.

Amygdalo-hippocampectomy

The corticographic findings in the patients selected for amygdalo-hippocampectomy or *en bloc* resections are compared in table 2. The decision to perform amygdalo-hippocampectomy had been based on preoperative findings; notably electrographic evidence of a mesial temporal seizure onset (using depth or foramen ovale electrodes), the absence of radiological demonstrable pathology involving the lateral temporal neocortex, and evidence from the carotid amytal test of significant memory function in the affected temporal lobe. These criteria would of course tend to select for MTS and indeed the patterns of discharge in the ECoG and the hippocampal strips of the patients selected for amygdalo-hippocampectomy were essentially similar to those found in association with MTS. The detailed findings in the patients subjected to amygdalo-hippocampectomy are set out in table 3. It shows that following the procedure ECoG discharges were reduced or abolished in eight subjects; the discharge rate was unchanged in three and increased in the remainder. Only limited follow-up data are available so far but there is no trend to suggest that the presence or absence of ECoG discharge following this procedure is predictive of outcome.

Morphology of hippocampal discharges

Epileptiform discharges recorded from the hippocampal strip were of two types. Some negative spikes occurred, in isolation or bursts (figure 3). However, the most characteristic discharges, found in 26/28 subjects, consisted of a positive-going sharp wave of some 200 mseconds duration preceded by a small negative spike and sometimes followed by a slower negative potential, occasionally with superimposed faster components (figure 3).

Some of these discharges were confined to the hippocampal leads but in many instances they occurred more or less synchronously with surface negative spikes in the ECoG on the under surface of the temporal lobe and/or the lateral convexity. The often sharply localised topography of these neocortical spikes and the morphology which was considerably different from the relatively slow hippocampal sharp waves, suggested a synchronous electro-

Table 2 *Electrophysiological and pathological findings and operative procedure (For key see table 1)*

	Electrophysiological pattern										
	ECoG				*Hippocampal strip*				*Pathology*		
	1	*2*	*3*	*4*	*A*	*M*	*N*	*O*	*MTS*	*Other*	*NS*
Operation											
Amygdalo-hippo-campectomy	13	5	0	0	5	1	0	0	13	2	3
En bloc resection	8	5	8	1	11	9	1	1	9	8	5
Hippocampal histology											
Normal	5	4	7	0	7	5	1	0	0	8	8
Abnormal	16	6	1	1	9	5	0	1	22	2	0

Table 3 *Findings in patients receiving amygdalo-hippocampectomy*

Discharge pattern					
Before procedure		*After procedure*			
ECoG	*Hippocampus*	*Site*	*Change*	*Pathology*	*Outcome*
1	—	1	none	NS	unimproved
1	—	1	decrease	MTS	improved
2	—	1	decrease	MTS	seizure-free*
1	—		absent	MTS	improved
2	—	1	increase	NS	unimproved
1	—	1	increase	Tum	seizure-free*
1	A	3	increase	MTS	improved
1	—		absent	MTS	improved
2	—	3	increase	MTS	seizure-free**
1	—	3	decrease	MTS	unimproved
1	—	3	increase	MTS	improved
1	—		absent	MTS	seizure-free**
1	A	3	decrease	MTS	seizure-free**
1	A		absent	MTS	seizure-free*
1	—	2	increase	MTS	seizure-free**
2	A	1	increase	Tum	seizure-free*
1	A	1	none	MTS	seizure-free*
2	M	1	none	NS	improved

Key: Pathology
MTS = mesial temporal sclerosis or hippocampal sclerosis
NS = non-specific
Tum = tumour, or other mass lesion.
Outcome
improved = more than 75% seizure reduction
unimproved = less than 75% seizure reduction
*follow-up < 6 months
**follow-up > 6 months

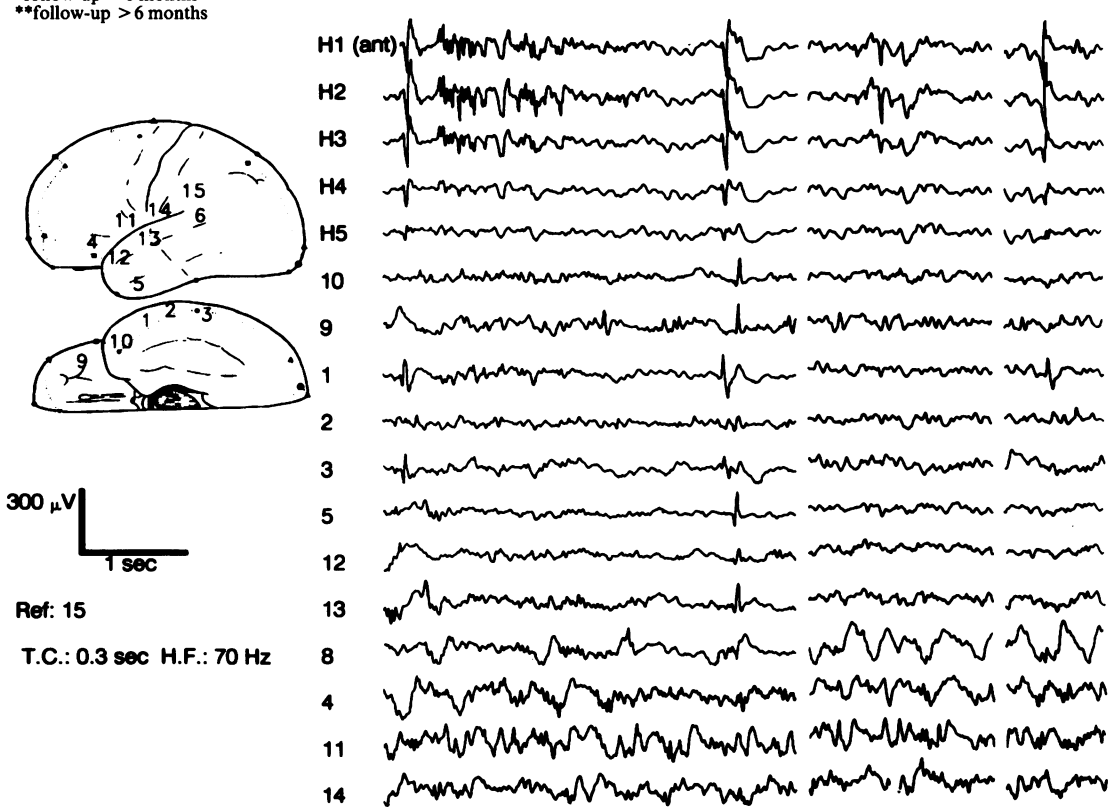


Fig 3 *Sharp waves at hippocampal leads H1–5, anterior pattern in MTS. (Downward deflection indicates positive polarity, with respect to reference electrode.) Also some bursts of negative hippocampal spikes.*

Table 4 *Pathological findings in resected temporal material*

Lesion	*Temporal lobectomy*	*Amygdalo-hippocampectomy*
Mesial temporal sclerosis	9	6
Hippocampal sclerosis	0	7
Hamartoma	1	2***
Cortical dysplasia	2	0
Tumour	1	0
Other	4*	0
Non-specific	5**	3
Total patients	22	18

Multiple Pathologies:
*includes 1 arteriovenous malformation combined with MTS and 1 long-standing scar combined with MTS.
**includes 1 small meningioma, with non-specific changes in temporal lobe and minimal hippocampal sclerosis.
***includes 1 hamartoma combined with hippocampal sclerosis.

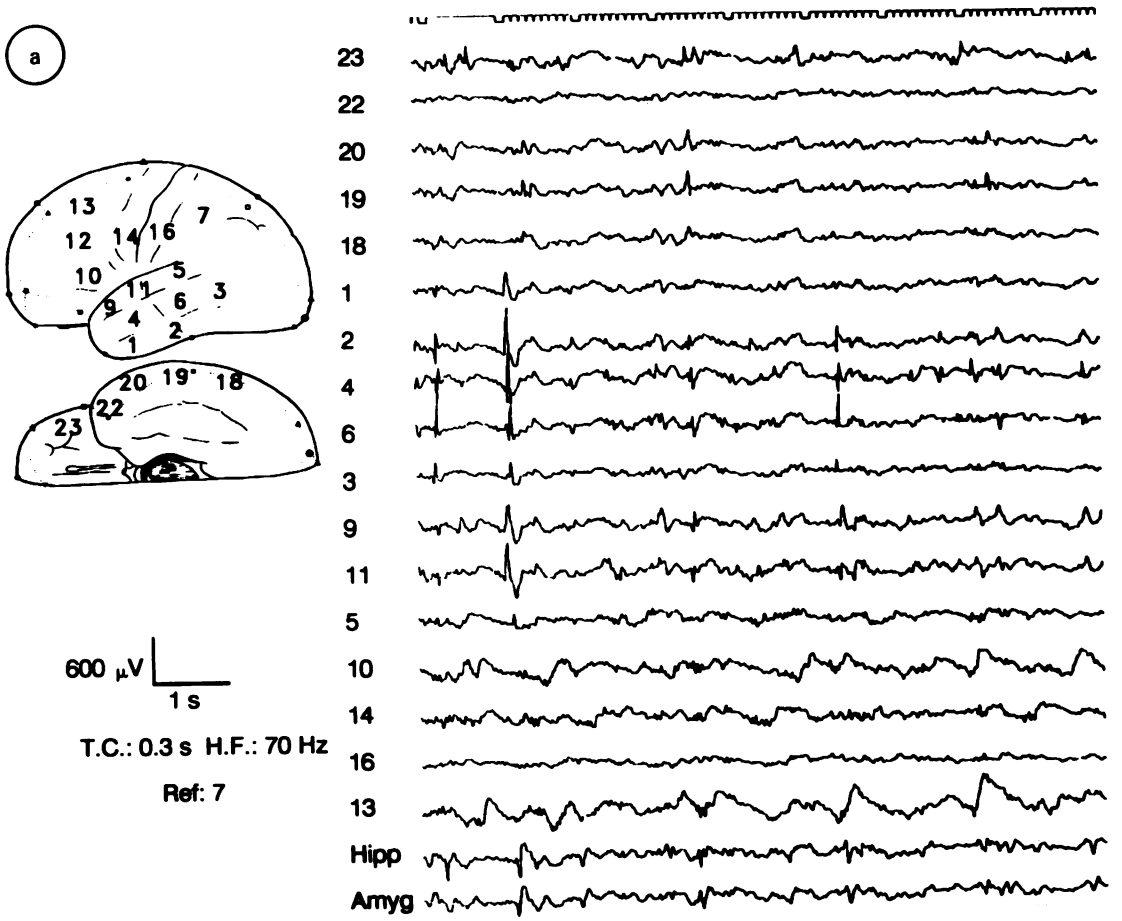
physiological event and not merely the negative end of a dipole generator producing the positive hippocampal sharp waves.

Pathology

The neuropathological findings in both surgical groups are set out in greater detail in table 4. It shows that three patients had a tumour or other lesion in combination with MTS, and for the purposes of the preceding account these have been classified according to the main pathology and not as MTS.

Discussion

The ECoG findings are perhaps predictable. The discrete mesial temporal abnormality might be expected to produce localised discharges, whereas lesions involving the lateral neocortex would be accompanied by more widespread electrophysiological disturbances. That electrographic patterns typical of patients with hippocampal abnormalities (predominantly mesial temporal sclerosis or hippocampal sclerosis in this series) should also be found in the patients selected for amygdalo-hippocampectomy is



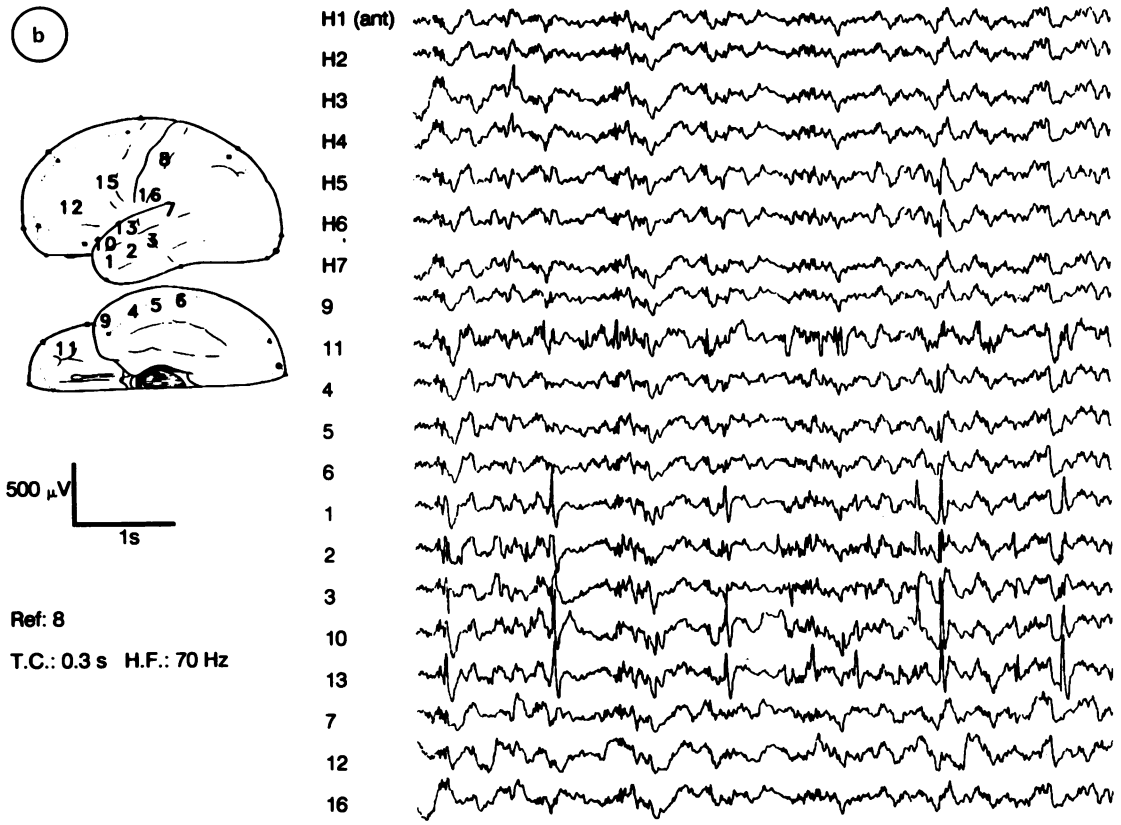


Fig 4 *Hippocampal sharp waves recorded with monopolar depth electrodes (last two channels of fig 4a) and hippocampal strips fig 4b. Posterior distribution of hippocampal discharges (contacts H5 and 6 maximum) and ECoG pattern 2, in patient with lateral neocortical tumour.*

also not unexpected as our criteria of selection for this procedure favour patients with discrete hippocampal or medial temporal pathology.

The results of the hippocampal strip recordings are however somewhat unexpected. Engel *et al*[13] described in two out of 76 patients positive-going hippocampal sharp waves (using monopolar depth electrodes) apparently not unlike the phenomenon described above. However, as their bipolar recordings referred the hippocampal contacts to the under-surface of the temporal lobe, it is not possible to determine whether they were in fact registering electro-positive events in the hippocampus or electro-negative waves on the under-surface of the lobe. In the present material posterior hippocampal sharp waves (whether or not the same as those described by Engel *et al*[13]) were an almost universal finding, as they were absent from only two out of 28 hippocampal recordings. In a few instances we also inserted monopolar depth electrodes, but abandoned this practice as it might have disturbed the subsequent hippocampal strip recordings. However, the morphology of the discharges recorded in this manner was very similar to that found using the strips (figure 4).

Engel *et al*,[13] using free-hand depth placements, were often unable to record any epileptiform activity in patients with MTS and suggested that the sclerotic hippocampus might produce no electrical activity. We anticipated similar findings but this was clearly not the case in the present material: the two hippocampi that failed to produce spikes or sharp waves, were both histologically normal and the lesion was found elsewhere.

Although electrocorticography is routinely performed during temporal lobe surgery for epilepsy we are not aware of any previous reports of the findings before and after amygdalo-hippocampectomy. The originators of this procedure[9 10] do not make use of electrocorticography; indeed as the question of excising an electrically mapped epileptogenic zone does not arise, electrocorticography is arguably unnecessary. However, our findings suggest a relationship between

the pattern of abnormal activity in the ECoG, particularly in the hippocampal strip recordings, and the site and nature of underlying pathology. If these trends are maintained in a more extensive series, using improved electrode technology for the hippocampal recordings, it may be necessary in some patients to base a final decision concerning the choice of operative procedure on the findings at acute electrocorticography.

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