Acta Neurochir (2012) 154:1337–1342
DOI 10.1007/s00701-012-1379-0

CLINICAL ARTICLE

Neuropsychological outcome after extra-temporal epilepsy surgery

Yassine El Hassani · Maryll Fournet · Shahan Momjian · Claudio Pollo · Margitta Seeck · Alan Pegna · Karl Schaller

Received: 31 December 2011 / Accepted: 1 May 2012 / Published online: 12 May 2012

Abstract
Background The neuropsychological results of temporal lobe epilepsy surgery are well reported in the literature. The aim of this study was to analyse the neuropsychological outcome in a consecutive series of patients with extra-temporal epilepsy.
Methods We retrospectively analysed the data of patients operated between 1996 and 2008 for extra-temporal epilepsy. Standard neuropsychological tests were applied. We assessed the neuropsychological outcome after surgery and the correlation of the neuropsychological outcome with (1) side and localisation of surgery, (2) Engel scale for seizure outcome and (3) timing of surgery.
Findings Patients had a better neuropsychological outcome when undergoing non-frontal resection [$\chi2$ (2) =6.66, p=0.036]. Subjects who had undergone left or right resection showed no difference in outcome [$\chi2$ (2) =0.533, p=0.766]. The correlation between the Engel scale for seizure re-occurence and the neuropsychological scores showed only a tendency for better outcome (Spearman $\rho=-0.437$; p=0.069). The global measure of change did not correlate significantly with delay of surgery (Spearman $\rho=-0.163$; p=0.518).
Conclusions Resective epilepsy surgery improves neuropsychological status outcome in patients with extra-temporal epilepsy even if the patient did not become seizure free. The outcome is better for non-frontal localisation.

Keywords Resective surgery · Extratemporal epilepsy · Neuropsychology

Y. El Hassani (✉) · S. Momjian · K. Schaller
Department of Neurosurgery, Geneva University Hospitals,
Rue Gabrielle-Perret-Gentil 4 (ex-rue Micheli-du-Crest 24),
1211 Genève 14, Switzerland
e-mail: yassine.elhassani@hcuge.ch

M. Fournet · M. Seeck · A. Pegna
Department of Neurology, Geneva University Hospitals,
Geneva, Switzerland

C. Pollo
Department of Neurosurgery,
Centre Hospitalier Universitaire Vaudois,
Lausanne, Switzerland

Introduction

Approximately 20 % to 40 % of individuals with a diagnosis of chronic epilepsy have seizures that are not adequately controlled by antiepileptic drugs [10, 13, 17]. Extra-temporal epilepsy refers to seizure originating from outside the temporal lobe and accounts for around one third of all cases [27].

In light of the above, resective surgery has been proved to be an important and effective treatment for many patients with pharmaco-resistant epilepsy [14, 15]. Surgery for extra-temporal epilepsy represents the minority of interventions with approximately 15–20 % of resective surgical cases [7, 9].

Detailed neuropsychological testing is indispensable for the pre-surgical evaluation as well as the post-surgical outcome analysis, as it allows focus determination and case selection [22].

However, the majority of neuropsychological studies have focussed on temporal epilepsy with less interest to extra-temporal epilepsy, because of the paucity of the latter cases. Therefore, this study addresses the question whether resective epilepsy surgery improves the neuropsychological outcome. Our hypothesis was that neuropsychological functioning should improve globally after surgery.

Methods and materials

Patients

We retrospectively analysed the data of all the patients investigated in the epilepsy unit of the department of neurology (n=457) between 1996 and 2008.

Among the patients who underwent surgery (n=261), (n=146) were operated for temporal epilepsy and (n=63) for extra-temporal epilepsy.

In order to ensure a reliable comparison between the pre- and postoperative data and the homogeneity of neuropsychological testing, we excluded (1) patients younger than 12 years, (2) patients with no postoperative follow-up in our centre, (3) patients who underwent more than one surgical procedure, (4) patients who underwent hemispherotomy and those who underwent vagus nerve stimulation. Therefore, our final sample consisted of 18 subjects aged 12 to 55 years at the time of surgery (mean=28.4 years; SD=12.7 years); 61 % (n=11) were women and 39 % were men (n=7). Subjects had a follow-up of 3 to 120 months (mean=14 months) after surgery. The latest examination was considered to estimate the prognosis.

Neuropsychological assessment

Patients went through standard neuropsychological examination investigating various cognitive functions. Language abilities were assessed by image naming using a short version of the Boston naming test [30], oral fluency tests including semantic and alphabetical cues (respectively animals names and words beginning with the letters "P" or "S" over a 2-min period) [3], and a clinical evaluation of written language (reading aloud, writing sentences spontaneously or under dictation).

Clinical evaluations of calculation on oral and written modalities, of visual agnosia and upper limb apraxia were also performed. Executive functioning was investigated with Luria's alternating graphic sequences [19], non-verbal fluency test [24], the Victoria version of the Stroop test [26] and Trail Making Test [19]. Verbal and visuospatial spans were assessed using forward digits span with three trials for each span length and the Corsi Block Tapping Test with the same procedure [19]. Episodic memory tests were used in both verbal and visual modalities with adaptations of the Rey Auditory-Verbal Learning Test [19] and the Rey Visual Design Learning Test [26].

Outcome analysis

To assess the evolution of the neuropsychological state, we compared the preoperative and the last neuropsychological assessment as available from our database.

According to the sample size, descriptive statistics on specific neuropsychological functions and inferential tests give a global outcome indicator. This was consistent with test our hypothesis that neuropsychological functioning should globally improve after surgery. We thus chose to determine the frequency of deterioration, the absence of change and the improvement across subjects for each test.

The criteria to attribute the scores were the following: if a negative evolution was seen in three or more tests (≥3), the patient was considered to have deteriorated. If a positive evolution was seen in three or more tests (≥3), the patient was considered to have improved. Any change in fewer than two tests (≤2) was considered an absence of change.

Change in performance itself was defined as improvement or deterioration in normative data of at least 1 point on the z-score or 34 points if centiles were used. When functions were not investigated with standardised tasks (e.g., writing, visual gnosia), a rating was given by a trained examiner.

The side (left-right) of surgery and the localisation of resection were analysed too. The anterior localisation represents the frontal resection, and the posterior localisation represents the remaining lobes (insular, parietal and occipital).

Epileptological outcome was assigned according to the Engel classification scheme: class I, seizure free or auras only since surgery; class II, rare seizures (<2/year or only non-disabling nocturnal seizures); class III, reduction of seizure frequency>75 %; and class IV, unchanged (<75 % reduction of seizure frequency) [11].

Correlations were investigated between the neuropsychological outcome and (1) the side of surgery; (2) localisation of surgery; (3) delay between age of onset seizures and surgery; (4) Engel scale for seizure occurrence evolution. Statistical analysis was performed using the SPSS 16.0 software for Windows.

Results

Patient’s characteristics

Eighteen patients were analysed; 61 % (n=11) were women and 39 % (n=7) were men. The mean age of surgery was 28 (12–55) years. The mean delay of surgery was 15.5 (1–37) years.

Imaging and epileptological workup

Indication for surgical intervention depended on the congruence of the EEG, MRI findings, PET and SPECT. In 33 % (n=6) patients, the non-invasive investigations did not allow identification of an epileptogenic focus, and they underwent invasive investigations with subdural grids, strip electrodes and depth electrodes, respectively.

Resective surgery

Equal numbers of patients (n=9) underwent operations on the left and right hemispheres; 45 % (n=8) had an anterior (frontal) localisation, and 55 % (n=10) had a posterior (insular, parietal and occipital) localisation (see Table 1).

Operative complications

Thirty-three percent (n=6) had no operative complications. For the remaining 64 % (n=12) complicated patients, 28 % (n=5) of the patients had transient neurological deficits. This figure also takes into account the "expected consequences" when resecting a part of an eloquent region, such as a visual field defect in the occipital region. 11 % (n=2) presented as a persistent visual field defect. Eleven percent (n=2) had to be re-operated, one for epidural haematoma and one for hydrocephalus with ventriculo-peritoneal shunting. All infections were controlled by adapted antibiotics (see Table 2).

Table 1 Repartition by side, localisation, neuropsychological scoring and Engel classification

Patient	Side	Localisation	Neuropsychological scoring	Engel classification at last control
1	Left	Anterior	Worsing	1
2	Right	Posterior	Improvement	1
3	Left	Posterior	Improvement	1
4	Right	Posterior	Improvement	1
5	Left	Posterior	Improvement	1
6	Left	Posterior	No change	4
7	Right	Anterior	Worsing	2
8	Left	Anterior	No change	1
9	Left	Posterior	Improvement	1
10	Left	Anterior	No change	4
11	Right	Posterior	Improvement	1
12	Right	Anterior	Worsing	2
13	Left	Posterior	Improvement	1
14	Right	Anterior	Improvement	1
15	Right	Anterior	No change	1
16	Left	Posterior	Improvement	1
17	Right	Posterior	No change	1
18	Right	Anterior	Improvement	3

Pathology

There was only one patient with normal histological findings. The remaining cases were abnormal with 28 % (n=5) cases of focal cortical dysplasia, 17 % (n=3) with cavernomas, 11 % (n=2) with oligodendrogliomaand 11 % (n=2) with dysembryoplastic neuroepithelial tumours (see Table 2).

Engel classification outcome

At the last control at 3 to 120 months (mean=14 months), 72 % (n=13) were Engel class I, 11 % (n=2) were Engel class II, 5 % (n=1) were Engel class III and 11 % (n=2) were Engel class IV (see Table 1).

Neuropsychological outcome

The hypothesis was that an improvement of cognitive functioning should be observed after surgery. This hypothesis was then tested against theoretical results "expected results", where no improvement after surgery would appear. This was implemented as 50 % subjects with deterioration, 50 % with no change in cognitive function and none with improvement.

On the preoperative neuropsychological assessment, most of patients had a deficit in a several cognitive functions. Preoperative results showed 45 % (n=8) language deficit, 17 % (n=3) praxis skills deficit, 55 % (n=10) attentionnal skills deficit, 72 % (n=13) executive function deficit, 50 % (n=9) verbal memory deficit and 33 % (n=6) visual memory deficit.

Postoperative results showed 45 % (n=8) language deficit, 17 % (n=3) praxis deficit, 39 % (n=7) attentionnal skills deficit, 61 % (n=11) executive function deficit, 33 % (n=6) verbal memory deficit and 28 % (n=5) visual memory deficit.

Our results showed a significant difference between the expected and the observed distribution [$\chi 2$ (2)=52,485.89, p=0.0001] with only 17 % (n=3) of patients showing a decrease in the postoperative results, 28 % (n=5) showing an absence of change and 55 % (n=10) showing an improvement.

Independent chi-square tests were then performed to determine any difference in neuropsychological outcome regarding the side and localisation of surgery. The results indicate that the distribution of scores according to localisation of surgery is significantly different from a random effect [$\chi 2$ (2) =6.66, p=0.036] with a better outcome for patients who underwent posterior (insular, parietal and occipital) resection; chi-square concerning the side of surgery was not significant [$\chi 2$ (2) =0.533, p=0.766] for subjects

Table 2 Repartition by localisation, pathology and complications

Patient	Side/localisation	Pathology	Complications
1	Left frontal lobectomy	Focal cortical dysplasia	None
2	Right parieto-occipital lesionectomy	Oligodendroglioma grade III	Persistant hemianopsia
3	Left parietal lesionectomy	Subcortical hypomyelinisation, ectopic neuron	Infection, regressive Gerstmann syndrome
4	Right parietal lobectomy	Periventricular heterotopia, polymicrogyria	Regressive hemianopsia
5	Left parietal cortectomy, lesionectomy	Tuberous sclerosis	Epidural haematoma evacuated surgically
6	Left cingulotomy	Normal	None
7	Right frontal lobectomy	Post-traumatic fibrosis	Parenchymal haematoma, infection
8	Left frontal cortectomy, lesionectomy	Focal cortical dysplasia	Regressive left paresis
9	Left parietal cortectomy	DNET	None
10	Left frontal lobectomy	Post-traumatic fibrosis	Infection
11	Right occipital lesionectomy	DNET	Persistant quadranopsia
12	Right frontal lobectomy	Oligodendrogliome grade II	Hydrocephalus shunted
13	Left insular and singular lesionectomy	Cavernoma	Left hyposmia
14	Right frontal lesionnectomy	Cavernoma	None
15	Right frontal lobectomy	Focal cortical dysplasia	Regressive left hemiparesis
16	Left parieto-occipital lesionectomy	Focal cortical dysplasia	None
17	Right insular lesionectomy	Cavernoma	Regressive left hemiparesis
18	Right frontal lesionectomy	Focal cortical dysplasia	None

who had undergone left and right resection showing the same pattern of evolution.

The correlation with the global cognitive outcome and the Engel scale for seizure occurrence evolution showed a strong tendency for a better outcome (Spearman $\rho=-0.437$; $p=0.069$), but did not reach significance. Furthermore, our global measure of change did not correlate significantly with the delay between the onset of seizures and the time of surgery (Spearman $\rho=-0.163$; $p=0.518$).

Discussion

Epilpetogenic outcome

Patients with extra-temporal lobe epilepsy are often particularly difficult to treat medically, and they are often equally difficult surgical candidates [12]. Some authors report that in extra-temporal pharmaco-resistant epilepsy, the outcome after cortical resection is less certain and the prognosis is generally less favourable than in temporal pharmaco-resistant epilepsy [2, 14]. However, a strictly unifocal, interictal epileptiform pattern on the scalp EEG can predict a successful post-surgical outcome in these patients [14].

In view of the above, the success rate for operations for extra-temporal epilepsies is lower when compared to temporal lobe epilepsy, with seizure-free rates varying from 55 % to 85 % for temporal locations and from 30 % to 60 % for extra-temporal locations [6, 15, 25, 31].

Patients with temporal lobe epilepsy have a 2.7-fold higher chance to benefit from surgery than patients with extratemporal lobe epilepsy. Within both groups, the presence of structural epileptogenic lesions is also related to a 2–3 times higher chance to become seizure-free postoperatively, as identified in a recent review [29]. Histological abnormalities were associated with significantly better outcomes in a study of 60 patients with extratemporal lobe epilepsy [32]. In our series 72 % (n=13) became seizure-free, and only one patient had normal histological findings.

Until the last 2 decades, surgical outcome in epilepsy surgery has been evaluated in terms of the degree of seizure reduction or cessation of seizures. However, recent clinical studies have shown that seizure reduction or cessation cannot be the sole and ultimate goal of epilepsy surgery, since patients who had been seizure-free may have serious psychosocial problems that might be intolerable, causing a poor quality of life [28]. Kim et al. reported that the most common morbidity after extratemporal resective surgery is hemiparesis in 18 % of cases [16]. In our data 17 % (n=3) presented a transient postoperative hemiparesis. In a series collected by Cascino et al. 8 % of patients required a surgical procedure to treat the operative complication [4]. This is in line with our findings, as we had to re-operate 11 % (n=2) of our patients.

Neuropsychological outcome

Cognitive function is now recognised as a critical component of quality of life in patients with epilepsy and is now included along with seizure control as an important outcome variable in research studies on the efficacy of medication treatment and the effect of resective surgery [1, 8].

Thus, neuropsychology has played a prominent role throughout the modern era of epilepsy surgery. It was employed originally to identify patients at risk for significant postoperative memory impairment after anterior temporal lobectomy for bilateral mesial temporal lobe dysfunction [21]. Neuropsychological evaluation is based on comparing the patient's performances on a variety of standardised tests and questionnaires to norms derived from the general population [18]. Previously, we demonstrated that the use of a post-ictal neuropsychological examination can yield lateralising and sometimes localising information, even for extra-temporal foci [23].

There are only a few studies looking specifically into the cognitive and psychosocial outcome of adult patients with extratemporal lobe epilepsy. The first prospective clinical study focussing on quality of life specifically in patients with extra-temporal epilepsy was performed by Tanriverdi in 23 patients, and the main finding of their results was that surgery clearly improved the overall quality of life compared to the preoperative status [27, 28].

In our series 55 % (n=10) of the patients showed an improvement in their neuropsychological status, and only 17 % (n=3) of the patients exhibited a worse neuropsychological status compared to the preoperative one. Descriptive statistics indicate that improvement occurred mainly for memory, executive functions and attention. Patients operated on at anterior localisations tended to have a better recuperation in visual memory. Patients operated on at posterior localisations tended to have a better outcome in language and executive functions. More studies should be done with larger samples and inferential analysis to investigate which cognitive functions have better prognoses. Comparison between the global cognitive outcome and the Engel scale for postoperative seizure occurrence showed a strong tendency for a better cognitive performance of patients with class I or II.

Our global measure of change did not correlate significantly with the delay time of surgery in our patient population. This might be different in smaller children, where the rapid diagnosis of pharmacoresistance and referral to surgical treatment, if indicated, is much more crucial [5]. Since the immature brain is supposedly more adaptive than the mature one, children may recover functions to a better degree after surgery and thus are subject to separate studies, albeit there are not many [20].

In a series of 126 patients with extra-temporal epilepsy presented by Holmes, the specific locations from which seizures arose did not have a significant relationship with outcome. Moreover, the time of operation, gender, family history of epilepsy and the presence of focal neurological signs also had no significant relationship with outcome [14]. Our results are in general in line with these observations; however, our findings suggest that patients with a frontal resection had a worse prognosis in terms of seizure outcome. Descriptive statistics suggest that these patients show a preoperative deficit in linguistic skills, attention and verbal memory more frequently. Also they tend to present a less positive outcome in language and executive function than patients operated on at posterior sites. However, we need further investigations with a larger sample size and inferential statistics. This may help to establish a prognosis regarding to the preoperative deficit.

Our study provided encouraging results for patients with surgically amenable extratemporal lobe epilepsy. Most patients improved or remained stable, a finding that may help in the counselling of patients. This report nevertheless has several limitations: first, it is based on retrospective and small sample size data; second, extratemporal epilepsy varies by hemisphere, lobe (with some being multilobar) and surgical approach; third, it is restricted to adult patients who may differ from paediatric patients in terms of their cerebral plasticity and potential for cognitive recovery.

Conclusion

Surgery in extra-temporal epilepsy is safe and beneficial; the results presented herein suggest that epilepsy and neuropsychological outcome significantly improve. A large sample size will provide clinically more reliable and meaningful information.

Conflicts of interest None.

References

1. Barr WB (2007) Epilepsy and neuropsychology: past, present, and future. Neuropsychol Rev 17:381–383
2. Berg A VB (1998) Outcome measures In: Engel Jr J PT, editors (ed) Epilepsy :a comprehensive textbook. Lippincott-Raven Philadelphia, pp 1891–1899
3. Cardebat D, Doyon B, Puel M, Goulet P, Joanette Y (1990) Evocation lexicale formelle et sémantique chez des sujets normaux: performances et dynamiques de production en fonction du sexe, de l'âge et du niveau d'études. Acta Neurol Belg 90:207–217
4. Cascino GD, Sharbrough FW, Trenerry MR, Marsh WR, Kelly PJ, So E (1994) Extratemporal cortical resections and lesionectomies for partial epilepsy: complications of surgical treatment. Epilepsia 35:1085–1090
5. Centeno RS, Yacubian EM, Sakamoto AC, Ferraz AF, Junior HC, Cavalheiro S (2006) Pre-surgical evaluation and surgical treatment in children with extratemporal epilepsy. Childs Nerv Syst 22:945–959
6. Cohen-Gadol AA, Wilhelmi BG, Collignon F, White JB, Britton JW, Cambier DM, Christianson TJ, Marsh WR, Meyer FB, Cascino GD (2006) Long-term outcome of epilepsy surgery among 399 patients with nonlesional seizure foci including mesial temporal lobe sclerosis. J Neurosurg 104:513–524

7. Elsharkawy AE, Behne F, Oppel F, Pannek H, Schulz R, Hoppe M, Pahs G, Gyimesi C, Nayel M, Issa A, Ebner A (2008) Long-term outcome of extratemporal epilepsy surgery among 154 adult patients. J Neurosurg 108:676–686
8. Elsharkawy AE, Pannek H, Schulz R, Hoppe M, Pahs G, Gyimesi C, Nayel M, Issa A, Ebner A (2008) Outcome of extratemporal epilepsy surgery experience of a single center. Neurosurgery 63:516–525, discussion 525–516
9. Engel J Jr (1996) Surgery for seizures. N Engl J Med 334:647–652
10. Engel J Jr (2001) Intractable epilepsy: definition and neurobiology. Epilepsia 42(Suppl 6):3
11. Engel Jr J VNP, Rasmussen TB, Ojemann LM (1993) Outcome with respect to epileptic seizures. In: Engel JE (ed) Surgical Treatment of The Epilepsies. Raven Press New York, pp 609–622
12. Gartner B, Seeck M, Michel CM, Delavelle J, Lazeyras F (2004) Patients with extratemporal lobe epilepsy do not differ from healthy subjects with respect to subcortical volumes. J Neurol Neurosurg Psychiatry 75:588–592
13. Gursahani R (2008) Management in refractory epilepsy: beyond epilepsy surgery. J Pediatr Neurosci 3:35–40
14. Holmes MD, Kutsy RL, Ojemann GA, Wilensky AJ, Ojemann LM (2000) Interictal, unifocal spikes in refractory extratemporal epilepsy predict ictal origin and postsurgical outcome. Clin Neurophysiol 111:1802–1808
15. Kan P, Van Orman C, Kestle JR (2008) Outcomes after surgery for focal epilepsy in children. Childs Nerv Syst 24:587–591
16. Kim SK, Wang KC, Hwang YS, Kim KJ, Chae JH, Kim IO, Cho BK (2008) Epilepsy surgery in children: outcomes and complications. J Neurosurg Pediatr 1:277–283
17. Kwan P, Brodie MJ (2000) Early identification of refractory epilepsy. N Engl J Med 342:314–319
18. Lassonde M, Sauerwein HC, Gallagher A, Theriault M, Lepore F (2006) Neuropsychology: traditional and new methods of investigation. Epilepsia 47(Suppl 2):9–13
19. Lezak MD (1995) Neuropsychological assessment. Oxford University Press New York
20. Liu S et al (2007) Pediatric intractable epilepsy syndromes: reason for early intervention. Brain Dev 29(2):69–78
21. Loring DW (1997) Neuropsychological evaluation in epilepsy surgery. Epilepsia 38(Suppl 4):S18–S23
22. Matsuoka H (2001) Neuropsychology of epilepsy. Epilepsia 42 (Suppl 6):42–46
23. Pegna AJ, Qayoom Z, Gericke CA, Landis T, Seeck M (1998) Comprehensive postictal neuropsychology improves focus localization in epilepsy. Eur Neurol 40:207–211
24. Regard M, Strauss E et al (1982) Children's Production on verbal and non-verbal fluency tasks. Pcp Mot Skills 55:839–844
25. Schramm J, Clusmann H (2008) The surgery of epilepsy. Neurosurgery 62(Suppl 2):463–481, discussion 481
26. Spreen O, Strauss E (1998) A Compendium of Neuropsychological Tests. Administrations, norms and commentary. Oxford University Press New York
27. Tanriverdi T, Olivier NP, Olivier A (2008) Quality of life after extratemporal epilepsy surgery: a prospective clinical study. Clin Neurol Neurosurg 110:30–37
28. Tanriverdi T, Poulin N, Olivier A (2008) Psychosocial outcome after extratemporal epilepsy surgery: a prospective clinical study. Turk Neurosurg 18:114–124
29. Tellez-Zenteno JF, Hernandez Ronquillo L, Moien-Afshari F, Wiebe S (2010) Surgical outcomes in lesional and non-lesional epilepsy: a systematic review and meta-analysis. Epilepsy Res 89:310–318
30. Thuilliard Colombo F, Assal G (1992) Adaptation française du test de dénomination de Boston. Versions abrégées. Eur Rev of Appl Psychol 42:67–73
31. Tonini C, Beghi E, Berg AT, Bogliun G, Giordano L, Newton RW, Tetto A, Vitelli E, Vitezic D, Wiebe S (2004) Predictors of epilepsy surgery outcome: a meta-analysis. Epilepsy Res 62:75–87
32. Zentner J, Hufnagel A, Ostertun B, Wolf HK, Behrens E, Campos MG, Solymosi L, Elger CE, Wiestler OD, Schramm J (1996) Surgical treatment of extratemporal epilepsy: clinical, radiologic, and histopathologic findings in 60 patients. Epilepsia 37:1072–1080