Cognitive outcomes of temporal lobe epilepsy surgery in older patients.

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Abstract

Purpose: To examine the cognitive risks of temporal lobe surgery in patients aged 50 years and older.

Methods: We analysed data from 55 patients who underwent temporal lobe surgery (26 left-sided:29 right sided)from 1988 – 2012 at our centre. Pre-surgical and one year post-operative memory and naming capacity were compared to data obtained from two younger cohorts ; 185 aged 18-30 and 220 aged 31-49.

Results: Pre-operative memory impairments were most marked for the oldest cohort and were associated with a longer duration of epilepsy. Naming capacity improved with age and better performance was associated with a later age at epilepsy onset. Post-operative declines were largest in older patients, achieving statistical significance for **verbal memory**, naming and subjective ratings. Left temporal lobe resections carried the greatest risk of memory and naming decline. Cognitive outcomes were unrelated to seizure outcome, VIQ or mood.

Conclusion: Our findings indicate the cognitive risks of TLE surgery are greater for older patients. Cognitive outcomes need to be considered when assessing the efficacy of epilepsy surgery in older cohorts and pre-operative performance levels need to be taken into account.

key words: epilepsy surgery, temporal lobe epilepsy, memory, cognitive outcome, elderly

1. Introduction

Increasingly, surgical treatment for temporal lobe epilepsy (TLE) is being offered to older patients and this trend will continue with improved life expectancies and reports of favourable seizure outcomes (1). The cognitive impact of TLE surgery on an aging brain, with likely compromised function remains unclear. The risk of worsening memory is a frequent concern raised by older surgical candidates and their families but the evidence base for counselling is limited.

Few studies have investigated the cognitive outcome of TLE surgery in older cohorts and findings are inconsistent. Sirven et al 2000 (2) failed to find increased cognitive vulnerability in seventeen patients undergoing surgery over the age of fifty years. All but four underwent right sided resections, a group known to have lower cognitive risks (3). Girvas et al 2006 (4) explored cognitive outcomes in 34 patients who underwent TLE surgery at 50 years or older. Post-operative cognitive losses were greater than gains, and lower pre-operative performance levels were associated with poorer cognitive outcomes particularly for verbal memory and surgeries undertaken after 65 years. The memory performance of the older group was already weak pre-operatively and the authors stressed the importance of taking this into account when assessing the cognitive impact of TLE surgery.

Costello et al (2009) reported that 10/42 older patients had adverse cognitive changes post-operatively, nine of whom had undergone temporal lobe resections (5). Memory test data was only available on 4/9 and only 2/4 were classified on the basis of this as having declined. Patra et al 2014 observed post-operative memory decline in a subset of older patients in a combined group of temporal and extra temporal surgeries (6). Murphy et al 2010 did not find evidence of memory decline in their older surgical cohort with hippocampal sclerosis (7) while Chapin et al 2013 found decreased susceptibility to memory decline in their older cohort (8).

TLE surgery in the speech dominant hemisphere also carries a risk of language difficulties and declines in confrontational naming have been recorded (9, 10). While language deficits rarely meet the diagnostic criteria of an aphasic disorder they often can affect social functioning and confidence. Word-finding difficulties are the most frequently reported cognitive complaint of people with TLE yet few studies have explored changes in language in older surgical cohorts. Costello noted four patients experienced transient word-finding difficulties lasting less than three weeks with one case receiving speech and language therapy (5). Murphy et al reported naming decline in association with left temporal lobe resections but those aged 50 years or older were not at an increased risk (7).

The aim of this study was to examine pre and post-operative memory and language function of people undergoing TL resections at fifty years or older. We aimed to address the following questions

1. Are pre-operative memory and language difficulties more severe in older patients undergoing TLE surgery and is this related to the chronicity of the epilepsy?
2. Are older patients at greater risk of post-operative cognitive declines?
3. What factors differentiate older patients who experience post-operative cognitive declines from those who do not?

2. Methods.

Participants

The participants were selected from a database of individuals with TLE who had undergone surgery at our centre between 1988 and 2012. Patients undergo neuropsychological assessments pre-operatively and at three months and twelve months as a matter of routine. Patients were included who had cognitive data available preoperatively and at one year post surgery and were assessed to be left hemisphere dominant for language (based on post-ictal dysphasia, Wada test findings to 2002, and latterly fMRI (11). All patients included had an IQ of > 69. Fifty-five patients were identified who were at least 50 at the time of surgery. Patients included represented 93 % of the total temporal lobe surgeries undertaken. Demographic and clinical characteristics are presented in table 1. Most patients underwent standard en bloc resections (LTLE =22;Right TLE = 24) but seven underwent lesionectomies (3

LTLE; 4 RTLE) and one person had a tailored resection following intracranial recordings. The predominant pathology was hippocampal sclerosis.

Table 1: Demographic and clinical characteristics of the three TLE age cohorts who underwent cognitive testing pre-operatively and one year post-operatively.

	18-30 years	31-49 years	50 years +
Number/ total number of surgeries	185/199	220/248	55/57
Age at surgery Median (range)	25 (18-30)	37 (31-49)	54 (50-69)
Gender Male, N (%)	80 (43%)	111 (51%)	24 (44%)
Age of seizure onset Median (range)	8.0 (1-27)	12.0 (1-43)	13.0 (1-58)*
Duration of epilepsy Mean (SD)	16.0 (1-28)	25.0 (3-45)	38.0 (3-62)*
Surgical side Left, N (%)	107 (58%)	110 (50%)	26 (47%)
Pathology HS, N (%)	143 (77%)	183 (83%)	42 (76%)
Seizure free @ 1 yr N (%)	116 (62%)	153 (69%)	37 (67%)
VIQ Mean(SD)	91.5 (13.2)	93.9 (13.1)	93.4(13.5)

$*P<0.001$

Comparable data were available from two younger cohorts aged 18 to 30 years (N= 185) and 31 to 49 years (N= 220) at the time of surgery. Age groupings were selected to reflect the age bandings of the memory test norms (see below). There were no significant differences between the groups with respect to gender, side of surgery, hippocampal pathology, seizure freedom rates at one year and intellectual level. The older surgical group had a later seizure onset and had longer seizure histories ($P<0.001$).

Cognitive measures

Pre-operative performance was compared to performance one year following surgery.

Memory

The List Learning and Design Learning subtests from the Adult Memory & Information Processing Battery (AMIPB) and its successor the BIRT Memory and information processing battery (BIMPB) form part of our routine assessments (12). On the list learning task the subject is read a list of fifteen words and asked to recall as many as possible over five consecutive trials (verbal learning: max =75 items) and after a second list (delayed recall: max = 15). On the design learning task the person is shown a design comprising nine features on a structured grid for 10 seconds and then asked to reproduce it on a blank grid. There are five learning trials and delayed recall following a second design leading to a maximum of 45 points for learning and 9 for recall. These tests have been previously described and have been reported to be sensitive to temporal lobe pathology and temporal lobe surgery (13).

Patients also rated their memory on a four point scale relating to the degree of impairment experienced in daily life. Ratings ranged from 0 for no nuisance to 3 for a severe nuisance.

Post-operative cognitive change.

Memory

For each individual, memory test outcome was classified separately for visual and verbal memory. A change in score was classified as a decline if the learning and/or recall subtest score post-operatively fell more than would be expected from retesting on the basis of the reliable change indices with a confidence interval of 90%. Similarly, a change in score was classified as improved if the test scores increased more than would be expected from retesting. Subjective memory ratings were classified as changed if a category shift occurred (eg rating change from 2 a moderate nuisance to 3 a severe nuisance) and rated as improved or declined depending on the direction of that shift.

Naming

The Graded Naming Test was employed to assess naming capacity (14). This measure consists of thirty line drawings of objects and animals, placed in order of difficulty. The performance indicator is the number of items correctly named. This measure has been found to be sensitive to dominant temporal lobe resections (9). Naming capacity was classified as deteriorated if the post-operative score decreased more than expected from the effects of retesting (15).

Mood

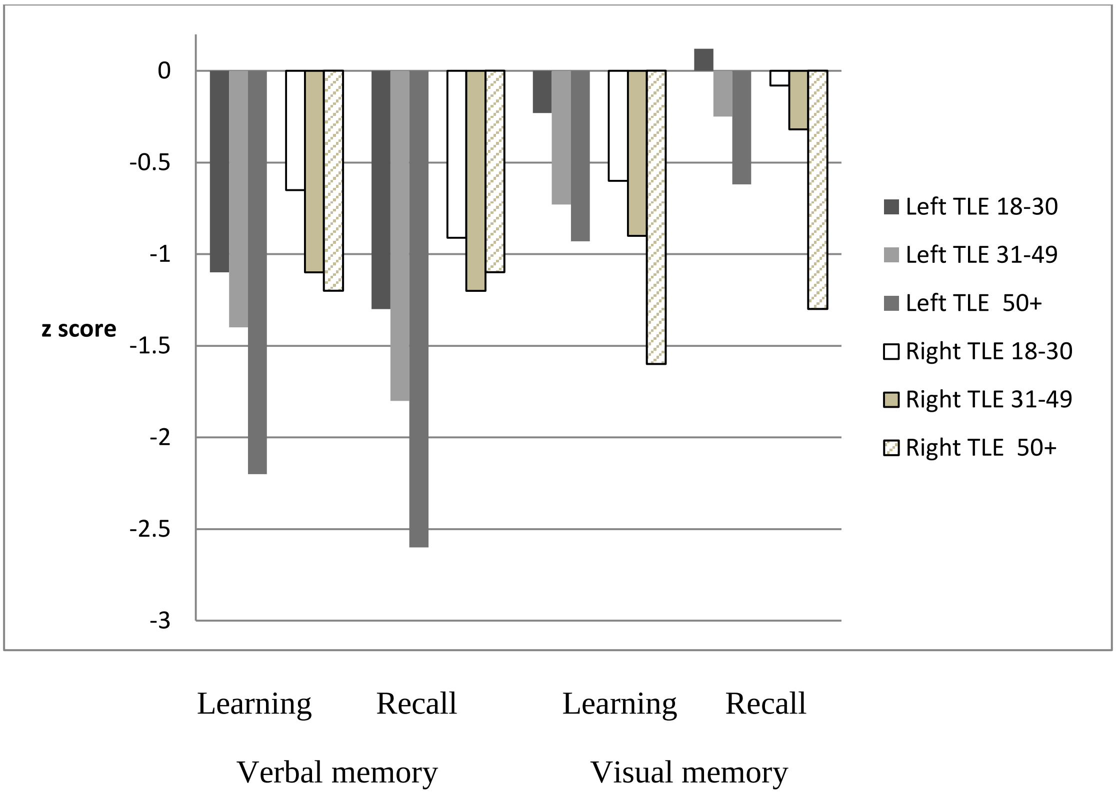
The Hospital Anxiety and Depression Scale was employed to assess levels of anxiety and depression (16).

3. Results

Pre-operative cognitive performance.

Memory test scores were converted into z scores based on age related norms. All three groups performed well below average for their age with most marked deficits observed for the left TLE group who performed more than two standard deviations below age matched controls on verbal memory measures and up to one standard deviation below on visual memory measures (figure 1).

Figure 1: Pre-operative verbal and visual memory test performance by age group and TLE laterality expressed as z scores.



Age

There was a significant effect of age for right LTE for verbal learning ($F=4.1$; $p<0.02$) visual learning ($F=6.4$;$p<0.002$) and visual recall ($F=9.1$; $p<0.0001$) and for left TLE for verbal learning ($F= 9.7$; $p<0.0001$); verbal recall ($F=12.2$;$p <0.0001$); visual learning ($F=4.9$ $p<0.008$); and visual recall ($F=5.0$ $p<0.007$) with poorer performance associated with increasing age. There was no effect of age on subjective memory ratings. There was an effect of age on the performance of the Graded Naming Test with naming capacity increasing with age ($F=6.5$;$p< 0.02$)

Duration of epilepsy

Significant correlations were observed between memory test scores and the duration of epilepsy, with lower scores associated with longer duration for verbal learning (Pearson correlation: -.18;$p<0.0001$), verbal recall (Pearson correlation -.16;$p<0.001$), visual learning (Pearson correlation: -.21;$p<0.0001$) and visual recall (Pearson correlation:-.26;$p<0.0001$). Memory ratings and naming capacity were not associated with chronicity of epilepsy.

Age of onset

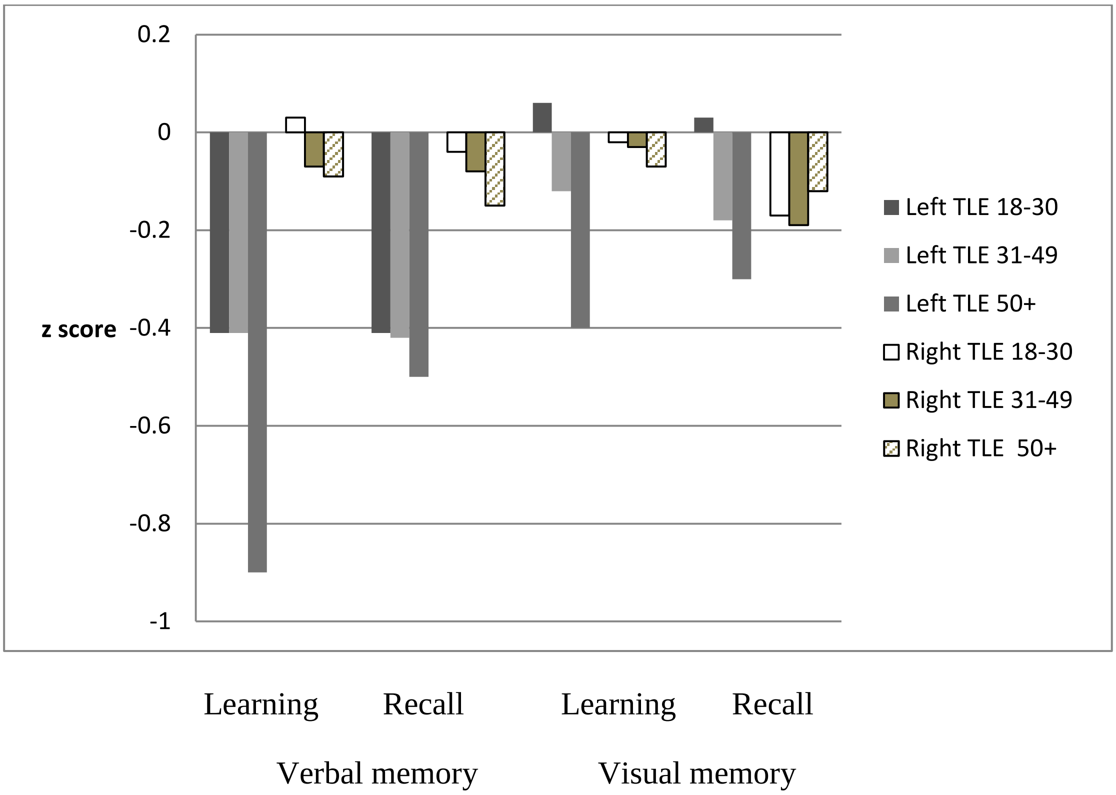
No correlations were observed between memory test performance or subjective memory ratings and the age of seizure onset. Naming proficiency did correlate with the age of seizure onset; lower scores were associated with an earlier onset (Pearson correlation +.23; $p<0.0001$).

Post-operative cognitive change

Memory

No group differences were found for changes in memory test scores post-operatively. The biggest fall of .9 of a standard deviation was observed in the left TLE group on verbal memory tests (see figure 2). This was not significant.

Figure 2: Post-operative verbal and visual memory test change by age group and laterality expressed as z scores



At an individual subject level, people in the elderly cohort were more likely to be classified with memory decline than memory improvement (see table 2). The differences between the groups was significant for verbal memory, with more patients classified as memory declined in the oldest cohort (X^2 5.6; $p<0.05$).

Subjective memory ratings

Few of the older group rated their everyday memory functions as improved and almost half reported a decline following surgery. Differences between the groups were significant for improvements in subjective memory ratings, with gains being reported less frequently in the oldest group (X^2 =4.6; $P<0.05$). No associations were observed between changes in subjective memory ratings and post-operative levels of anxiety and depression.

Table 2: Post-operative change in memory and naming for the three TLE age cohorts expressed as the % of individuals.

	improved	declined
verbal memory		
18- 30	16%	**25%**
31-49	17%	**28%**
50+	12%	**44%***
Visual memory		
18-30	13%	14%
31-49	13%	16%
50+	9%	21%
Memory rating		
18-30	**25%**	28%
31-49	**28%**	30%
50+	**5%***	46%
Naming		
18-30	12%	**5%**
31-49	16%	**10%**
50+	6%	**33%****

Bold text denotes clinical significance: ***p<0.05 : **p<0.01**

Naming

There was a significant difference in the rates of naming decline post-operatively between the groups. More individuals were rated as declined in the oldest cohort (X^2 =14.6; $p<0.01$).

Risk factors for decline

For the older cohort left sided surgery was associated with poorer verbal memory (X^2 =4.0; $p< 0.05$) and poorer naming outcomes (X^2 = 4.5; $p<.03$). Other factors including seizure outcome, type of surgery, pathology (HS versus other), VIQ and mood were not associated with post-operative cognitive decline.

4. Discussion

Memory impairments were more severe in our older TLE patients prior to surgery. Poorer performance associated with a longer duration of epilepsy although the magnitude of the correlation was small. Post-operative verbal memory decline occurred more frequently in our oldest cohort and this group also rated their memory less positively following surgery. Poorer verbal memory outcomes were associated with left temporal lobe resections.

Severe memory impairments in older patients with epilepsy have been highlighted previously. The nature of the problems described are in keeping with those observed in individuals diagnosed with mild cognitive impairment, an identified precursor of dementia (17, 18). In TLE it has been reported memory difficulties are present toward the outset of the epilepsy and as a consequence of normal age related declines deficits become evident earlier in life (19, 20). A role for abnormal aging processes also has been proposed; with older brains having the potential for an increased vulnerability to seizure induced cognitive declines (21, 22). Our finding of an association between epilepsy duration and memory impairments lends some support for this and seizure frequency was not explicitly explored. A further possibility, for those with later onset TLE, is that the seizures are an early indicator of a neurodegenerative process of which a failing memory is a feature (23) . Such patients might be expected to have a poorer cognitive prognosis with memory decline accelerated by insults such as surgical treatment.

We found post-operative verbal memory decline was greater in our oldest surgical group as assessed at the individual but not the group level. Chapin et al reported 50% of their younger group showed memory decline post-operatively versus 25% of their older group. The pre-operative memory test scores of their older cohort however were lower before surgery (8). To assess the meaning of post-operative memory decline pre surgical performance levels need to be taken into account (4) and this possible interpretation was acknowledged in the discussion of their findings. Even a decline of small magnitude may have a major impact on daily functioning for an individual with already compromised memory function. The subjective rating changes made by our older cohort also indicated less favourable memory outcomes than in our younger groups.

Pre-operatively our older cohort performed at a higher level on a naming test that our younger groups and poor performance was associated with an earlier age of epilepsy onset. No relationship was found with the duration of epilepsy perhaps indicating an early cognitive vulnerability for the development of semantic memory. Our older cohort however were at risk of greater declines in confrontation naming post-operatively a finding previously reported and associated with non-hippocampal pathologies (24). There was no evidence from our study that naming decline was pathology driven.

We found left sided surgery was a significant risk factor for verbal memory decline with 44% of our older cohort classified as having experienced a decline post-operatively. Seizure freedom was not associated with memory or naming outcomes. A higher cognitive reserve, as assessed by IQ in our study was not associated with better cognitive outcomes. Cognitive reserve has been found to be accompanied by more favourable cognitive changes following surgery in older (8) and in younger groups (22).

Our older group, although larger than most studies, is small and this limited the statistical analysis that could be undertaken particularly regarding risk factors. All underwent temporal lobe resections and the majority had hippocampal sclerosis. Follow up data was restricted to one year but longer cognitive monitoring is needed. We have not considered AED treatment which is known to have adverse cognitive effects which may be expected to increase in the aging damaged brain (25). It is practice at our centre that medication changes generally are not undertaken until one year post-surgically and are unlikely to have had a major impact on our findings.

5. Conclusion

Our findings indicate that while the seizure outcomes are comparable to younger cohorts the cognitive risks of TLE surgery are greater for older patients particularly those undergoing left temporal lobe resections. Cognitive outcomes need to be considered when assessing the efficacy of surgical treatment in older cohorts and pre-operative performance levels should be taken into account. A small decline in a memory that is already compromised may have dramatic effects on daily life. Elderly patients with TLE considering surgical treatment need to be aware of this possibility. Further research is needed on the impact of surgery in older patients with epilepsy, a cognitively vulnerable group.

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