Surgery of children with frontal lobe lesional epilepsy: Neuropsychological study

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Abstract

Aim of the study was to provide new data about the evolution of neuropsychological findings in patients with lesional frontal lobe epilepsy (FLE) operated on with lesion excision. Patients and methods Twelve patients with lesional FLE underwent full clinical examination including neurological, neuropsychological and developmental assessments, high-resolution magnetic resonance imaging (MRI), ictal and interictal prolonged EEG monitoring and evaluation of seizure semeiology before and after surgery. The mean follow-up duration was 2 years and 10 months (range = 14 months–7 years). Another group of lesional temporal lobe epilepsy, matched for the age at surgery and side of surgery, was likewise studied in order to compare neuropsychological patterns and to try to find out specific features in frontal lobe epilepsy evolution. Results All patients resulted seizure free at outcome except one belonging to Engel’s class II. Before surgery general intelligence was similar in FLE as well as in TLE group. Executive functions and motor coordination were frequently affected in FLE whereas patients with TLE often presented with deficits in naming, visual memory and visuo-spatial attention. After surgery there was a frequent decline of IQ in FLE group together with a slight deterioration, especially of executive functions in some patients. An improvement of behaviour was often observed in both groups. Conclusions As already reported in literature, neuropsychological pre-surgical data confirms the involvement of attention and executive functions in lesional FLE. No significant neuropsychological improvement was produced by surgery that determined in some cases a slight decline of general intelligence and specific frontal abilities. Yet, generally behaviour improved and seizures were controlled. © 2010 Published by Elsevier B.V.

Keywords: Frontal epilepsy; Epilepsy surgery; Child neurodevelopment

1. Introduction

Frontal lobe (FL) includes different anatomical areas accounting for several complex functions going from the motor to the higher cognitive competences. That is the cause of the known protean disorders that may arise from its injuries. However, it may be frequently hard to establish a direct relationship between injury site and kind of disorder due to the complex organization of this lobe.

Several neuropsychological studies are available concerning frontal lobe epilepsies (FLE) in children [1–9], when development is particularly florid with variable emergence times of frontal functions [10]. Morphological studies showed, in fact, that frontal lobes maturation occurs late in adolescence [11,12]. So, patterns of functions and quality of dysfunctions may largely vary with
children age. The variability of neuropsychological results depends also on the complex neuronal organization related to different brain areas and on the particular character of epileptogenesis in FLE [13] to which corresponds a large array of seizure patterns [14,15].

To the best of our knowledge, only one is the neuropsychological study on children affected with lesional FLE who underwent surgery [16]. Difficulty to diagnose FLE and the frequent poor outcome of patients operated on are the reasons evoked to account for the rare studies on this topic [16].

Aim of this study is to provide new information in the field by reporting the results of a neuropsychological study on 12 children operated on for lesional FLE whose age at surgery was between 1 and 15 years (six patients were 5 year old or less), with a follow-up period ranging between 2 and 7 years. A control group of lesional temporal lobe epilepsies (TLE) operated on was also included to compare neuropsychological patterns and try to find out specific features in frontal lobe epilepsies and their evolution after surgery.

2. Participants and methods

Twelve children affected with lesional FLE who was operated on at the Child Neurosurgery Unit of the Catholic University were enrolled in the study. In parallel, 12 other children with lesional TLE operated on in the same institution, matched for the age at surgery and side of surgery (six right and six left in each group), were enrolled too.

All the participants underwent full clinical examination including neurological and developmental assessment, high-resolution magnetic resonance imaging (MRI), ictal and interictal prolonged EEG monitoring, and evaluation of seizure semiology. The evaluation was performed before surgery and at the last follow-up control.

Neuropsychological assessment included global cognitive scales and specific function tests. Cognitive scales varied according to age. Griffiths' developmental scales (1996) [17] including five subscales (concerning locomotion, language, personal-social, performance, and eye-hand coordination) were used in the first four years of life. The general cognitive quotient was determined after 4 years using WIPPSI (Wechsler preschool and Primary Scale of Intelligence) at preschool age and WISC-R (Wechsler Intelligence Scale for Children-revised: 1992) [18] after the age of 6 years.

Specific abilities were assessed with:

Language: (a) Primary Language Test (PLT) for basic naming and comprehension in children younger than 3 years and (b) Language evaluation (Test di Valutazione del Linguaggio: TVL) [19] in children between 3 and 6 years; (c) Boston naming test in children between 6 and 12 years (Goodglass and Kaplan, 1972; Riva, 2000)); (d) Peabody test (comprehension in children between 6 and 12 years); (e) BADA test (Batteria per l’Analisi dei Deficit Afasici), lexical naming and comprehension beyond 12 years [22].

Memory tasks: (a) Verbal memory task, digit span and word learning list (immediate, delay recall and recognition) [23]; (b) Visual memory task, recall of a complex geometric figure design (Delayed recall of Rey–Osterreith complex figure) [24]; (c) Working memory: Digit Span, WISC-R; Visuoperceptual tasks: The Beery Developmental Visual-Motor Integration Test [25]; Visuo-spatial attention tasks: The Bells Test Revised [26];

Executive functions: (a) Word fluency: by phonological and semantic criteria [27], Italian standardization (Riva, 2002) [3]; (b) Tower of London [28]. Motor coordination, i.e. ability of copying sequences of left/right unimanual hand movements and complex bimanual sequences, was performed following the test of Luria (1973) [29].

All specific abilities were evaluated as variations of ±1 in Z scores, except verbal memory and motor coordination considered as normal or abnormal.

Behaviour assessments was performed after 18 months with Achenbach Child Behaviour Checklist for ages 1½–5 (CBCL/1½–5) [30]; Child Behaviour Checklist 4/18 [31] was used in children over 5 years. Raw and T scores as well as the profile of results in different syndromes (emotionally reactive, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems, aggressive behaviour) and internalizing or externalizing scores were calculated in each assessment. Statistical analysis.

The small number of cases whose assessment was partial because of the patient age and the possible lack of collaboration did not allow to perform reliable detailed statistical analysis concerning neuropsychological data. We used only the Fisher’s exact test to compare clinical data between the two groups, TLE and FLE.

3. Results

We report in Table 1 the main demographic and clinical data of frontal (FLE) and temporal group (TLE).

Histopathological diagnosis included two kinds of lesion, low grade tumours in 21 cases (2 gangliogliomas, 3 dysembryoplastic neuroepithelial tumour, 1 low grade astrocytomas and 3 cavernomas among frontal tumours and 2 gangliogliomas, 3 dysembryoplastic neuroepithelial tumour, 6 low grade astrocytomias and 1 cavernoma among temporal ones). As to the location of FLE group, it was right dorsal lateral in four and left in two, right premotor dorsal in 1 and left in two, right mesial in 1 and left in 2; lesions in TLE were all mesial, left in six and right in six. The type of surgery was a pure lesionectomy in all cases.

Neurological examination was normal in all patients at admission, no clinical deterioration was observed after surgery except one patient of TLE group that
became hemiparetic. Differences between groups were not significant as to the age of seizure onset, gender ratio (and educational degree) as well as age of surgery, follow-up duration, and seizure outcome. Five patients with FLE and six with TLE required more than two antiepileptic drugs before surgery. None was administered more than two drugs after surgery.

The neuropsychological data are reported in Table 2.

The developmental quotient (DQ) or the intelligence quotient (IQ) before surgery were in the normal range in all cases but two (one borderline and one mildly retarded) in FLE group; three presented an abnormal cognitive development (two borderline and one mildly retarded) in TLE group, corresponding to a symmetrical distribution in the two groups with regard to pre-surgical development. All cases in FLE group persisted in the same category after surgery even though in five patients there was an IQ decline of more than ten points. Three changes of category occurred in TLE group: one borderline became in normal range and two normal eventually showed borderline values.

As to specific abilities, in the FLE group sporadic defects were found before surgery; executive functions and motor coordination were more frequently affected. In TLE group impairments, namely of language, verbal and visual memory as well as visuo-spatial attention and executive functions are more diffusely observed. It should be underlined that executive functions have obviously been assessed in more aged children (over six).

Considering changes after surgery (Graph. 1a and 1b), generally remained stable, showing an improvement only sporadically. There was a deterioration in some cases of the FLE group as to executive functions, visuo-spatial attention, and only episodically in language naming and visuomotor integration, whereas definitely less were the patients in the TLE group with a function degradation (language naming and visual memory). Behaviour disorders, present before surgery

Table 1
Demographic and clinical data.

<table>
<thead>
<tr>
<th></th>
<th>FLE (n = 12)</th>
<th>TLE (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (Males/females)</td>
<td>7/5</td>
<td>8/4</td>
</tr>
<tr>
<td>Mean age of seizure onset</td>
<td>5.6 (range: 8 m–12.2 y)</td>
<td>5.8 (range: 3 m–14.6 y)</td>
</tr>
<tr>
<td>Seizure frequency (d/w/m/y)</td>
<td>3/4/3/2</td>
<td>2/7/2/1</td>
</tr>
<tr>
<td>Pre-surgery aed (&gt;2)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Mean age (years) of surgery</td>
<td>7.5 (range: 14 m–17 y)</td>
<td>8.2 (range: 9 m–17 y)</td>
</tr>
<tr>
<td>Side of lesion</td>
<td>R7/L5</td>
<td>R6/L6</td>
</tr>
<tr>
<td>Mean follow-up duration</td>
<td>2.10 (12 m–6.5 y)</td>
<td>3.4 (12 m–6.4 y)</td>
</tr>
<tr>
<td>Post-surgery aed (&gt;2)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Seizure outcome

<table>
<thead>
<tr>
<th></th>
<th>FLE (n = 12)</th>
<th>TLE (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engel’s I class</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Engel’s II class</td>
<td>1</td>
<td>2</td>
</tr>
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</table>

Table 2
Patients with defective neuropsychological results.

<table>
<thead>
<tr>
<th></th>
<th>FLE</th>
<th>TLE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-surgery</td>
<td>Post-surgery</td>
</tr>
<tr>
<td>DQ/IQ</td>
<td>17% (2/12)</td>
<td>17% (2/12)</td>
</tr>
<tr>
<td>Naming</td>
<td>0 (0/11)</td>
<td>0 (0/12)</td>
</tr>
<tr>
<td>Comprehension</td>
<td>10% (1/10)</td>
<td>0 (0/12)</td>
</tr>
<tr>
<td>Verbal memory</td>
<td>22% (2/9)</td>
<td>10% (1/10)</td>
</tr>
<tr>
<td>Visual memory</td>
<td>17% (1/6)</td>
<td>11% (1/9)</td>
</tr>
<tr>
<td>Working memory</td>
<td>0 (0/7)</td>
<td>17% (2/12)</td>
</tr>
<tr>
<td>Visual-motor integration</td>
<td>20% (2/10)</td>
<td>17% (2/12)</td>
</tr>
<tr>
<td>Visuo-spatial attention</td>
<td>0.0 (0/9)</td>
<td>27% (3/11)</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>57% (4/7)</td>
<td>50% (5/10)</td>
</tr>
<tr>
<td>Tower of London</td>
<td>20% (1/5)</td>
<td>29% (2/7)</td>
</tr>
<tr>
<td>Motor coordination</td>
<td>50% (6/12)</td>
<td>42% (5/12)</td>
</tr>
<tr>
<td>Behaviour disorders</td>
<td>50% (6/12)</td>
<td>17% (2/12)</td>
</tr>
</tbody>
</table>

Cognitive/developmental quotient was considered abnormal when it was not in normal range.
In brackets, number of abnormal patients divided total number of assessed patients.
* Results were calculated in Z scores in all the assessments but verbal memory: scores with values <−1 were considered abnormal. In verbal memory abnormal results referred to scores <27.35.
in half of the cases, both frontal and temporal, were generally improved (in 8 out of 12 patients). The small number of cases did not allow considering any reliable relationship between neuropsychological data and nature as well as location of lesions, age of seizure onset, age at surgery and frequency of seizures before the surgical treatment.

4. Discussion

The young age of our series and the almost complete absence of seizures after surgery make our experience more suitable for the analysis of the effects of the lesion excision on development and neuropsychological evolution.

The seizure outcome in our cohort of lesional FLE was significantly better than that reported in adults [32–35] as well as in other few children series [16,36–38]. All our patients resulted seizure free after surgery excepted one case belonging to the second class of Engel’s classification. The evidence of focal and well delimited MRI changes of brain lesions may have contributed to the extremely favourable outcome in our cohort, as previously suggested [39]. These results are believed to support early surgical treatment in children with refractory epilepsy to control seizures and possibly to improve brain functional re-organization after surgery.

The comparison of the FLE series with a control group of TLE, matched for the age at operation and side of surgery as advised by several previous studies aiming at better discriminating neuropsychological results [16,35,40–43] documented a similar pre-surgery general intelligence: FLE group included only two mental defective (borderline or mildly delayed) patients whereas three were mentally delayed (borderline or mildly retarded) in TLE group. That was different from Lendt’s series, unique neuropsychological study in children who underwent neurosurgery, as well as from other adult series [1,44] that showed definitely better results in frontal than in temporal patients. A further difference concerned the motor coordination generally impaired in other child and adult cohorts with lesional FLE and troubled only in half of our cases. One of the factors which might have contributed to these differences is age of surgery, definitely higher in other series including Lendt’s children cohort whose mean age was about 6 years older than ours.

The most frequent defects of specific abilities before surgery concerned verbal memory, visuomotor integration, and especially executive functions (word fluency), consistently with what has been previously reported both in adults and children with FLE. It is well known that executive functions including planning, attention self-control behaviour and thinking organization are mediated by the frontal lobe. Their disorders together with impaired motor coordination were frequently observed in adults with FLE, including those produced by lesional causes [2,45,46]. A similar involvement of executive functions was found in children with FLE [5,47]. According to Hernandez et al. the maturation of frontal functions is a key factor in determining performances in children with FLE: the Tower of London was the most sensitive measure of FL dysfunction in their study stressing the “impulsive” behaviour in executing the test together with a longer time of execution; in this context, a primary inadequate impulse control due to a dysfunction of the frontal lobe has been advocated. Verbal fluency resulted particularly impaired in FLE, especially as compared to TLE. The different competence of the two lobes and the physiological delay of maturation in frontal lobe might have contributed to this result. The impairment of executive functions in our series confirmed the literature data supporting the hypothesis that frontal lobes at an earlier stage of development are more sensitive to epileptic insults.
Normal memory with impaired executive functions was found both in children [41] and adults [42] with FLE, differently from what has been reported in TLE showing memory impairment with rather normal executive functions. That is why some authors [4] distinguished “temporal type” impairment, characterized from memory deficits from a “frontal type”, characterized by defects in frontal lobe abilities. Yet, a relevant involvement of memory in FLE, rarely reported in adults [43], was especially observed in children whose memory was even more impaired than in TLE [6,16], in association with attention problems and behaviour disorders. These controversial data are confirmed by our patients a minority of whom with FLE showed before surgery particularly poor results in memory tests such as the immediate recall of the Rey–Osterrieth Complex Figure. If encoding problems might account for memory deficits in TLE, whereas failing in strategies in organizing materials might be the cause of memory deficit in FLE [6], variability of results could be due to the different contribution of frontal and temporal involvement in the various patient series.

Language was not generally affected in our FLE cohort independently from the side of the lesion. On the contrary, TLE patients presented often problems in this area (especially in naming) with a definite predominance in left sided lesions. That was consistent with results of Lendt’s series but differed from previous studies [40] that found no difference between groups (FLE and TLE). Some inconsistency of results in the literature concerning the comparison of FLE and TLE could be due to the generally small cohorts but also to a certain overlap of these two functional areas (frontal and temporal) because of the known possible inter-lobe propagation of epileptic discharges.

Concerning the effects of surgical treatment on general cognitive abilities (DQ/IQ), our patients showed in several cases a decline of more than ten points of IQ although there was no change in mental impairment categories. A mild deterioration of performances had been reported in adults by various authors [48]; in some studies it has been stressed the role played by the size of the surgically removed lesions [44,49]. Unfortunately, no comparison of our patients can be made with other children series [16] because no post surgery assessment of general intelligence was reported. As to specific cognitive abilities, in comparison with what has been previously reported by Lendt et al. [16] a higher rate of patients with FLE in our series showed after surgery a tendency to a deterioration of executive functions and attention after surgery, whereas verbal memory and naming were improved in TLE. Also in adults with FLE, Morris and Cowey [46] reported slight difficulties of executive functions after surgery.

Indeed, one of the most favourable effect of the surgical treatment concerns the improvement of behaviour possibly mediated by the seizure control. In summary, our neuropsychological pre-surgical data confirms the involvement of attention and executive functions in lesioned FLE even though with a mild inconsistence of results as already reported in literature. Though early surgery is expected to favour brain reorganization, in some of our cases general intelligence and specific frontal cognitive abilities tended to a slight decline after surgery. Yet, the surgical treatment is strongly indicated for seizure control and behaviour improvement.

Relevant limit of our study like several other studies in literature is the small sample size that makes impossible dealing with the influence on cognitive abilities of the precise location of the lesion inside each lobe on the cognitive abilities and evaluating the related epileptic course before surgery. The difficulty to collect enough children especially belonging to the first ages in only one centre suggests the opportunity of a multicenter study aimed at further elucidating the actual role of the excision of a focal epileptogenic lesion of the frontal lobe.

Acknowledgement

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References


