Journal of Neurology, Neurosurgery, and Psychiatry 1987;**50**:167–176

Relationships between neuropathology and cognitive functioning in temporal lobectomy patients

T M McMILLAN, G E POWELL, I JANOTA, C E POLKEY

From the Institute of Psychiatry, London, University of Surrey, Guildford, and the Maudsley Hospital, London, UK

SUMMARY Cognitive functions were examined before operation and 4 weeks after operation with respect to pathology in 40 patients who underwent temporal lobectomy for epilepsy. Hippocampal sclerosis was associated with febrile convulsions, an earlier onset of regular seizures, poorer pre-operative intelligence and with a tendency towards greater cognitive improvement across the operation than found in patients with tumour-like malformations or non-specific pathology. Damage to the amygdala was associated with a poorer outcome for the retention in memory of verbal and non-verbal material. The absence of any specific abnormality in the resected tissue was not associated with a poorer cognitive outcome 4 weeks after the operation.

A previous paper discussed the short-term cognitive outcome of temporal lobectomy for chronic drug-resistant epilepsy, and related these effects to clinical variables.[1] The present study is concerned with relationships between cognitive functioning and evidence for brain damage obtained from investigation of the resected temporal lobes of these temporal lobectomy patients.

Approximately 50% of institutionalised epileptics who die of natural causes disclose a brain lesion at necropsy known as Ammon's Horn Sclerosis.[2 3] This lesion, which was first noted macroscopically in 1825 by Bouchet and Cazauvieillh and was later described by Sommer in 1880, refers to nerve cell loss and gliosis in the hippocampus.[3] Falconer and Taylor[2] however, recommended the term "mesial temporal sclerosis" because the lesion which has been described as "par excellence a lesion of the limbic system,"[3] may involve not only the hippocampus, but also the amygdala, the uncus and even extend further into the parahippocampal and fusiform gyri to affect there the second and third layers of the cerebral cortex.

It has been suggested that mesial temporal sclerosis often results from hypoxia which may be associated with febrile convulsions in infancy.[3 4] This contrasts with the view that mesial temporal sclerosis is secondary to a generalised convulsion rather than its cause.[5] Falconer[3] further argued that if convulsions nurture the extent of mesial temporal sclerosis, then temporal lobectomy in children will prevent more widespread pathology, and this position has gained support.[6 7] The development of the lesion may however involve a more complex mechanism of metabolic imbalance.[8]

Falconer[9] related post-operative seizure frequency to neuropathology in a group of 100 chronic temporal lobe epileptics who were followed up for 1–24 years. Patients with mesial temporal sclerosis were more often fit-free after the operation (51% of cases) when compared with those with other pathology who were combined to form a single group (34% fit-free). Successful outcome overall was defined as having fewer than three fits per year.[10] This was found in 60% of patients who had mesial temporal sclerosis and in 62% of patients with other specific lesions, but in only 32% of cases where specific lesions were not found. Only 4% of cases with mesial temporal sclerosis had seizure frequencies which were greater than 50% of the pre-operative number, whereas 26% of those with other lesions revealed this relatively poor outcome.

These data have recently received general support from a clinicopathological study of 249 temporal lobectomy cases operated on by Murray Falconer, and which represent the original Maudsley Series.[11] Forty-three percent of these patients were found to have Ammon's horn sclerosis and the lesion extended beyond the hippocampus in all of these cases. Febrile convulsions or birth injuries were found in 65% of patients, and 80% of those with mesial temporal

Address for reprint requests: TM McMillan, PhD, Department of Clinical Psychology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK.

Received 24 January 1986 and in revised form 9 May 1986.

Accepted 15 May 1986

sclerosis had "improved" or "greatly improved" seizure frequencies post-operatively. Indefinite pathology (in 10% of cases) or non-specific lesions (16% of cases) were associated with a poorer outcome (only 41% improved).

Considering other criteria for pathology-related outcome, there is little published information. Taylor and Falconer[12] reported a tendency for social and psychiatric status to improve more often if a focal lesion (mesial temporal sclerosis or hamartoma) was found but this was only based on evidence from a semi-structured interview. Bruton[11] also reported social functioning in the 249 Falconer patients. Improvement was found more often in mesial temporal sclerosis cases (60%), than in others with indefinite abnormality (20%), or non-specific pathology (20%) or in seven patients with cortical scars following trauma (none improved).

Evidence concerning cognitive functioning as related to neuropathology in temporal lobectomy patients is extremely sparse. Clinical reports have commented that IQ is slightly lower in mesial temporal sclerosis patients than in those with other pathology,[14] but the opposite has also been stated,[15] and details are not given in either publication. More recently Taylor[13] compared temporal lobectomy patients with mesial temporal sclerosis or "alien tissue" on a pre-operative measure of verbal IQ. In this instance "alien tissue" referred to small cryptic tumours or hamartomas, and the definition of mesial temporal sclerosis was not given. Verbal IQ was lower in sub-groups of left temporal lobectomy patients. These were males with "alien tissue" and females with mesial temporal sclerosis. Pre- and post-operative verbal and performance IQs were presented descriptively, but without the benefit of statistics interpretation of group differences is difficult. Side of lesion, sex and seizure type have otherwise not been found to relate to neuropathology and outcome.[2 12 15]

In summary, few studies have examined neuropathology in relation to outcome of temporal lobectomy. In general, they suggest a better outcome in terms of seizure frequency and social functioning in patients with mesial temporal sclerosis, compared to those with other types of pathology, and more especially a relatively poor outcome has commonly been found in patients who were found to have normal specimens or non-specific lesions. On this basis it was predicted that cognitive outcome would be better post-operatively in patients who have mesial temporal sclerosis in contrast to those who have non-specific lesions or other pathology. In addition it was thought likely that pre-operative cognitive abilities would be poorer in patients with mesial temporal sclerosis, because early onset of epilepsy has been associated with mesial temporal sclerosis[4] and with poorer cognitive functioning in patients with temporal lobe epilepsy[1] or generalised seizures.[16 17]

This paper will examine these hypotheses on the basis of preoperative and 4 week post-operative neuropsychological assessments in temporal lobectomy patients.

Methods

Subjects Neuropathology and neuropsychology reports were available for 40 adult patients from the New Maudsley Series,[1] who were operated upon by one of the authors (CEP). An additional five patients from this Series were excluded because reports were incomplete, as were a further 14 cases who had been operated upon by Mr M Falconer. Only patients who were left hemisphere dominant for language were included in the study.[1] Basic characteristics of the group as a whole are listed in table 2.

Testing procedures All patients were tested by a neuropsychologist pre-operatively and 4 weeks post-operatively. Tests included a short version of the Wechsler Adult Intelligence Scale[18] which comprised vocabulary, comprehension, similarities, block design and object assembly sub-tests. The sum of object assembly and block design minus vocabulary yields in addition a spatial IQ (SIQ) that is independent of verbal IQ (VIQ) as described in the factor analytic study by Maxwell.[19]

The Wechsler Memory Scale logical memory sub-test and the Rey-Osterrieth Picture Test were given to estimate verbal and non-verbal memory. Further details of testing procedure are given in Powell *et al.*[1]

Operative procedures The operation itself was based on the en bloc technique pioneered by Mr M Falconer[9] and was detailed in the previous paper in this series.[1]

Neuropathological investigation Macroscopic details of the resected temporal lobe specimens were obtained from formal neuropathology reports. Information included details of external examination, weight of specimen and photographs of coronal slices. Slices were selected for embedding in paraffin wax and microscopy. All of this evidence was reviewed in the preparation of the present report.

Mesial temporal sclerosis was defined here by evidence for lesions in both the hippocampus and amygdala (loss of nerve cells and astrocytosis).

Results

Distribution of pathology variables (see table 1) The frequency of occurrence of mesial temporal sclerosis (20% of cases) was lower than that reported in previous studies,[3 11] but the incidence of hippocampal sclerosis was more similar (60%) to that reported for mesial temporal sclerosis in other studies. Frequencies of cysts and tumours were lower than those found by Falconer. A smaller proportion of patients with non-specific abnormalities or with apparently normal specimens may well reflect differences in selection of patients for the operation in the current series.

Table 1 *Neuropathology in 40 temporal lobe epileptics selected for lobectomy*

Neuropathology		*Left lobectomy*	*Right lobectomy*	*% Total*
Hippocampus	No pathology	5	8	32·5
	Sclerosis only*	13	11	60·0
	Sclerosis and/or other pathology	0	2	5·0
	Unknown	1	0	2·5
Amygdala	No pathology	13	9	55·0
	Sclerosis only*	3	4	17·5
	Sclerosis and/or other pathology	1	5	15·0
	Unknown	2	3	12·5
Mesial temporal sclerosis* (that is, sclerosis in hippocampus and amygdala)		3	5	20·0
Normal specimen or non-specific lesions		2	4	15·0
Space occupying malformation		4	4	20·0
Tumour		0	3	7·5
Cyst		1	0	2·5
Scarring		1	2	7·5

(*Loss of nerve cells and astrocytosis).

Distribution of clinical variables (see table 2) An early onset of regular seizures (that is, before 11 years of age, see Powell *et al*[1]) was found in 18/24 (75%) of patients who had hippocampal sclerosis or mesial temporal sclerosis, whereas only two of the remaining 16 patients (13%) with other specific pathology or non-specific abnormality/normal specimens had an early onset of regular seizures, and one of these cases had hippocampal sclerosis with additional malformation (chi squared = 12·6, $p < 0·001$). The difference between age at operation and age of onset of regular seizures represents the duration of epilepsy; however, differences between hippocampal sclerosis, other specific pathology and non-specific normal specimen groups were non-significant for this measure ($F\ 2, 35 = 1·83$).

Febrile convulsions were found together with hippocampal sclerosis and with an early onset of regular seizures in 10/11 patients (91%). Seven remaining cases who had hippocampal sclerosis or mesial temporal sclerosis and an early onset of regular seizures had anoxia or suspected head injury before 4 years of age. However, suspicion of early brain damage was found in only 1/6 (17%) patients with hippocampal sclerosis and a later onset of regular seizures (chi squared = 9·57, $p < 0·01$). Hence there was a close association between hippocampal lesions, early onset of regular seizures and suspected brain damage in infancy.

All patients with mesial temporal sclerosis or non-specific abnormality/normal specimens had low frequencies of generalised seizures (less than 1 per year), whereas patients with other specific pathology had relatively high numbers of generalised seizures. Differences in the frequencies of generalised seizures between hippocampal sclerosis, other specific pathology and non-specific abnormality/normal specimens groups were however non-significant ($F\ 2,35 = 1·61$). Frequencies of partial seizures were more similar between groups. Once more patients with non-specific abnormality/normal specimens tended to have fewer seizures, and again variance in hippocampal sclerosis and other specific pathology groups were large ($F\ 2,35 = 0·84$).

Weights of resected specimens differed significantly between groups ($F\ 2,33 = 4·7$, $p < 0·02$), being heaviest in patients without specific abnormality, and lightest in cases where hippocampal sclerosis was found (see table 2). More generally, there was a tendency for more tissue to be removed during right temporal lobectomy (42·9 ± 13·5 g) than in left temporal lobectomy (36·2 ± 6·2 g) cases ($t\ 1,28 = -1·98$,

Table 2 *Distribution of patient and clinical variables in neuropathology groups*

	Hippocampal sclerosis	*Other specific pathology*	*Non-specific lesions*
Number of cases (female)	24 (11)	10 (6)	6 (3)
Left Lobectomy	13	6	2
Febrile seizures/infantile brain damage	18	1	1
Age at operation (yrs)	23·8 ± 7·8	24·5 ± 8·6	29·0 ± 14·8
Age at onset of regular seizures	14·2 ± 18·9	15·6 ± 7·1	22·2 ± 13·8
Partial seizures per month	26·1 ± 29·8	35·8 ± 35·7	15·7 ± 15·4
Generalised seizures per year	8·0 ± 26·1	24·1 ± 39·9	0
Weight of resected specimen (g)	35·1 ± 6·2	41·8 ± 7·5	46·0 ± 15·1

$p < 0.06$). This may reflect that atrophy is more commonly found in the left temporal cases to some extent.The interaction between side of lobectomy and pathology with respect to weight was not significant; ($F\ 2, 29 = 0.47$).

Frequencies of generalised and partial seizures, age at operation, duration of epilepsy and weight of resected specimens were also examined by pathology *and* side of operation. Interactions between side and pathology were significant only for age at operation ($F\ 2,29 = 4.94$, $p < 0.02$). Patients with right temporal lobectomy tended to be older at operation in those with other specific pathology (25·7 years) or non-specific abnormality/normal specimens (35·5 years) rather than hippocampal sclerosis (19·8) whereas left temporal lobectomy patients were older in those with other specific pathology (22·8 years) or hippocampal sclerosis (24·5) and youngest in those with non-specific abnormality/normal specimens (16 years). This interaction was also significant when only hippocampal sclerosis and other pathology groups were considered ($F\ 1,35 = 6.18$, $p < 0.02$); paired comparisons revealed significant differences between right temporal cases with hippocampal sclerosis or other pathology ($t\ 1,19 = 2.34$, $p < 0.04$) but not between left temporal cases with hippocampal sclerosis or other pathology ($t\ 1,16 = 1.34$).

The presence or absence of lesions in the amygdala (where known) or the length of resected hippocampus, was not associated with significant differences in clinical variables. One exception was a higher frequency of partial seizures in patients with lesions in the amygdala (49.2 ± 36.0), in contrast to those where no evidence of amygdaloid damage was found (14.0 ± 15.2), ($t\ 1,16 = 3.46$, $p < 0.003$).

Cognitive Variables and Pathology

Differences in cognitive variables between pathology groups and side of lesion were investigated pre-operatively, 4 weeks postoperatively and as change scores across the operation using analysis of variance.

Predictions were made regarding patients with mesial temporal sclerosis; however, few cases in the sample fulfilled the criteria for such a classification, and analysis concentrated on differences between the larger hippocampal sclerosis group (which includes mesial temporal sclerosis cases) and patients who had other pathology.

1. *Hippocampal sclerosis versus other pathology*

The hippocampal sclerosis group (n = 24) consisted of 16 patients with astrocytosis or nerve cell loss in the hippocampus alone, together with a further seven cases where such damage extended to the amygdala. One other case was included where astrocytosis clearly extended beyond the hippocampus, but where the condition of the amygdala was not known. If, in addition to these lesions in the hippocampus, other pathology, such as arteriovenous malformation was found, such patients were *excluded* from this group, (see table 1). The remaining 16 patients formed a heterogenous "other pathology" group which included cases with tumour-like malformations and a normal (n = 8) or abnormal (n = 2) hippocampus and others with non-specific lesions or normal specimens (n = 6).

(a) *Intelligence* (see table 3 and fig 1) Analysis of variance between hippocampal sclerosis and other specific pathology groups by side of lobectomy did not reveal significant interactions for VIQ, PIQ, SIQ or VIQ-PIQ differences pre- or post-operatively or for change scores across the operation. Hence differences beween pathology groups were not found with respect to side of operation.

Differences between pathology groups were however found independently of the side of operation. Verbal IQ was higher in other pathology cases than in hippocampal sclerosis cases pre-operatively ($F\ 1,29 = 7.56$, $p < 0.01$). Significant changes in VIQ were not found across the operation ($F\ 1,26 = 0.48$, $p > 0.05$), although a tendency for VIQ to fall in other pathology cases led to postoperative differences which only approached significance ($F\ 1,32 = 3.38$, $p < 0.08$).

Performance IQ was also found to be higher in other pathology cases preoperatively ($F\ 1,24 = 4.35$, $p < 0.05$). A non-significant tendency ($F\ 1,26 = 1.84$) for PIQ to increase across the operation in hippocampal sclerosis patients (+3 IQ points) and to decrease in other pathology cases (−5 IQ points) led to non-significant post-operative effects ($F\ 1,31 = 0.81$). Differences between verbal and performance IQ were non-significant pre- ($F\ 1,26 = 0.78$) and post-operatively ($F\ 1,26 = 2.08$).

Spatial IQ did not differ significantly between groups pre- ($F\ 1,29 = 0.73$) or post-operatively ($F\ 1,32 = 1.95$) or as change scores across the operation ($F\ 1,26 = 3.19$).

(b) *Memory* (see table 4 and fig 2) The expected total score in a group of normal subjects would be approximately 18·5 for total immediate verbal recall[20] and a few points before this score for delayed recall.[21] Considering pre-operative immediate verbal recall, an interaction between pathology and side of lobectomy was found ($F\ 1,3 = 10.3$, $p < 0.004$). Both left and right temporal cases with hippocampal sclerosis scored 16·9; however left temporal lobectomy patients with other pathology had a poor recall (mean total score = 9·0) whereas right lobectomy cases with other pathology had an above average recall (mean total score = 22·4). A similar interaction was found post-operatively ($F\ 1,3 = 6.40$, $p < 0.02$);

Table 3 *Intelligence and pathology*

Intelligence variables	*Group*	*Pre-operative testing*			*Post-operative testing*		
		n	*Mean*	*SD*	*n*	*Mean*	*SD*
VIQ	HS	18	98·3	17·5	20	98·2	14·0
	OP	15	114·7	15·6	16	109·6	18·5
	OSP	8	117·5	14·8	10	108·8	19·9
	NS	6	112·8	18·4	5	110·2	19·6
PIQ	HS	18	95·8	16·8	19	99·6	19·6
	OP	15	106·9	17·2	16	100·5	16·6
	OSP	8	111·9	16·2	10	103·1	18·5
	NS	6	103·0	18·9	5	97·4	14·1
SIQ	HS	18	97·4	19·2	20	102·3	18·1
	OP	15	97·8	12·8	16	92·4	17·0
	OSP	8	101·9	13·5	10	94·1	17·6
	NS	6	94·2	11·8	5	90·8	18·9

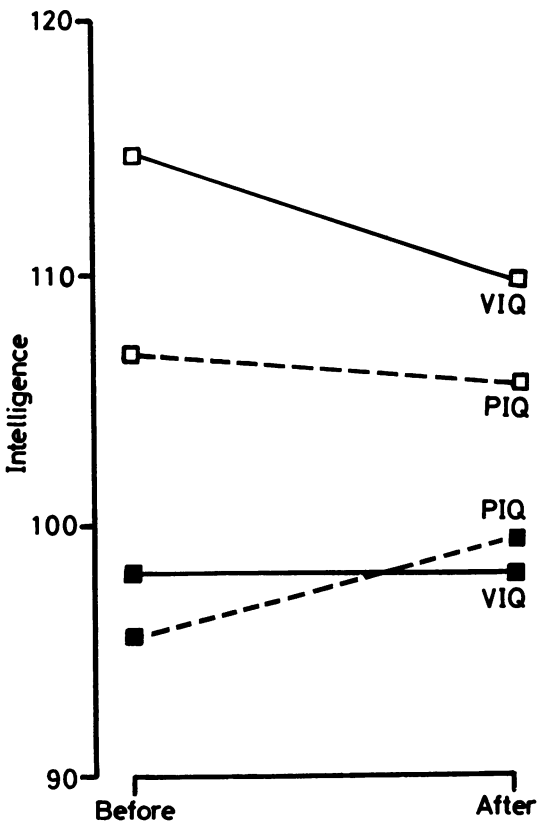

Fig 1 *Verbal and performance IQ before and after temporal lobectomy for epilepsy in patients found to have hippocampal sclerosis ■, or other pathology □, from resected tissue. Both measures of intelligence were lower in HS cases but only pre-operatively ($p < 0·05$).*

again differences were not apparent between left (mean = 15·0) and right temporal (mean = 15·4) cases with hippocampal sclerosis, whereas scores for left temporal cases with specific pathology indicated some impairment (mean = 12·2), and right temporal cases with other specific pathology once more had good immediate recall (mean = 27·6). Changes across the operation were significant between pathology groups ($F\ 1,22 = 6·24$, $p < 0·02$), revealing improvement in other pathology cases (+5 points) and a slight worsening on average in hippocampal sclerosis cases (−2 points).

A significant pre-operative interaction was also found for delayed verbal recall ($F\ 1,3 = 7·30$, $p < 0·01$). Once more little difference was found between left (mean = 10·0) and right temporal (mean = 11·9) cases with hippocampal sclerosis preoperatively, the differences lying largely within the other pathology group, where left temporal cases again revealed poor memory (mean = 5·0) and right temporal cases showed good delayed recall (mean = 20·4). Changes in delayed recall across the operation approached significance between pathology groups ($F\ 1,22 = 3·44$, $p < 0·08$), where hippocampal sclerosis cases showed little change (mean = +1·0) and other specific pathology 3·44, $p < 0·08$), where hippocampal sclerosis cases showed little change (mean = +0·1) and other specific pathology cases improved somewhat (mean = +3·7). Post-operatively the interaction between pathology and side of lobectomy remained significant ($F\ 1,3 = 12·45$, $p < 0·002$). In the hippocampal sclerosis group a tendency for delayed recall to be impaired was found in left temporal patients (mean = 13·3) and this was accentuated in right temporal cases (mean = 10·3). However, clearer differences were again found in the other specific pathology group where impairment was found once more in left temporal cases (mean = 7·0) and the score for right temporal cases was above average (mean = 25·3).

Table 4 *Memory and pathology*

Memory variables	Group	Pre-operative testing			Post-operative testing		
		n	*Mean*	*SD*	*n*	*Mean*	*SD*
Immediate verbal recall	HS	18	17·1	4·8	20	15·1	5·7
	OP	15	16·9	8·4	16	21·0	11·1
	OSP	10	18·9	9·4	10	21·8	12·4
	NS	5	13·0	4·7	5	20·0	10·5
	AD	13	19·9	6·4	12	21·3	10·6
	AN	16	15·3	6·3	18	15·7	8·1
Delayed verbal recall	HS	18	11·2	6·2	19	11·4	6·7
	OP	15	13·7	9·7	15	17·7	11·9
	OSP	10	16·1	10·6	9	19·9	12·9
	NS	5	9·0	6·0	5	13·4	11·4
	AD	13	15·7	8·8	10	17·8	13·4
	AN	16	9·9	7·5	18	12·8	8·4
Percent verbal recall	HS	19	66·0	26·3	20	73·1	27·1
	OP	16	66·1	34·2	15	78·9	27·4
	OSP	10	73·4	32·6	9	87·1	17·8
	NS	6	54·0	36·4	5	57·8	31·9
	AD	13	74·2	23·0	11	72·9	29·3
	AN	18	57·0	34·7	19	77·2	25·4
Delayed non-verbal recall	HS	19	24·2	6·8	20	25·9	8·3
	OP	14	29·0	6·9	16	27·0	10·9
	OSP	8	32·1	5·5	10	27·9	9·3
	NS	5	23·6	6·7	5	22·2	12·8
	AD	12	29·0	6·5	12	24·4	11·3
	AN	15	25·4	7·8	18	27·9	7·9
Percent non-verbal recall	HS	19	53·8	14·2	20	56·3	16·9
	OP	14	63·1	15·3	16	58·3	22·9
	OSP	8	68·6	12·5	10	60·2	19·5
	NS	5	53·0	13·5	5	48·4	27·3
	AD	12	64·1	13·4	12	52·8	23·5
	AN	15	55·5	17·1	18	60·7	16·2

Percent recall (delayed/immediate recall × 100) did not differ between pathology groups pre-operatively (F 1,27 = 0·03) or as an interaction with side of lobectomy (F 1,3 = 2·47). An interaction was found post-operatively (F 1,3 = 8·65, p < 0·007) such that percent recall was slightly above average in left temporal cases with hippocampal sclerosis (83·1% recall) and right temporal cases with other pathology (86·8%), whereas recall in left temporal cases with other pathology (58·4%) and right temporal cases with hippocampal sclerosis (59·0%) was below the average expected for a normal population (i.e. 80%).[22] Changes in percent recall across the operation did not differ between pathology groups (F 1,22 = 0·23) or as an interaction with side of lobectomy (F 1,3 = 0·65).

Differences between groups for non-verbal memory were all non-significant.

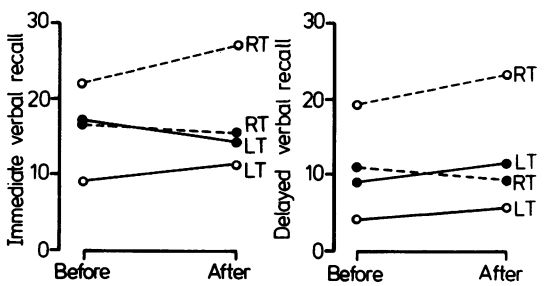

Fig 2 *Immediate and delayed recall of short prose passages in patients who had left (LT) or right (RT) temporal lobectomies, and who were found to have hippocampal sclerosis ●, or other pathology ○.*

Non-specific pathology

Outcome of temporal lobectomy in terms of seizure frequency has been reported to be poorer in patients with normal specimens or non-specific lesions.[9 11] For this reason differences in cognitive functioning were examined in patients with non-specific abnormality/normal specimens (NS) despite the small numbers (n = 6).

Differences of intelligence variables between hippocampal sclerosis, other specific pathology (OSP) and non-specific abnormality/normal specimens groups were found to be non-significant by analysis of variance (p > 0·05), with the exception of pre-operative VIQ (F 2,29 = 4·2, p < 0·03). However, VIQ in the non-specific abnormality/normal specimens group was not below the average for a normal population and was midway between the other two groups (see table 3).

With regard to memory, differences were found

between groups pre-operatively for both delayed ($F\ 2,29 = 4{\cdot}5$, $p < 0{\cdot}02$) and percent ($F\ 2{\cdot}29 = 3{\cdot}2$, $p < 0{\cdot}05$) recall of the Rey figure. In both cases scoring by the non-specific abnormality/normal specimens group approximated to that of the hippocampal sclerosis group and was lower than that found in the other pathology group (see table 4). Across the operation immediate verbal recall worsened slightly in the hippocampal sclerosis group ($-1{\cdot}5$ points), and improved somewhat in other specific pathology cases ($+2{\cdot}9$ points) 4·5 and markedly in non-specific abnormality/normal specimen cases ($+9{\cdot}0$ points), these differences being significant overall ($F\ 2,28 = 6{\cdot}9$, $p < 0{\cdot}005$).

These results do not support the view that non-specific abnormality/normal specimens cases have a relatively poor outcome, at least shortly after operation.

Memory and amygdaloid lesions (see table 4) Thirteen patients were found to have lesions in the amygdala. Of these, seven had sclerosis which extended to the hippocampus. The remaining six revealed tumour-like lesions, and one of these also had an abnormal hippocampus. Patients in this group were compared with others where no evidence for amygdaloid damage was found ($n = 22$). Five additional patients were excluded because it was not known whether or not amygdaloid lesions had occurred.

Differences were not found for any verbal or non-verbal test pre- or post-operatively using *t* tests. However, changes across the operation varied between groups. Percent recall of short prose passages improved in patients with a normal amygdala (AN), increasing by $+19{\cdot}6 \pm 28{\cdot}7\%$, whereas a decrease of $-0{\cdot}5 \pm 17{\cdot}6\%$ was found in cases where damage to the amygdala (AD) was evident ($t\ 1,25 = 2{\cdot}07$, $p < 0{\cdot}05$). If no damage to the amygdala was found delayed recall of the Rey figure improved across the operation by $+2{\cdot}3 \pm 5{\cdot}0$ points, but worsened in cases with amygdaloid lesions by $-4{\cdot}2 \pm 8{\cdot}4$ points ($t\ 1,23 = 2{\cdot}60$, $p < 0{\cdot}03$). Percent recall of the Rey figure also improved across the operation in cases with a normal amygdyla by $4{\cdot}5 \pm 9{\cdot}7$ points and worsened by $-10{\cdot}7 \pm 18{\cdot}5$ points in cases with a normal amygdyla ($t\ 1,14 = 2{\cdot}5$, $p < 0{\cdot}03$).

In summary these results indicate changes across the operation which result in improved verbal and non-verbal retention in patients where no evidence for damage to the amygdala was found but poorer retention in cases with amygdaloid lesions. When groups were further subdivided into patients with hippocampal sclerosis only, amygdaloid lesions only, pathology in both of these structures or in neither, differences in memory tasks did not form any clear pattern.

Memory and the length of resected hippocampus
In 10 patients only the pes or anterior part of the hippocampus was present in the resected specimen. These were compared with seven patients in which the body of the hippocampus was also included. Differences between groups were not found by *t* test for any memory tests whether pre- or post-operative, verbal or non-verbal.

Weight of resected tissue and cognitive functioning
Correlations between intelligence variables and the weight of resected tissue did not approach significance ($p > 0{\cdot}05$). However association between resected weight and immediate verbal recall approached significance pre-operatively ($r\ (32) = 0{\cdot}28$, $p < 0{\cdot}06$) and became significant post-operatively ($r\ (35) = 0{\cdot}45$, $p < 0{\cdot}003$). Delayed verbal memory correlated with weight resected both before ($r\ (32) = 0{\cdot}32$, $p < 0{\cdot}04$) and after operation ($r\ (33) = 0{\cdot}30$, $p < 0{\cdot}05$). Correlations between non-verbal memory and weight were non-significant. These results imply better memory with increased weight of resected tissue. However, this does *not* imply that outcome for memory is dependent on the weight of resected tissue because change scores across the operation were non-significant. This finding could be more easily explained by differences in weight between pathology groups as the latter revealed memory differences also.

Discussion

The clear association between the presence of hippocampal sclerosis or mesial temporal sclerosis, early onset of regular seizures and suspicion of brain damage from febrile convulsions or trauma in infancy lends support to the findings of Falconer.[3] Taken together with a low incidence of generalised seizures in patients in the hippocampal sclerosis group, these results are consistent with the view that hippocampal sclerosis or mesial temporal sclerosis is related to early anoxia[3] or metabolic imbalance[8] rather than being the result of generalised seizures. The virtual absence of febrile convulsions and the presence of *relatively* high frequencies of generalised seizures in patients with other specific pathology also supports this position. Where non-specific lesions or a normal resected specimen was found, no generalised seizures were reported and the aetiology of epilepsy in this group is less easily postulated. Longer term outcome of seizure frequency has previously been found to be poorest in patients with non-specific abnormality/normal specimens.[9] It is therefore encouraging that the proportion of cases belonging in this category has fallen from 26% in the Falconer series[11] to 15% in patients reported here, suggesting

improvement in selection of candidates for lobectomy in this respect.

Reports from large scale studies have failed to find IQ deficits in *children* who had febrile convulsions, except for cases known previously to have neurological abnormalities.[23 24] However, present findings indicate that IQ may be lower in an additional sub-section of patients who had febrile convulsions and later developed temporal lobe epilepsy. As these cases were *adult* when tested, the longer term effects of seizures and presence of hippocampal sclerosis cannot however be dissociated from febrile convulsions as being contributory to lower pre-operative IQ. Increased severity of brain damage, a greater possibility of bilateral impairment and reduced brain plasticity might occur in patients with a longer duration of intractable epilepsy, and early operations have been recommended in order to prevent more widespread development of mesial temporal sclerosis.[3 6] Different durations of epilepsy between groups could have potentially confounding effects on analyses of cognitive functioning with respect to pathology because greater impairment could be associated with a longer history of regular seizures rather than pathology. However, this was not found to be the case in the current series where the time between age at onset of regular seizures and age at operation did not vary significantly between groups.

Pre-operative intellectual functioning was in general mildly below average in the hippocampal sclerosis group and somewhat above average in the other pathology group. The mean discrepancy of 16·5 IQ points for VIQ and 11·1 IQ points for PIQ between these two groups indicates poorer pre-operative intellectual ability in hippocampal sclerosis patients (see table 3). Bearing in mind the poorer intellectual functioning reported in patients who have an earlier onset of epilepsy[16 17] and the strong association between hippocampal sclerosis and early onset of regular seizures, this finding is consistent with the prediction that cognitive functioning would be worse in patients who have hippocampal sclerosis and an early onset of regular seizures. However, it was also postulated that hippocampal sclerosis cases would improve more across the operation, and although changes were in the expected direction, the evidence here is less clear. A more crucial test of this hypothesis requires a longer term follow-up especially as post-operative improvements in IQ have been reported to continue for some years after temporal lobectomy.[25]

With regard to memory, no overall differences were found between pathology groups, and scores approximated to those expected in the normal population. However, when account was taken of the side of lobectomy a complex picture emerged. It became apparent that the presence of other pathology in the left temporal lobe was associated with an especially poor verbal memory. This is in direct contrast to the above average verbal memory found when other pathology occurred in the right temporal lobe. These findings could suggest that whereas the verbal memory abilities of an undamaged left temporal lobe are relatively unaffected by contralateral temporal lobe impairment, an undamaged right temporal lobe is unable to subserve verbal memory functions adequately when functions of the left lobe are impaired. Pre-operative differences in verbal memory were unremarkable between left and right cases with hippocampal sclerosis, and overall mild impairment placed these groups intermediately between left and right temporal cases with other pathology (see fig 2).

A possible explanation of these findings would be that the mature brain is less able to compensate for brain damage and also that hippocampal sclerosis has more deleterious consequences for verbal memory. This could account for the poor verbal memory in left temporal cases with other pathology because the mature brain was less able to compensate pre- or post-operatively. Right temporal patients with other pathology were relatively unaffected despite a later onset of seizures because the left temporal lobe normally subserves verbal memory. Concerning hippocampal sclerosis, such cases may have been more able to adapt pre-operatively because of the earlier onset of brain injury. Here, left temporal lobectomy is more likely to have resulted in the removal of tissue which may never have subserved memory function because of the early onset of the lesion. Hence interference by the epileptic focus with other brain areas which may have substituted for the damaged left temporal region and become involved with verbal memory, was removed by the operation allowing verbal retention to improve. In right temporal cases with hippocampal sclerosis, the decrease in verbal retention across the operation was therefore unexpected, and recovery to result in little overall change or improvement might be predicted at longer term follow-up.

Significant effects were not found for non-verbal memory. This may indicate that whereas verbal memory is more sensitive to dysfunction and may be subserved by other brain areas with more difficulty, non-verbal memory develops in a relatively robust fashion, and may readily map more easily on to a greater variety of brain areas.

The absence of specific lesions did not reflect clear abnormality or poorer cognitive functioning despite the greater weight of resected tissue in these cases. It has been reported that outcome in terms of seizure frequency is poorer in this group.[9 11] The present findings are not necessarily inconsistent with those for seizure outcome, because the latter is reported at long

term follow-up. The continuation of seizures in temporal lobectomy patients with non-specific abnormality/normal specimens might therefore be expected to produce further brain damage and greater impairment in cognitive functioning also at long term follow-up.

Damage to the amygdala has been associated with deficits in learning and memory in animals and man, particularly when lesions are bilateral.[26 27] Impairment of memory was not found pre-operatively in patients who were later found to have a damaged amygdala in the present study. However, a dramatic improvement in the retention of verbal information occurred across the operation in patients where evidence for amygdaloid damage was not found. In contrast, the retention of non-verbal material actually became worse across the operation in patients where damage to the amygdala was found. These findings might be explained by postulating a tendency for damage to the amygdala to occur in association with contralateral mesial temporal dysfunction. A view of bilateral damage in patients with amygdaloid lesions may gain further support from the high frequency of partial seizures found in this group (49·1 $\pm$ 36·0) compared with those without amydgaloid damage (14·0 $\pm$ 15·2). An alternative hypothesis would be that damage to the amygdala is associated with more widespread unilateral damage. This is less attractive because of the failure to find any clear relationships between cognitive impairment and groups with lesions in *both* the hippocampus and amydgala, in either, or in neither structure.

Neither the length of resected hippocampus nor the total weight of resected tissue were found to have important implications for cognitive functioning, and this may in part reflect the uniformity with which the operation is carried out.

The patients comprising this study were highly selected for the operation and hence the generality of findings to the total population of temporal lobe epileptics may be limited. The relative influences of onset, and pathology or of a combination of these variables is difficult to ascertain because of the rarity of patients with hippocampal sclerosis and later onset of seizures (n = 6) and more especially of patients with other pathology and an early onset (n = 3). Low frequencies of patients in these groups may be related to aetiology or result from rejection for the operation because of poor cognitive functioning or bilateral dysfunction. However, the latter interpretation may be questioned because no gross pre-operative impairments in memory or intellectual ability were noted here in either of these sub-groups.

Despite these reservations a pattern of cognitive functioning did seem to emerge in the largely early onset hippocampal sclerosis cases which was distinct from later onset other pathology patients, and which remains to be confirmed at longer term follow-up.

References

1 Powell GE, Polkey CE, McMillan TM. The New Maudsley Series of temporal lobectomy. I: Short-term cognitive effects. *Br J Clin Psychol* 1985;**24**:109–24.

2 Falconer MA, Taylor DC. Surgical treatment of drug-resistant epilepsy due to mesial temporal sclerosis. *Arch Neurol* 1968;**19**:353–61.

3 Falconer MA. Mesial temporal (Ammon's Horn) sclerosis as a common cause of epilepsy. *Lancet* 1974;**2**:767–70.

4 Davidson S, Falconer MA. Outcome of surgery in 40 children with temporal lobe epilepsy. *Lancet* 1975;**1**:1260–1.

5 Scholz W. Cerebral lesions found in epileptics: details about sclerosis of Ammon's Horn. *Acta Neurol Belg* 1956;**56**:43–60.

6 Rasmussen T. Cortical resection in children with focal epilepsy. In: M Parsonage *et al.* (eds) *Advances in Epileptology:* 14th International Epilepsy Symposium, New York: Raven Press, 1983:249–61.

7 Vaernet K. Temporal lobectomy in children and young adults. In H Parsonage *et al.* (eds) *Advances in Epileptology:* XIVth Epilepsy International Symposium, New York: Raven Press, 1983.

8 Meldrum BS, Corsellis JAN. Epilepsy. In: J Hume *et al* (eds) *Greenfield's Neuropathology,* London: Edward Arnold, 1984.

9 Falconer MA. Surgical treatment of temporal lobe epilepsy. In RN Hetherington (ed) *Current Problems in Neuropsychiatry.* Ashford: Headley Brothers, 1969:95–100.

10 Penfield W, Paine K. Results of surgical therapy for focal epileptic seizures. *Can Med Assoc J* 1955;**73**:515–31.

11 Bruton CJ. *Neuropathology of Temporal Lobectomy.* MD. Thesis, University of London, 1984.

12 Taylor DC, Falconer MA. Clinical socio-economic and psychological changes after temporal lobectomy for epilepsy. *Br J Psychiatry* 1968;**114**:1247–61.

13 Taylor DC. Brain surgery lesions, surgery, seizures and mental symptoms. In: EH Reynolds, MR Trible (eds) *Epilepsy and Psychiatry,* London: Churchill Livingstone 1981:229–41.

14 Falconer MA. (Discussant) *Proced R S Med* 1958;**51**:613–6.

15 Falconer MA, Cavanagh JB. Clinico-pathological considerations of temporal lobe epilepsy due to small focal lesions. *Brain* 1959;**82**:483–504.

16 Dikman S, Mathews CG, Harley JP. Effect of early versus late onset of major motor epilepsy upon cognitive-intellectual performance. *Epilepsia* 1975;**16**:73–81.

17 O'Leary DS, Seidenburg M, Berent M, Ball TJ. Effects of age of onset of tonic-clonic seizures on neuropsychological performance in children. *Epilepsia* 1981;**22**:197–204.

18 Wechsler D. *Wechsler Adult Intelligence Scale.* The Psychological Corporation, New York, 1955.

19 Maxwell AE. Obtaining factor scores on the Wechsler Adult Intelligence Scale. *J Ment Science* 1960;**106**:1060–2.
20 Wechsler D. A standardised memory scale for clinical use. *J Neurol Neurosurg Psychiatry* 1954;**15**:54–8.
21 Lezak MD. *Neuropsychological Assessment*, Oxford: Oxford University Press, 1983.
22 Brooks DN. Wechsler Memory Scale performance and its relationship to brain damage after severe closed head injury. *J Neurol Neurosurg Psychiatry* 1976;**39**:593–601.
23 Ellenberg JH, Nelson KB. Febrile seizures and later intellectual performance. *Arch Neurol* 1978;**35**:17–21.
24 Verity CM, Butler NR, Golding J. Febrile convulsions in a national cohort followed up from birth. II Medical history and intellectual ability at 5 years of age. *Br Med J* 1985;**290**:1311–5.
25 Milner B. Psychological aspects of focal epilepsy and its neurosurgical management. In: DP Purpura *et al* (eds) *Advances in Neurology*, New York: Raven Press 1975;**8**:299–321.
26 Sarter M, Markowitsch HJ. The amygdala's role in human mnemonic processing. *Cortex* 1985;**21**:7–24.
27 Saunders RC, Murray EA, Mishkin M. Further evidence that amygdala and hippocampus contribute equally to recognition memory. *Neuropsychologia* 1984;**22**:785–96.