Epileptic Disord 2011; 13 (3): 284-90

Superselective anterior temporal resection in mesial temporal lobe epilepsy

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Received April 16, 2011; Accepted August 5, 2011

ABSTRACT – We report the case of a patient with pharmacoresistant mesial temporal lobe epilepsy presenting psychomotor seizures with onset at early childhood. MRI showed a blurred internal structure of the right hippocampus and right mammillary body atrophy. Neuropsychological testing revealed deficits in selective attention and visual planning. Non-invasive recording was not sufficient to precisely detect the seizure onset zone. Invasive recording showed seizure onset in the temporo-polar neocortex, with spread to the amygdalum and hippocampus. A superselective resection of the temporal pole and amygdalum was performed with preservation of the hippocampus. Histology revealed the presence of focal cortical dysplasia (Palmini type Ib). Seizure frequency was reduced after surgery, and seizure freedom for two years was achieved with optimisation of the antiepileptic drug regime. Memory functions were preserved, and selective attention and visual planning improved following limited resection. This case suggests that, in selected cases, highly targeted resections with preservation of memory-relevant structures may be the best choice considering both seizure control and unimpaired cognitive functioning.

Key words: epilepsy surgery, resection, mesial, temporal lobe, epilepsy, focal cortical dysplasia

Temporal lobe epilepsy (TLE) is the most common form of epilepsy in the adult population, often caused by mesial temporal generators which are reported to be present in around 60-70% of the patients (Commission, 1989; Watson *et al*., 1992). Epileptogenic structures can comprise the hippocampus itself, the parahippocampal gyrus, the amygdala, and adjacent structures (Vermathen *et al*., 2002). Since many patients are resistant to pharmacological treatment, surgical resection of the epileptogenic area may be indicated (Semah *et al*., 1998; Volcy Gomez, 2004). There is an ongoing debate, however, regarding the extent of resection necessary to achieve seizure control. Progressive advances in diagnostic evaluation allow a more precise determination

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doi:10.1684/epd.2011.0460

of the ictal focus which may open options for superselective resections.

We present the case of a patient with mesiotemporal epilepsy who underwent a highly selective surgical procedure sparing the hippocampus and achieved favourable seizure outcome and improvement in cognitive performance.

Case report

A right-handed 52-year-old man was admitted for presurgical evaluation of his epilepsy. Since the age of two years he suffered from complex partial seizures characterised by behavioural arrest, staring, impairment of consciousness, oroalimentary and manual automatisms and head deviation to the left side with preserved language functions, and secondary generalised tonic-clonic seizures. Seizure frequency was from one to three per month. There was comorbidity of severe depression and hypothyroidism. The first epileptic episodes occurred in his early childhood; in the course of the disease, pharmacoresistance against phenytoin, oxcarbamazepine, topiramate, lamotrigine and clobazam was documented.

Therapy at the time of admission was 300 mg/d lamotrigine, 1,200 mg/d oxcarbazepine, 10 μg/d vitamin B12 and 125 μg/d levothyroxin. Physical examination was unremarkable. Neurological examination showed normal findings except for facial hypoaesthesia due to a former facial trauma. Routine laboratory testing showed no relevant abnormalities.

He was working as an international manager in a large German company. Neuropsychological evaluation revealed above average general intellectual abilities. There were specific deficits in the domains of selective attention and visual planning while the other cognitive functions were average or even above average (including verbal and visual declarative memory). Clinical psychological examination showed depressive symptoms and increased anxiety.

High resolution MRI (3T) showed a blurred internal structure of the right hippocampus without clear atrophy or signal change *(figure 1)* and right mammillary body atrophy. An interictal FDG-PET was non-localising.

EEG revealed interictal sharp waves recorded with maximum amplitude over the right sphenoidal electrodes extending to adjacent temporo-anterior contacts. Ictal recordings showed a widespread rhythmic activity over the right temporal lobe with later propagation to left temporal and bifrontal areas. Precise focus localisation within the right temporal lobe was not possible. In order to define the role of the hippocampus in seizure generation, the patient underwent stereotactic implantation of two depth electrodes with a lateral approach targeting the right amygdala and hippocampal head. Moreover, temporobasal and temporo-lateral subdural strip electrodes were implanted *(figure 2)*. Invasive recordings showed extended interictal spiking in the amygdala, hippocampus, as well as in the temporo-basal and temporo-polar areas *(figure 3)*. Ictal recordings showed seizure onset with low-amplitude fast activity over the polar neocortex and rhythmic spiking in the amygdalum, with spread to the hippocampus after a few seconds.

Since the hippocampus was not the primary seizure generator, and since the patient was unwilling to risk memory deterioration following surgery, the patient was offered a superselective surgical procedure preserving the hippocampus which was assumed to carry relevant function in memory processing. Therefore, selective resection of the right amygdala, uncus and temporal pole with preservation of the hippocampus

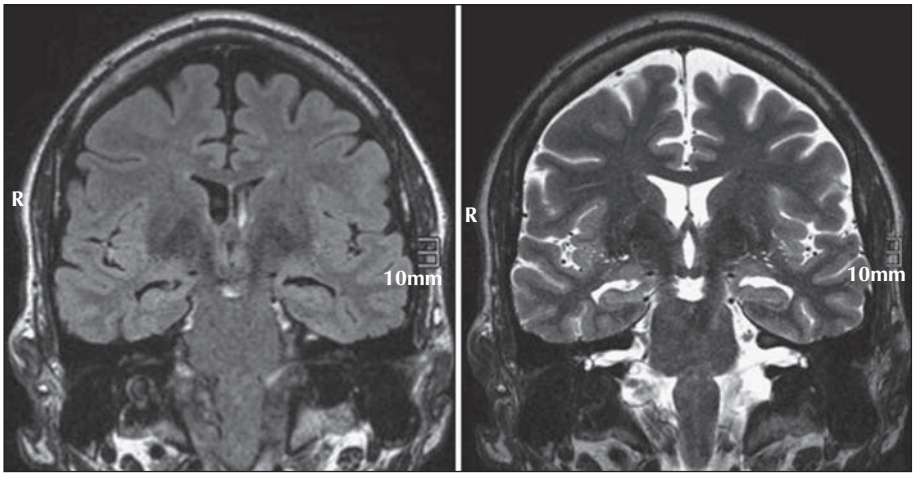

Figure 1. High resolution MRI (3T) shows a blurred internal structure of the right hippocampus without clear atrophy or signal change.

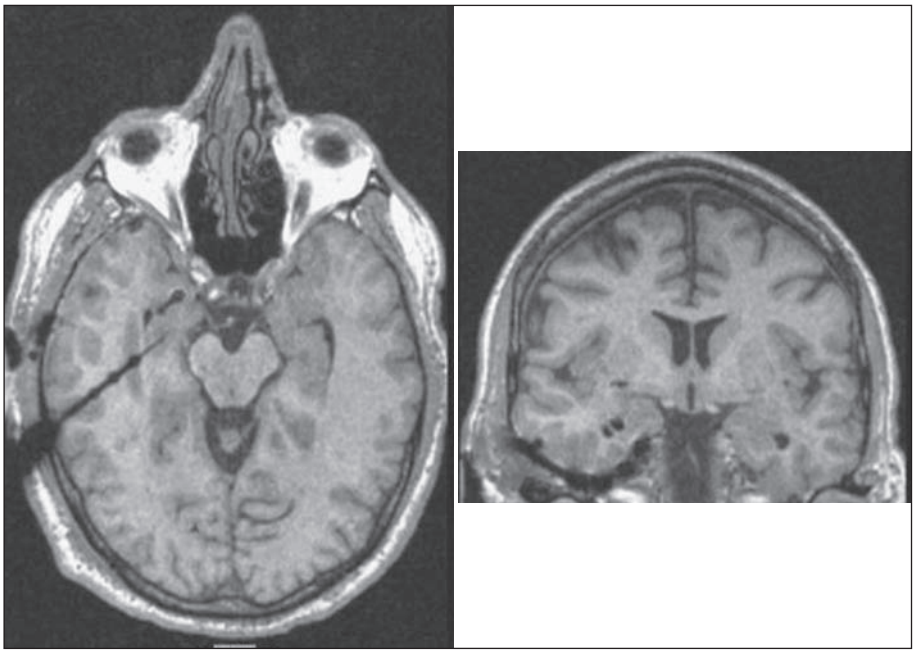

Figure 2. MRI showing the positions of depth electrodes targeting the right amygdala and hippocampus as well as the temporo-basal and temporo-lateral strips.

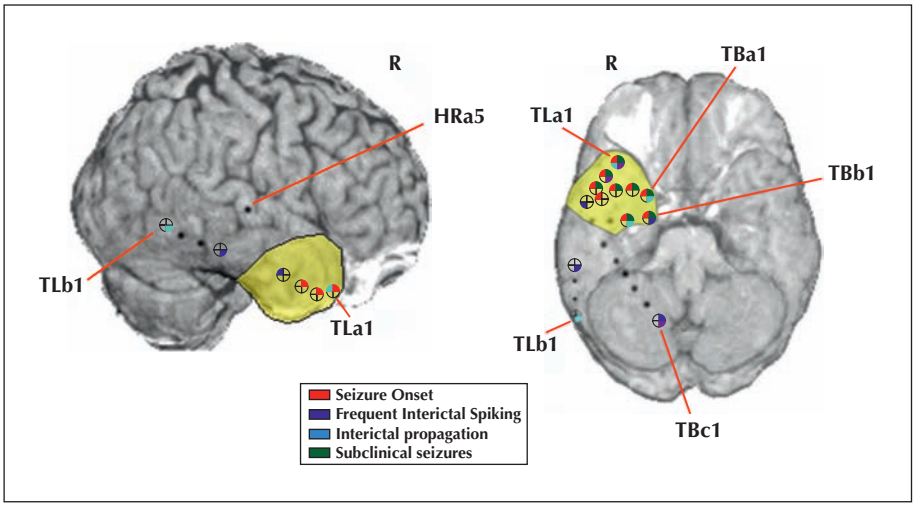

Figure 3. Results of invasive recordings showing ictal onset in the right temporal pole and amygdala, and delay between anterior ictal onset and hippocampal involvement; superselective resection preserving the hippocampus was planned (yellow shaded area).

and parahippocampal gyrus was performed. Histological analysis revealed the presence of focal cortical dysplasia (Palmini type Ib).

Within the first three months after surgery, the patient continued to have complex partial seizures at a lower frequency. Visual fields were unchanged. Neuropsychological performance concerning selective attention and visual planning improved to an average level, and declarative memory performance remained unchanged *(figure 5)*. Depressive symptoms were still present. MRI showed the resection of the right amygdala, uncus and temporal pole with mild surrounding gliosis *(figure 4)*. Routine interictal scalp EEG was free of epileptic activity.

With add-on introduction of levetiracetam in combination with oxcarbazepine, complete seizure freedom was achieved 11 months after the surgical procedure; the patient has now remained completely seizure-free (Engel 1a, Wieser 1) for 26 months. Depressive symptoms have resolved over this period, and due to his professional performance he was promoted to a higher position.

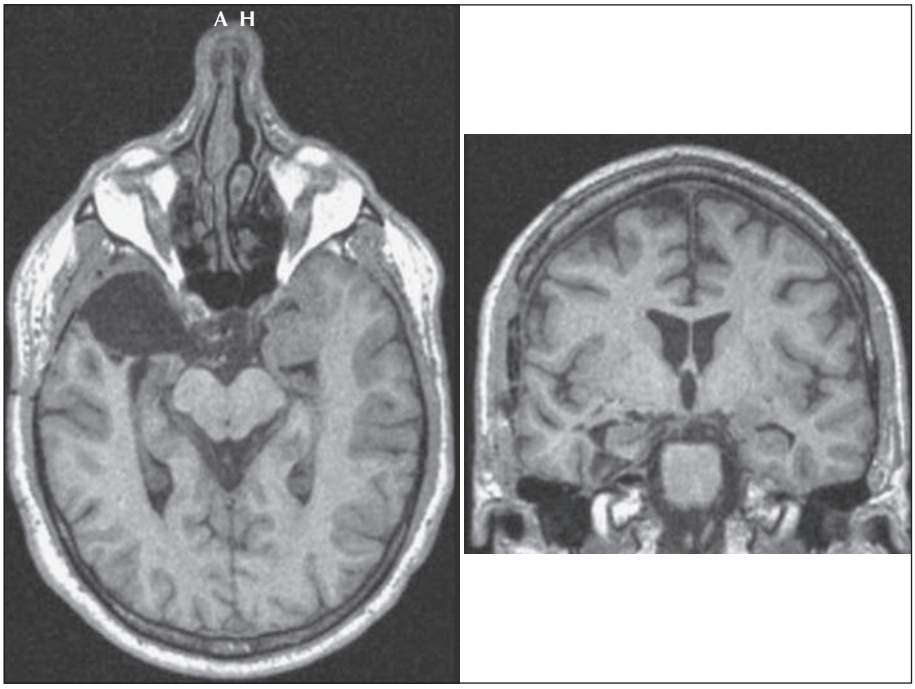

Figure 4. Postoperative MRI demonstrating the superselective resection of the temporal pole, uncus and amygdala with preservation of the hippocampus and parahippocampal gyrus.

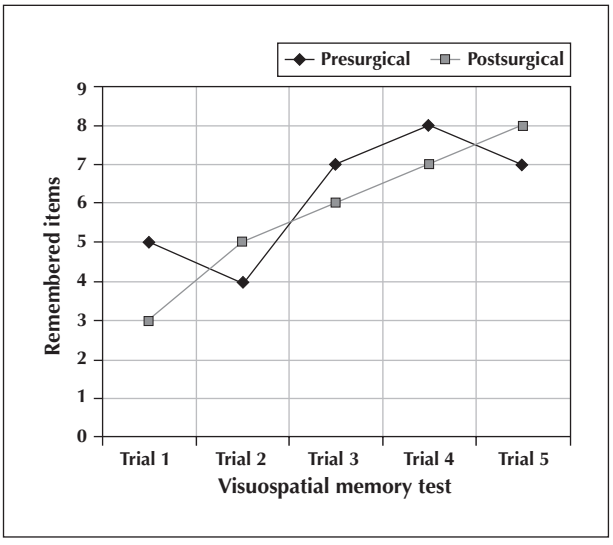

Figure 5. Pre- and postsurgical visual memory performance; lines show similar learning increment across the five trials and overall average visual memory performance at both time points.

Discussion

TLE is not a homogenous disease. Different neocortical and archicortical areas may contribute to epileptogenesis, corresponding to a large spectrum of histological abnormalities. Although the hippocampus (Gloor, 1991) is frequently the structure responsible for seizure generation, the amygdala (Zentner *et al*., 1999) and neocortical abnormalities, particularly focal cortical dysplasias (also as dual pathology) (Fauser and Schulze-Bonhage, 2006; Levesque *et al*., 1991), may also be seizure generators in TLE.

In general, intracerebral recordings have demonstrated that ictal patterns in mesial TLE (MTLE) are frequently first recorded from the hippocampus or simultaneously from the hippocampus and the amygdala. Although latencies between involvement of hippocampus and amygdala are often brief, an origin confined to the amygdala with some delay to the propagation to the hippocampus (*e.g*. five seconds) suggests an amygdalar seizure onset, which is found in only approximately 5% of patients with appropriate intracerebral recordings (Wieser, 2000). In a subsequent study, the Montreal group used phase-coherence analysis (Gotman and Levtova, 1996) and found that the amygdala was leading in 21% of focal mesial and in 53% of regional temporal lobe seizures. The hippocampus was leading in 48.5% of focal mesial and in 27% of regional temporal lobe seizures. In the remaining seizures, discharges were synchronous in these two structures.

In our patient, seizure onset in the amygdala and temporal pole clearly preceded hippocampal involvement, although both structures were part of the irritative zone and zone of early propagation. Involvement of

the hippocampus was thus considered to be secondary to the epileptogenic region in the anterior temporal lobe. The selective surgery performed in this patient with non-specific MRI and PET findings demonstrates that targeting the seizure onset zone and leaving a functional hippocampus intact may not only be efficacious but may also improve cognitive performance. In the case presented, the patient was highly dependent on unimpaired cognitive functioning and was not willing to take any risk associated with removal of a presumably normal functioning hippocampus. In the end, the epileptogenic zone was not completely removed during the limited resection, nevertheless, with the introduction of a second antiepileptic drug, the patient has now been rendered seizure-free for more than two years, and according to his unimpaired cognitive functioning, he is able to meet the demands of an international management position in his company. Consistent with the report of Fauser *et al*. (2008), the brief duration of epilepsy was likely to have offered good seizure outcome.

Selective approaches to TLE have been reported in recent case series. Takaya *et al*. (2009) described the effects of subtemporal SAH (selective amygdalohippocampectomy) in cognition and cerebral metabolism by means of FDG-PET in MTLE patients. A postoperative improvement was observed in delayed recall and attention/concentration scores, regardless of the resected side. PET analysis suggested that the selective subtemporal resection improved cerebral glucose metabolism in areas receiving projections from the affected mesial temporal lobe. These results would support the notion that cognitive improvement might result from seizure control and minimised postoperative functional impairment (Takaya *et al*., 2009). Kanner *et al*. (1995) reported 24 patients with anterotemporal seizure focus, referred for tailored anterior temporal lobectomy. In this series, the extent of resection was tailored by intraoperative electrocorticographic findings and functional mapping of eloquent cortex. In six patients, the amygdala and hippocampus were spared, nine patients had partial to total resection of the amygdala, eight patients had resection of the amygdala and anterior third of the hippocampus and one patient underwent resection of the amygdalum and anterior two thirds of the hippocampus. Complete or almost complete seizure relief (Engel class I) was achieved in 21 of the 24 patients; three patients had rare persisting seizures (Engel class II). These results suggested that sparing or limiting resection of the mesial temporal structures in appropriately selected patients with anterotemporal seizure focus is not necessarily associated with a poor seizure outcome, provided that the decision not to resect the hippocampus is based on an absence of epileptiform activity during intraoperative electrocorticography or extraoperative recordings using intracranial electrodes (Kanner *et al*., 1995).

Patients with epilepsy secondary to temporo-apical lesions visible on MRI may also benefit from highly selective approaches. Elsharkawy *et al*. (2011) reported related findings in a series of 61 patients with lesions in the apex of the temporal lobe and normal hippocampal aspect on MRI as well as intact memory function. These subjects underwent apical temporal resection, sparing the mesial temporal structures and contributed to the 80.9% of cases of Engel Class 1 at two years of follow-up. Memory outcome was favourable in most of patients while worsening was observed in only two patients (3.2%) (Elsharkawy *et al*., 2011).

Regarding lateralisation of cognitive functions, most authors describe patients with right-sided MTLE to show frequently impaired visuospatial memory performance (Fauser and Schulze-Bonhage, 2006; Giovagnoli *et al*., 1995; Ladavas *et al*., 1979; Majdan *et al*., 1996), caused by the underlying structural damage and epilepsy or after resection of the hippocampus. Glikmann-Johnston *et al*. (2008) reported on a series of TLE patients in which an extended assessment of spatial memory and hippocampal volumetry was performed. This analysis revealed that visuospatial memory impairment was neither dependent on the side of resection in ATL patients (anterior temporal lobectomy) nor on the side of hippocampal atrophy in unilateral non-operated TLE patients (Glikmann-Johnston *et al*., 2008). In order to explore the relationship between visuospatial memory and hippocampal metabolism, PET scans were performed in healthy participants during navigation-related tasks. As result, bilateral hippocampal activation was observed. Predominance at the right hippocampus was only detected by accurate navigation (Maguire *et al*., 1998). These findings suggest that visuospatial memory may relate to the integrity of both temporal lobe structures and the concept of task specificity could represent a useful description of patterns of lateralisation of visuospatial memory (Glikmann-Johnston *et al*., 2008; Saling, 2009).

In our case there was no impairment of visuospatial memory prior to or after surgery which suggests functional hippocampal integrity. An extensive literature review of clinical aspects after epilepsy surgery revealed an average rate of verbal memory decline in TLE patients of 44% for those operated on the left side versus 20% operated on the right side. For visual memory, the risk of loss was similar for both right and left temporal resections (23% and 21%, respectively) (Sherman *et al*., 2011). Even if the risk of visual memory loss is lower than that for verbal memory, superselective approaches may further decrease the risk of impairment. Postsurgical maintenance of hippocampal

functional integrity of our patient was evident from neuropsychological assessment three months after surgery, which revealed a stable general cognitive performance as well as an improvement of attention and visual planning. This postoperative functional recovery may have been promoted by a reduction of interictal spiking and complex partial seizures during the daytime. The standardised neuropsychological follow-up was relatively short, however, at two years after surgery the patient did not report any deterioration in declarative memory functions and was successful in his professional life. Our patient had normal functional memory and a hippocampus with normal appearance; this patient group has only recently been shown to be at particular risk of memory decline following resection of the hippocampus (Helmstaedter *et al*., 2011).

Current evidence supports the utility of highly selective surgical approaches in specific patients, aiming at the prevention of progressive cognitive deterioration due to poor seizure control. In contrast, total resection of the temporal lobe including the hippocampus may be associated with a higher risk of memory decline (Clusmann *et al*., 2002) and larger neocortical resections may correlate with cognitive impairment, which has been shown, at least, on the language dominant side (Alpherts *et al*., 2008). Material-specific memory aspects after transsylvian SAH were compared to those after temporal pole resection with amygdalohippocampectomy (TPR+). Figural memory outcome was worse after right-sided surgery, mainly when the temporal pole was included (TPR+). Attention improved, independent of side or type of surgery, and language functions showed some improvement after right-sided surgery (Helmstaedter *et al*., 2008). This further points to the positive role of superselective surgical approaches; preservation of memory in our patient suggests that hippocampal sparing had a positive effect, whereas resection of the pole and amygdala alone may be well tolerated. In addition to the preservation of functional tissue, the effect on networks (Frings *et al*., 2009), including the contralateral temporal lobe, may contribute to postoperative improvement in cognition. Spectroscopic investigations may demonstrate these effects (Vermathen *et al*., 2002).

With the goal to use minimally invasive surgical modalities, several authors have performed stereotactic lesioning of limbic targets and in particular, the amygdala, as treatment for TLE. Reviewing the literature, Ojemann and Ward (1975) and Ravagnati (1987) concluded that overall results of stereotactic approaches were inferior compared to resective surgery. Regarding the treatment of TLE due to amygdalar epilepsy, only limited data on long-term efficacy of amygdalotomy are available (Hood *et al*., 1983; Narabayashi and Mizutani, 1970; Narabayashi, 1976; Ravagnati, 1987; Siegfried and Wieser, 1988). Research is ongoing to define the number of patients who are completely "cured" (*i.e.* seizure-free for several years without taking antiepileptic drugs [AEDs]) by epilepsy surgery versus a switch to pharmacoresponsiveness. In the study of Schmidt *et al*. (2004), following temporal lobe surgery, approximately one in four adult patients were reported to become seizure-free for five years without AEDs. However, as 55% of patients preferred not to discontinue their medication despite seizure freedom, it is impossible to know if they were cured.

It is possible that more selective approaches may be associated with a higher dependency of pharmacotherapy, as well as later relapse. Wieser (2000) reported the case of a patient with amygdalar epilepsy who was referred for stereotactic amygdalotomy. After a seizure-free outcome of 11 years, he required selective amygdalohippocampectomy due to recurrent seizures. Therefore, the long-term outcome of our patient concerning his seizures as well as memory functions should be observed. However, even considering these risks, particular aspects, such as the high cognitive demand necessary for the patient's professional position reported here, may turn the balance in favour of a limited resection which has allowed him to advance in his career in the years following epilepsy surgery.

Epileptic foci can be very limited (Fauser and Schulze-Bonhage, 2004) and even electrode impalement can have a curative effect (Schulze-Bonhage *et al*., 2010). Thus, additional options of even more focused approaches may be chosen for appropriate patients. Constant advances in the methodology available for presurgical investigation allow for a more refined identification of targets for epilepsy surgery. Further studies with longer follow-up are required to define the role of superselective approaches in patients with a very localised epileptogenic zone. □

Disclosure.
None of the authors has any conflict of interest or financial support to disclose.

References

Alpherts WCJ, Vermeulen J, van Rijen PC, da Silva FHL, van Veelen CWM. Standard versus tailored left temporal lobe resections: differences in cognitive outcome? *Neuropsychologia* 2008; 46: 455-60.

Clusmann H, Schramm J, Kral T, *et al*. Prognostic factors and outcome after different types of resection for temporal lobe epilepsy. *J Neurosurg* 2002; 97: 1131-41.

Commission on classification and terminology of international league against epilepsy: proposal of revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989; 30: 389-99.

Elsharkawy AE, Pannek H, Woermann FG, *et al*. Apical temporal lobe resection; "tailored" hippocampus-sparing resection based on presurgical evaluation data. *Acta Neurochir (Wien)* 2011; 153: 231-8.

Fauser S, Schulze-Bonhage A. How large must an epileptic focus be to cause an electrographic status epilepticus - a case report. *Clin Neurophysiol* 2004; 115: 2274-9.

Fauser S, Schulze-Bonhage A. Epileptogenicity of cortical dysplasia in temporal lobe dual pathology: an electrophysiological study with invasive recordings. *Brain* 2006; 129: 82-95.

Fauser S, Bast T, Altenmüller D, *et al*. Factors influencing surgical outcome in patients with focal cortical dysplasia. *J Neurol Neurosurg Psychiatr* 2008; 79: 103-5.

Frings L, Schulze-Bonhage A, Spreer J, Wagner K. Remote effects of hippocampal damage on default network connectivity in the human brain. *J Neurol* 2009; 256: 2021-9.

Giovagnoli AR, Casazza M, Avanzini G. Visual learning on a selective reminding procedure and delayed recall in patients with temporal lobe epilepsy. *Epilepsia* 1995; 36: 704-11.

Glikmann-Johnston Y, Saling MM, Chen J, *et al*. Structural and functional correlates of unilateral mesial temporal lobe spatial memory impairment. *Brain* 2008; 131: 3006-18.

Gloor P. Mesial temporal sclerosis: historical background and an overview from a modern perspective. In: Lüders H. *Epilepsy surgery*. New York: Raven, 1991: 689-703.

Gotman J, Levtova V. Amygdala-hippocampus relationships in temporal lobe seizures: a phase-coherence study. *Epilepsy Res* 1996; 25: 51-7.

Helmstaedter C, Richter S, Röske S, *et al*. Differential effects of temporal pole resection with amygdalohippocampectomy versus selective amygdalohippocampectomy on material-specific memory in patients with mesial temporal lobe epilepsy. *Epilepsia* 2008; 49: 88-97.

Helmstaedter C, Petzold I, Bien CG. The cognitive consequence of resecting nonlesional tissues in epilepsy surgery-Results from MRI- and histopathology-negative patients with temporal lobe epilepsy. *Epilepsia* 2011; 52: 1402-8.

Hood TW, Siegfried J, Wieser HG. The role of stereotactic amygdalotomy in the treatment of temporal lobe epilepsy associated with behavioural disorders. *Appl Neurophysiol* 1983; 46: 19-25.

Kanner AM, Kaydanova Y, de Toledo-Morrell L, *et al*. Tailored anterior temporal lobectomy. Relation between extent of resection of mesial structures and postsurgical seizure outcome. *Arch Neurol* 1995; 52: 173-8.

Ladavas E, Umilta C, Provinciali L. Hemisphere-dependent cognitive performances in epileptic patients. *Epilepsia* 1979; 20: 493-502.

Levesque MF, Nakasato N, Vinters HV, Babb TL. Surgical treatment of limbic epilepsy associated with extrahippocampal lesions: the problem of dual pathology. *J Neurosurg* 1991; 75: 364-70.

Maguire EA, Burgess N, Donnett JG, *et al*. Knowing where and getting there: a human navigation network. *Science* 1998; 280: 921-4.

Majdan A, Sziklas V, Jones-Gotman MJ. Performance of healthy subjects and patients with resection from the anterior temporal lobe on matched tests of verbal and visuoperceptual learning. *J Clin Exp Neuropsychol* 1996; 18: 416-30.

Narabayashi H. Lessons from amygdaloid surgery in long-term observation. In: Gillingham FJ, Hitchcock ER, Nádvornik P. *Stereotactic treatment of epilepsy*. *Acta Neurochir* 1976; 23: 241-5.

Narabayashi H, Mizutani T. Epileptic seizures and the stereotactic amygdalotomy. *Confinia Neurol* 1970; 32: 289-97.

Ojemann GA, Ward Jr. AA. Stereotactic and other procedures for epilepsy. In: Purpura DP, Penry JK, Walter RD. *Adv Neurol* 1975; 8: 241-63.

Ravagnati L. Stereotactic surgery for epilepsy. In: Wieser HG, Elger CE. *Presurgical evaluation of epileptics*. Heidelberg, New York: Springer, 1987: 361-71.

Saling MM. Verbal memory in mesial temporal lobe epilepsy: beyond material specificity. *Brain* 2009; 132: 570-82.

Schmidt D, Baumgartner C, Löscher W. The chance of cure following surgery for drug-resistant temporal lobe epilepsy. What do we know and do we need to revise our expectations? *Epilepsy Res* 2004; 60: 187-201.

Schulze-Bonhage A, Dennig D, Wagner K, *et al*. Seizure control resulting from intrahippocampal depth electrode insertion. *J Neurol Neurosurg Psychiatr* 2010; 81: 352-3.

Semah F, Picot MC, Adam C, *et al*. Is the underlying cause of epilepsy a major prognostic factor for recurrence? *Neurology* 1998; 51: 1256-62.

Sherman EMS, Wiebe S, Fay-McClymont TB, *et al*. Neuropsychological outcomes after epilepsy surgery: systematic review and pooled estimates. *Epilepsia* 2011; 52: 857-69.

Siegfried J, Wieser HG. The actual role of stereotactic operations on deep brain structures in the treatment of medically refractory epilepsies. In: Broggi G. *The rational basis of the surgical treatment of epilepsies* (*Current Problems in Epilepsy 5)*. London, Paris: John Libbey, 1988: 113-9.

Takaya S, Mikuni N, Mitsueda T, *et al*. Improved cerebral function in mesial temporal lobe epilepsy after subtemporal amygdalohippocampectomy. *Brain* 2009; 132: 185-94.

Vermathen P, Ende G, Laxer KD, *et al*. Temporal lobectomy for epilepsy: recovery of the contralateral hippocampus measured by (1)H MRS. *Neurology* 2002; 59: 633-6.

Volcy Gomez M. Mesial temporal lobe epilepsy: its physiopathology, clinical characteristics, treatment and prognosis. *Rev Neurol* 2004; 38: 663-7.

Watson C, Andermann F, Gloor P, *et al*. Anatomic basis of amygdaloid and hippocampal volume measurement by magnetic resonance imaging. *Neurology* 1992; 42: 1743-50.

Wieser HG. Mesial temporal lobe epilepsy versus amygdalar epilepsy: late seizure recurrence after initially successful amygdalotomy and regained seizure control following hippocampectomy. *Epileptic Disord* 2000; 2: 141-52.

Zentner J, Wolf HK, Helmstaedter C, *et al*. Clinical relevance of amygdala sclerosis in temporal lobe epilepsy. *J Neurosurg* 1999; 91: 59-67.