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Verbal learning and memory outcome in selective amygdalohippocampectomy versus temporal lobe resection in patients with hippocampal sclerosis

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ABSTRACT

Purpose: With the advent of new very selective techniques like thermal laser ablation to treat drug-resistant focal epilepsy, the controversy of resection size in relation to seizure outcome versus cognitive deficits has gained new relevance. The purpose of this study was to test the influence of the selective amygdalohippocampectomy (SAH) versus nonselective temporal lobe resection (TLR) on seizure outcome and cognition in patients with mesial temporal lobe epilepsy (MTLE) and histopathological verified hippocampal sclerosis (HS).
Methods: We identified 108 adults (>16 years) with HS, operated between 1995 and 2009 in Denmark. Exclusion criteria are the following: Intelligence below normal range, right hemisphere dominance, other native languages than Danish, dual pathology, and missing follow-up data. Thus, 56 patients were analyzed. The patients were allocated to SAH ($n = 22$) or TLR ($n = 34$) based on intraoperative electrocorticography. Verbal learning and verbal memory were tested pre- and postsurgery.
Results: Seizure outcome did not differ between patients operated using the SAH versus the TLR at 1 year ($p = 0.951$) nor at 7 years ($p = 0.177$). Verbal learning was more affected in patients resected in the left hemisphere than in the right ($p = 0.002$). In patients with left-sided TLR, a worsening in verbal memory performance was found ($p = 0.011$). Altogether, 73% were seizure-free for 1 year and 64% for 7 years after surgery.
Conclusion: In patients with drug-resistant focal MTLE, HS and no magnetic resonance imaging (MRI) signs of dual pathology, selective amygdalohippocampectomy results in sustained seizure freedom and better memory function compared with patients operated with nonselective temporal lobe resection.

1. Introduction

Epilepsy surgery is widely accepted as an effective therapeutic option in patients with drug-resistant mesial temporal lobe epilepsy (MTLE) [1–3]. However, it remains a matter of controversy whether to use a small resection with the risk of failing to obtain sustained seizure freedom or to use a large resection with the risk of causing additional neuropsychological impairment. With the advent of new techniques like thermal laser ablation [4] and MRI-guided focused ultrasound ablation [5], the controversy will gain new attention. These new techniques make promises for future much less invasive and very selective tissue destruction for the treatment of MTLE, and if proven, safe and efficient will be of utmost importance for more patients to be included in the epilepsy surgery evaluation program.

Temporal lobe resection (TLR) has been the surgical approach of choice for temporal lobe epilepsy [6,7]. There is a well-known risk of verbal memory decline after TLR in the language dominant hemisphere [8,9]. Because of this potential risk of memory impairment, more selective approaches have been developed, the most restricted one being the selective amygdalohippocampectomy (SAH) [7,10–12]. Some studies have found SAH to give as good a seizure outcome as TLR with a better postoperative cognitive and memory outcome [13–16], while others have not [3,17]. Because of the heterogenous surgical approaches, patient referrals, and preoperative evaluations, meta-analysis is difficult

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to perform. Of the two most recent papers, one indicates that SAH has a similar seizure outcome as TLR, and a better cognitive outcome [18], while the other paper indicates that seizure outcome is worse after SAH [19]. No randomized controlled trials with regard to the extent of lateral temporal resection have been performed and most studies include patients with different pathology, which have different influence on the cognitive outcomes [13,14,16,17,20].

Here, we present data on cognitive function and seizure outcome in a homogeneous group of patients operated by the same neurosurgeon and with histopathological verified HS. Our aim was to compare the effect on verbal learning, verbal memory, and seizure outcome in patients after SAH compared with TLR.

2. Material and methods

2.1. Patients

We identified all 108 adults (>16 years) with histopathologically verified HS, operated between 1995 and 2009 in Denmark. Only left hemisphere dominant patients were included (12 left handed or ambidextrous patients with right hemisphere dominance or no WADA test was excluded). Additional patients were excluded because of intelligence level below normal range (n = 9), native language other than Danish, in which the neuropsychological tests were done (n = 8), or dual pathology (n = 6). Patients were excluded because of dual pathology if the written conclusion from the presurgical MRI scan described a potential epileptogenic lesion additional to HS. The exclusion diagnoses were the following: dysembryoplastic neuroepithelial tumor (n = 1), bilateral hippocampal sclerosis (HS) (n = 2), focal cortical dysplasia (n = 1), changes caused by cortical contusion (n = 1), and hypoplasia in the temporooccipital area, which could be caused by meningoencephalitis (n = 1). Follow-up data were not available in 17 patients. Thus, 56 patients remained, and these were analyzed in the present study. Approval for using data from patient records without consent from the individual patient was given by the Danish Health and Medicines Authority (sagsnr. 3-3013-1030/1) and the Danish Data Protection Agency.

2.2. Surgery

All patients were operated by the same neurosurgeon. Resection of amygdala and hippocampus is done in all patients. Selective amygdalohippocampectomy was performed in 22 cases and additional resection of temporal neocortex, TLR, was done in 34 patients. There was no difference in the extent of mesial resection between the groups with SAH and TLR (details are given in Section 3.3). In 47 patients, the decision about resection type SAH or TLR and the extension of the TLR was guided by intraoperative electrocorticography (ECoG). In three patients, the TLR approach was chosen because of technical problems with the surgical entrance. In one additional case, TLR was used because a vascular malformation in the temporal lobe was suspected during the operation, but not found on the preoperative MRI, and histopathology described a small vascular area only suspicious of vascular malformation. In four patients undergoing TLR and one patient undergoing SAH, there were no detailed descriptions of the basis for decision-making.

The ECoG was performed prior to the cortical resection, and a 4-electrode strip was placed in the lateral ventricle through a 1.5 cm linear opening anterior in the superior-temporal sulcus. The strip covered the anterior 3 cm of the hippocampus. Furthermore, a 4×5 electrode grid was placed on the lateral and inferior aspects of the temporal lobe [21]. Electrocorticography was recorded for several minutes. When spikes were unequivocally identified on the strip but not on the grid, a SAH was performed. In all other cases, a TLR was performed. In SAH, the surgical entrance was always made through the superior temporal sulcus. The TLR operation was a tailored procedure based on the ECoG findings. Identification of spikes decided the degree of the lateral resection.

2.3. Seizure outcome

Seizure outcome was assessed using the Engel classification at 1 and at 7 years after surgery. Patients in Engel class I were considered seizure-free and compared with patients in Engel classes II–IV. At one-year follow-up, seizure outcome was described in the medical records, no data were missing. At seven-year follow-up, seizure outcome was rated from the medical records or when missing by a telephone interview. In three patients, seven-year follow-up was not possible: two had been reoperated and one had emigrated. Data did not exist for three patients who had died.

2.4. Neuropsychological assessment

In 2006, the neuropsychological follow-up together with other follow-up measures was decided to be changed from a one-year to a two-year follow-up at our hospital. Thus, in 41 patients, the follow-up test was performed 1 year after surgery; in 14 patients, 2 years after surgery; and in one subject, 3 years after surgery. Verbal learning and memory were assessed by a Danish version of 15 Verbal Paired Associated words, containing 7 semantically related/easy pairs (e.g., mouse – cheese) and 8 unrelated/hard pairs (e.g., chimney – coat) [22]. Parallel test versions have been used. The paradigm requires a deeper conceptual processing and is believed to represent two distinct memory systems, the semantic and the episodic [23,24]. First, the word pairs are presented once. Hereafter, the patient is cued by the first word in the pair, and asked to mention the associated word. Once the word pair is learned, it is put aside. All 15 word pairs are to be learned in 1–10 trails, errors are counted. This is interpreted as verbal learning. Retention with the cuing again by the first word is performed 1 h later, errors are counted. This is interpreted as verbal memory [22].

All patients were tested by Wechsler Adult Intelligence Scale (WAIS) Information [25] and Ravens Progressive Matrices, set 1 [26]. Normal range was defined as a scale score above 6 in WAIS Information and a score above 1.5 SD below mean [27] (Gade A, Mortensen EL. The influence of age, education, and intelligence on neuropsychological test performance, 1984, unpublished). Educational and occupational levels supported the test results. Only patients functioning in the normal range was included.

2.5. Statistical analyses

Three outcomes were considered: seizure outcome (at 1 year and at 7 years), verbal learning performance, and verbal memory performance.

A logistic regression was used to assess the effect of the surgical approach (SAH vs. TLR), the side of surgery (left vs. right hemisphere), and their interaction (SAH and left) on the seizure outcome.

A linear regression model was used to investigate the effect of the surgical approach, the side of resection (hemisphere), and their interaction on the verbal memory performance. To account for the difference in variance observed between approaches and hemisphere subgroups, a variance parameter specific to each subgroup was fitted. The model was adjusted for the occurrence of seizure after resection, which can influence the cognitive ability of the patients [28]. The same methodology was used to investigate the effect of the surgery approach and the side of surgery on the verbal learning.

Gender, chronological age, duration of epilepsy, age of onset of epilepsy, number of respectively SFS (simple focal seizures), CFS (complex focal seizures), and sGTC's (secondarily generalized tonic–clonic seizures) are possible confounders for the relation between the outcome and the surgical approach. Therefore, in addition to the previously mentioned models, a backward elimination procedure [29] with a threshold of $p < 0.1$ was used to identify variables associated with the outcome and to check the consistency of the results regarding the set of variables that was included in the model.

Statistics were calculated by use of SAS Enterprise Guide 6.1 for Windows and R 3.3.2 [30].

3. Results

Patient characteristics are listed in Table 1. The two groups showed similar characteristics in age at surgery, age at epilepsy onset, duration of epilepsy, and number of seizures preoperative.

3.1. MRI

All patients but one had a hyperintense hippocampus at the preoperative MRI corresponding to the side of the later resection, and all but six had hippocampal atrophy also corresponding to the side of the later resection. In one, the size of the hippocampus was not described. Patients with a potential epileptogenic lesion other than HS on the side of resection on the preoperative MRI were excluded, but the patients included could have one or more of the below mentioned changes, not considered epileptogenic: abnormal positioning of the hippocampi (n = 2), gliosis (n = 3), atrophy of the temporal lobe in the same hemisphere as the later resection (n = 4), atrophy of the hemisphere contralateral to the later resection (n = 1), slight atrophy of cerebellum (n = 1), ventricular ectasia (n = 2), nonspecific white matter changes (n = 3), arachnoid cyst (n = 3), asymmetric frontal lobes (n = 1), small hyperintense change next to hippocampus in the same hemisphere as the later resection (n = 1), and slight abnormal gray matter next to the temporal horn of the lateral ventricle (n = 1).

3.2. Pathology

All included patients had histologically verified HS. Patients were diagnosed before publication of the most recent international consensus classification of HS in temporal lobe epilepsy [31]. However, descriptions of neuronal cell loss and gliosis in subregions of hippocampus were available in 27/34 patients with TLR and in 17/22 patients with SAH. In 21/27 patients with TLR and in 12/17 patients with SAH, neuronal loss and gliosis dominated in CA1, and in 6/27 patients with TLR and in 5/17 patients with SAH, neuronal loss and gliosis were described in CA4, too. There was no significant difference in the description of neuronal loss and gliosis in CA1 and CA4 between the patients with SAH and the patients with TLR (Fisher's exact test, p = 0.7). In patients operated with the TLR approach, the only pathology found in tissue not from the hippocampus was gliosis (n = 14), and in one patient a small vascular area.

Table 2
Logistic regression model for the seizure outcome at one- and at seven-year follow-up, odds ratio estimates.

Seizure outcome at 1-year follow-up			
Variable	Odds ratio	Confidence interval of odds ratios	p-Value
		Test main effects	
Approach (SAH)	1.04	[0.30; 3.56]	0.951
Hemisphere (R)	1.62	[0.49; 5.42]	0.431
Seizure outcome at 7-year follow-up			
Variable	Odds ratio	Confidence interval of odds ratios	p-Value
		Test interaction	
Reference (R) SAH			
Hemisphere (L): approach (TLR)	0.08	[0.01; 1.16]	0.064
		Difference between subgroups	
Hemisphere (R): TLR vs SAH	5.10	[0.66; 33.55]	0.119
Hemisphere (L): TLR vs SAH	0.42	[0.08; 2.25]	0.309

3.3. Extent of mesial resection

The length of the hippocampus removed was measured and noted right after the resection. This gave us the opportunity to investigate differences in the extent of mesial resection between the group with SAH and TLR. In some cases, ultrasonic surgical aspiration was performed after this initial removal, and the neurosurgeon estimated the extra amount of tissue resected. In 19 patients, data on the length of the hippocampus removed were missing.

In the group with SAH, a mean of 30.2 mm (22 patients, 5 missing) (SD: 6.5, range: 18–40 mm) was resected compared with 29.7 mm (34 patients, 14 missing) (SD: 7.2, range: 22–48 mm) in the group with TLR (pooled *t*-test, p = 0.834). In the right hemisphere (31 patients, 10 missing), a mean of 31.0 mm (SD: 5.9, range: 20–40 mm) of the hippocampus was resected compared with 28.6 mm on the

Table 1
Patient characteristics of the two surgical groups (SAH vs. TLR).

Patient characteristics	SAH	TLR	Total
Number of patients	22	34	56
Gender (females)	9	17	26
Age at surgery (mean ± SD)	34.7 ± 10.3	36.0 ± 10.4	
Duration of epilepsy in years (mean ± SD)	27.5 ± 11.8	26.6 ± 11.4	
Age of onset of epilepsy (mean ± SD)	7.2 ± 6.3	9.4 ± 9.3	
Side of surgery (left/right hemisphere)	12/10	13/21	25/31
Educational level[a]			
High (left/right hemisphere)	4/5	5/11	9/16
Low (left/right hemisphere)	8/5	8/10	16/15
Number of simple focal seizures per month preoperative (mean ± SD)	12.2 ± 16.7[b]	19.4 ± 36.7[c]	
Number of complex focal seizures per month preoperative (mean ± SD)	6.1 ± 4.6[b]	8.7 ± 15.9	
Number of secondarily generalized tonic–clonic seizures per year preoperative (mean ± SD)	2.3 ± 7.8[d]	4.7 ± 10.0[d]	
Number of antiepileptic drugs taken preoperative (mean ± SD)	2.1 ± 0.7	2.2 ± 0.8	
Engel class postoperative (I/(II, III, IV))	16/6	25/9	41/15
Decisions on the surgical approach were based on			
Intraoperative electrocorticography	21	26	47
Technical reasons	0	4	4
Not described	1	4	5

[a] High educational level is defined by >3.5 years of education.
[b] Data from 2 patients missing.
[c] Data from 6 patients missing.
[d] Data from 1 patient missing.

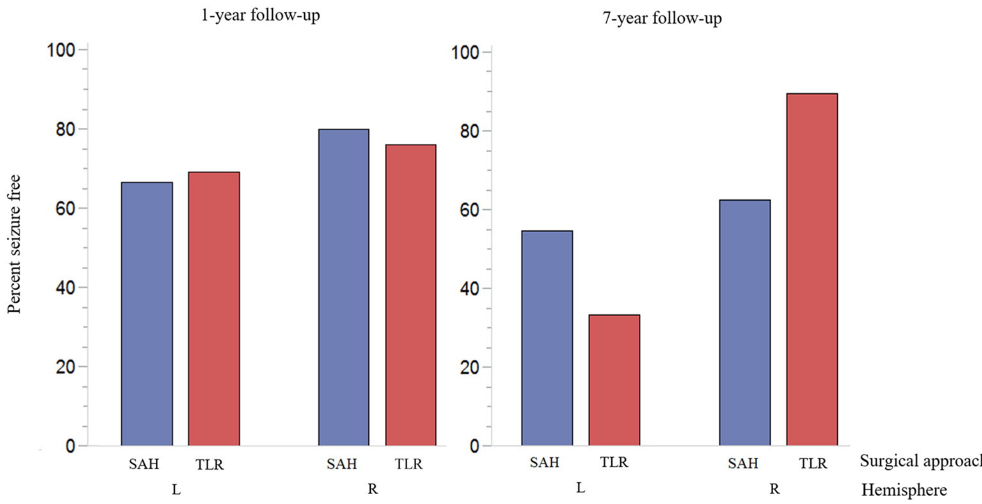

Fig. 1. Bar chart of percent seizure-free (Engel class I) at one-year and at seven-year follow-up in selective amygdalohippocampectomy (SAH) versus temporal lobe resection (TLR) in the right (R) and the left (L) hemispheres.

left (25 patients, 9 missing) (SD: 7.7, range: 18–48 mm) (pooled *t*-test, $p = 0.293$).

3.4. Seizure outcome

Altogether, 73.2% of the patients were seizure-free (Engel class I) at one-year follow-up, 73.5% in the group with TLR (25/34), and 72.7% in the group with SAH (16/22). No interaction between side of surgery (hemisphere) and approach was identified by the logistic model: The effect of the surgical approach and the effect of the side of resection on the seizure outcome can be interpreted separately. There was no significant difference in seizure outcome between patients in the group with TLR compared with patients in the group with SAH ($p = 0.951$) and no significant difference in seizure outcome between patients operated in the left and in the right hemisphere ($p = 0.431$). Odds ratio estimates and confidence intervals are listed in Table 2, data are presented in Fig. 1. No variables were identified by the backward elimination procedure.

At seven-year follow-up, data were accessible in 50 patients (lost to follow-up ($n = 3$), data not existing ($n = 3$)). Altogether, 64.0% of the patients were seizure-free (Engel class I). The amount of seizure-free patients in each surgical group (SAH and TLR) and for each hemisphere is displayed in Fig. 1. A borderline interaction between hemisphere and surgical approach was found by the logistic model ($p = 0.064$) (odds ratio = 0.08), Table 2. Therefore, we need to take the hemisphere into account when we interpret the effect of having performed SAH versus TLR.

In patients operated in the right hemisphere, there was no significant difference in seizure outcome between patients operated with TLR compared with those operated with SAH ($p = 0.119$) (odds ratio 5.10). In patients operated in the left hemisphere, there was no significant difference in seizure outcome between patients operated with TLR compared with those operated with SAH ($p = 0.309$) (odds ratio 0.42). Therefore, given an operation side (hemisphere), we did not find any significant difference in seizure outcome between the SAH and the TLR approach ($p = 0.177$).

The backward elimination procedure identified the following variables: age at surgery and duration of epilepsy. Adjusting for these variables, patients resected in the right hemisphere with TLR was found to have a borderline significant higher chance of being seizure-free than patients resected in the right hemisphere with SAH ($p = 0.048$, odds ratio: 19.29, CI: (1.03; 362.83)). No significant effect of surgical approach was observed for patients operated in the left hemisphere.

3.5. Neuropsychological outcome

3.5.1. Verbal memory

A borderline significant interaction between hemisphere and surgical approach was found by the linear regression model ($p = 0.057$) with

Table 3
Linear regression model for the verbal memory and the verbal learning outcome, respectively. Each model is adjusted for the seizure outcome.

Verbal memory			
Variable	Estimated coefficients (unstandardized)	Confidence interval	p-Value
	Test interaction		
Reference (R) SAH			
Hemisphere (L) (SAH)	−0.11	[−3.02; 2.80]	0.941
Hemisphere (L): approach (TLR)	−3.72	[−7.46; 0.03]	0.057
	Difference between subgroups		
Hemisphere (L): TLR vs SAH	−3.49	[−6.75; −0.23]	0.036
Hemisphere (R): TLR vs SAH	0.23	[−1.61; 2.07]	0.807
Verbal learning			
Variable	Estimated coefficients (unstandardized)	Confidence interval	p-Value
	Test main effects		
Approach (TLR)	−0.10	[−7.13; 6.93]	0.978
Hemisphere (L)	−13.9	[−22.21; −5.59]	0.002

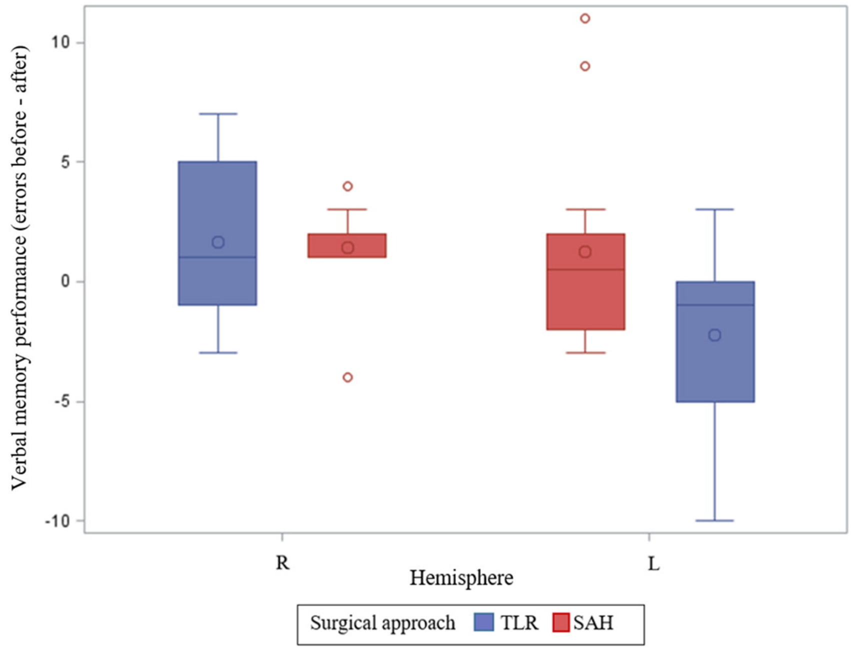

Fig. 2. Boxplot of verbal memory performance (errors before – after) in patients resected with selective amygdalohippocampectomy (SAH) versus temporal lobe resection (TLR) in the right (R) versus the left (L) hemisphere.

a punctual estimate of −3.72 (Table 3). Thus, we need to take the hemisphere into account when we interpret the effect of having performed SAH versus TLR. A worse performance was found in patients resected in the left hemisphere with the TLR approach compared with other patients ($p = 0.011$). This was also found when comparing the left hemisphere patients with TLR, specifically to the left hemisphere patients with SAH (punctual estimate: −3.49, $p = 0.036$). There was no significant difference between patients resected in the right hemisphere with either the SAH or the TLR ($p = 0.807$), and neither with patients operated on the left with SAH ($p = 0.941$). This is shown in Fig. 2, where the variables for the first three groups are comparable, but the fourth, representing patients operated in the left hemisphere with a nonselective approach (TLR), is shifted below the others. No variable was identified by the backward elimination procedure.

3.5.2. Verbal learning

No interaction between hemisphere and surgical approach was found by the linear regression model ($p = 0.574$). Patients operated in the left hemisphere performed significantly worse than patients operated in the right hemisphere ($p = 0.002$) with a punctual estimate of −13.9 (Table 3), as shown in Fig. 3. No effect of the surgical approach (SAH versus TLR) was found ($p = 0.978$).

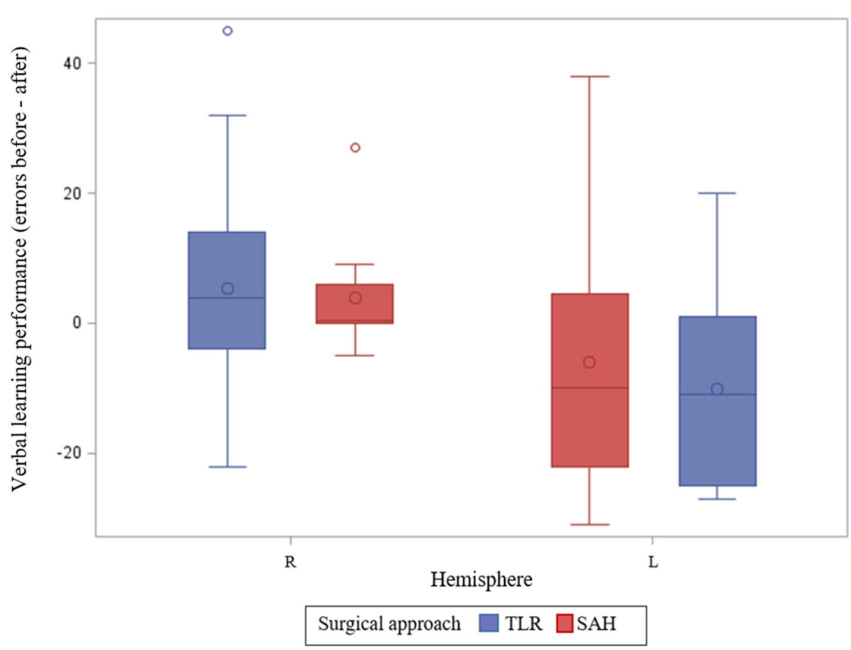

Fig. 3. Boxplot of verbal learning performance (errors before – after) in patients resected with selective amygdalohippocampectomy (SAH) versus temporal lobe resection (TLR) in the right (R) versus the left (L) hemisphere.

The backward selection procedure retained the following variables: age at surgery, number of CFS', duration of epilepsy, age of onset, and seizure outcome. A model accounting for these variables gave values consistent with the original model: no interaction between hemisphere and surgical approach was found with this approach either ($p = 0.811$). Patients operated in the left hemisphere performed significantly worse than patients operated in the right hemisphere ($p < 0.001$) with a slightly different punctual estimate of −15.5, no effect of the surgical approach ($p = 0.827$).

In our statistical analyses, we merge follow-up data from neuropsychological tests performed 1 year (41 patients), 2 years (14 patients), and 3 years (one patient) after surgery. Merging of neuropsychological test data is based upon the assumption that neuropsychological function stabilizes during the first year after surgery to the temporal lobe. Our material is not dimensioned to formally test this assumption; however, we performed a sensitivity analysis on the 41 patients tested 1 year after surgery. The secondary analysis showed effect sizes comparable to the primary analysis including all subjects.

4. Discussion

Epilepsy surgery is a safe and efficient treatment option in patients with medically resistant MTLE, but it is still controversial to which extent resection of the lateral temporal lobe in addition to the SAH affects seizure outcome and cognitive function. With the new option of thermal laser ablation and MRI-guided focused ultrasound ablation, it is becoming possible to make even more selective resections than SAH, and potentially with lesser risks for complications during the resection [4,5,32]. This possibility calls for a clarification of the old controversy.

The present study evaluated whether a selective (SAH) or a nonselective (TLR) approach to surgical treatment of MTLE has different impact on objective measures of cognitive function and seizure outcome or not. Postoperative neuropsychological follow-up was obtained more than 1 year after surgery, at a time when cognitive outcome is not directly affected by the operation and expected to be stable. Seizure outcome was evaluated 1 and 7 years after surgery.

4.1. Seizure outcome

The number of seizure-free patients (Engel class I) remained favorable at seven-year follow-up, 64.0% compared with 73.2% at one-year follow-up. No difference in seizure outcome between patients in the group with TLR compared with patients in the group with SAH was found at one-year follow-up ($p = 0.951$). This is in line with several other studies [13,14]. At 7 years, an unadjusted model showed no difference in seizure outcome between the surgical approaches in patients operated in the same hemisphere ($p = 0.177$). In Wendling's study from 2013 [13], no significant difference in seizure outcome between SAH and TLR, was found either, at a mean follow-up period of 7 years. These results are in favor of choosing a selective resection when operating patients with MTLE and HS. However, one must bear in mind that patients with a more widespread disease for example cortical dysplasia or dual pathology possibly still would get a better seizure outcome with a more extensive resection [3,19].

4.2. Verbal memory after left-sided TLR

The second main result in our study was a worsening in verbal memory performance in patients with left-sided TLR compared with all the other patient groups ($p = 0.011$), and compared specifically to patients with left-sided SAH ($p = 0.036$). In line with this finding, it was shown in Martin et al.'s study [33] that 48% of patients who underwent left-sided anterior temporal lobectomy and had moderate or severe HS performed worse in retrieval aspects of verbal memory, when comparing the preoperative score to a postoperative score measured 3 to 18 months after surgery.

The favorable neuropsychological outcome in SAH in the dominant hemisphere is widely theoretically explained by the sparring of temporal neocortex and the temporal stem. The temporal neocortical regions are by most considered critical to semantic processing, and the left hemisphere is considered especially important regarding language semantics [34,35]. The better verbal memory in the left SAH group compared with the left TLR group might as well be related to the sparring of neocortical tissue and thereby a theoretically relatively preservation of semantic processing. The verbal associate pair tests are thought to be sensitive to these processes because of the demands of a semantic function when associating words, and because of the highly semantic relation in half of the word pairs. In the temporal stem among others a fiber bundle, the uncinate fasciculus (UF), which connects the anterior temporal lobe with the orbitofrontal cortex and the anterior prefrontal cortex in a bidirectional way [36], is considered important in verbal learning and memory [37–39]. In our material, the UF was divided alongside its fiber length in the SAH approach, but across its fiber length in most of the TLR approaches, and we speculate that damage to this structure could explain the worse performance in verbal memory in the left TLR group. Disruption of the UF may cause problems in the expression of memory to guide decisions and in the acquisition of certain types of learning and memory [36]. In a recent study, abnormalities in the UF were found with diffusion tension magnetic resonance imaging showing positive correlations with disturbed verbal fluency and digit span test scores [40]. Others have argued that the UF might be compensated by alternative connections and regions in postoperative reorganization processes [41]. Functioning of the remaining posterior part of the hippocampus has been connected to verbal memory outcome in the first postoperative months [42,43] while reorganization to the contralateral hemisphere seems to be of importance for the verbal memory outcome at 12 months postsurgical [44]. The lack of consistent findings in verbal memory outcome studies comparing left SAH and left TLR might not only be due to heterogeneous patient characteristics and surgical methods but also to a substantial heterogeneity in task demands in the various verbal memory tests [45,46]. Our study supports the importance of applying various types of verbal memory tests that are sensitive to different aspect of memory processing and task demands. As a consequence, a much broader test battery is now used at our hospital.

4.3. Verbal learning and side of surgery

The third major result is that our data support the differing impact of the side of surgery (hemisphere) on verbal learning performances that has been reported for decades [47]. Patients operated in the left hemisphere had significantly worse performances in the verbal learning score than those operated in the right hemisphere ($p = 0.002$). This result is in line with the well-established material specific hypothesis [48].

In contrast to verbal memory, no significant difference was observed in verbal learning outcome between the left sided SAH and the left sided groups with TLR. Several other studies describe verbal learning decline both after left SAH and after different left TLR approaches, but to a lesser extent in left SAH [49–51]. Because both groups are declining following surgery, smaller differences might have been blurred by other factors, e.g., the potential trouble learning all the 15 word pairs (up to 10 trails). This might be exhausting to left patients with TLE who nearly all have some degree of language and learning problems in addition to the common executive problems [48].

4.4. Limitations

A potential limitation of this study is the procedure for allocating patients to the groups with SAH or TLR. Patients were not randomized. The decision about resection type SAH or TLR, and the extension of the TLR, was guided by intraoperative ECoG. A technique based on a limited time sampling of interictal epileptiform activity that can be changed when the neuronal tissue is affected by surgery and anesthetics [52]. Good results have been shown with this technique [53], but the seizure outcome has been found to be comparable between TLR guided by ECoG and standard TLR [54]. In one prospective study [55], patients with unilateral mesial temporal lobe sclerosis diagnosed on preoperative MRI, were investigated with pre- and postresective ECoG. They received the same standard resection independent of the ECoG results. No significant difference between patients with a good (Engel class I) and a poor (Engel classs II, III, IV) seizure outcome, was found, with respect to the share of patients having spikes in unresected neighboring areas before resection, residual spikes in neighboring areas after resection, and new spikes in areas distant from the resection. This study and a newer review therefore conclude that ECoG generally is not considered to be needed in patients with mesial temporal lobe sclerosis [55,56]. In this material, the seizure outcome corresponds to what has been presented in other studies not using intraoperative ECoG [1,57]. We would like to emphasize that the goal of the present study not was to elucidate whether ECoG is needed for the operative decision-making. We would also like to enhance that whether ECoG has been used or not, this study analyzed the pre- minus the postoperative score that is the change from baseline in the verbal learning and the verbal memory test, in each patient. Therefore, this study gives information about the influence of a selective versus a nonselective procedure and of resection in the right versus the left hemisphere on these neuropsychological functions despite the allocation procedure. Since data to this article goes back to the beginning of the Danish epilepsy surgery program, the exact data on related vs. unrelated word pairs were unavailable.

The methodological strengths of the present study are the very strict inclusion criteria (intelligence within the normal range, left hemisphere dominance, Danish as native language, histopathological verified HS, age above 16 years), operation by the same neurosurgeon (1995–2009), and accounting for potential confounders, which are important when assessing neuropsychological performance.

5. Conclusion

In patients with drug-resistant focal MTLE, HS and no MRI signs of dual pathology SAH results in sustained seizure freedom and better memory function compared with patients operated with nonselective TLR.

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Conflicts of interest

No conflicts of interest exist for any of the authors.

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