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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