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# Cognitive outcome two years after frontal lobe resection for epilepsy – A prospective longitudinal study

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ABSTRACT

*Purpose:* To investigate cognitive outcomes after frontal lobe resection (FLR) for epilepsy in a consecutive single centre series.
*Methods:* Neuropsychological examinations were performed prior to and two years (mean test interval 2.5 years) after surgery in 30 consecutive patients who underwent FLR. Cognitive outcome was evaluated with particular consideration to the site of surgery (lateral, premotor/SMA [supplementary motor area], mesial/orbital). Cognitive domains assessed were speed, language, memory, attention, executive functions and intelligence. 25 healthy controls were assessed at corresponding time points (mean test interval 3.0 years). Analyses were made both at group and individual levels.
*Results:* At baseline the patients performed below controls in variables depending on speed, executive functions, global and verbal intelligence. Two years after surgery, the analyses at the subgroup level indicated that the lateral resection group had less improvement than the controls in global intelligence, FSIQ ($p = .037$). However, at the individual level, the majority of the change scores (74–100%) were classified as within the normal range for all but one variable. The exception was the variable "Comprehension" (measuring verbal reasoning ability) with reliable declines in 44% (8/18) of the patients. This pattern of decline was observed in the lateral (4/7 patients) and premotor/SMA (4/7 patients) resection groups. Seizure outcome and side of surgery did not influence these results.
*Conclusion:* The main finding was cognitive stability at group level two years after FLR. A reliable decline in verbal reasoning ability was rather common at an individual level, but only in the lateral and premotor/SMA resection groups. The lateral resection group also had less improvement than the controls in global intelligence.



## 1. Introduction

Although frontal lobe epilepsy (FLE) is the second most common type of focal epilepsy, surprisingly few studies address neuropsychological characteristics of the disorder [1]. Existing reports from adult cohorts include heterogeneous FLE patient groups, both drug-resistant candidates for epilepsy surgery [2,3] and non-surgical candidates [4]. These studies show that patients with FLE often demonstrate reduced performance compared to controls and to patients with temporal lobe epilepsy (TLE) in aspects of executive functions such as working memory, concept formation and shift, anticipation and planning, verbal and non-verbal fluency, and proverb interpretation [5]. Reduced performance has also been observed in speed, attention, and motor coordination/sequencing [2,6]. Impairment in memory functions has also been reported but to a lesser extent than in TLE [1,3,7,8]. Upton and Thompson [4] highlighted the importance of a number

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of specific features of FLE that probably influence the cognitive profile and emphasised the importance of the rapid propagation of frontal lobe seizures both bilaterally and to other cortical regions.

Frontal lobe resection (FLR) is the second most common surgical treatment for drug resistant focal epilepsy but knowledge of its cognitive consequences is limited [1,9–13]. One recent study focusing on verbal fluency outcome showed that patients undergoing FLR for epilepsy are at risk of verbal fluency decline, especially if they have a high presurgical verbal fluency score, undergo a resection in the speech-dominant hemisphere, and have a poor seizure outcome [10]. It has been shown that surgery in different areas within the frontal lobes can affect different aspects of cognitive function [11,14]. In a short-term follow-up study including 33 FLR patients Helmstaedter et al. [11] found deterioration in motor coordination and speed/attention three months after surgery. Patients with resections in the premotor/SMA (supplementary motor area) region were at the highest risk for decline in response maintenance and inhibition. If surgery was performed on the left side there was also an increased risk for deterioration in language functions after surgery. On the other hand, seizure free patients improved in short-term memory. There is a lack of studies concerning cognitive functioning in adults beyond the first postsurgical months after FLR. The aim of the present study was therefore to investigate the cognitive outcome two years after FLR for epilepsy in a prospective and consecutive single centre series, both at group and individual level and compared to neurologically healthy controls.

## 2. Patients and methods

### 2.1. The patient group

The patient group consisted of 30 (19 male) consecutive FLE patients who underwent resection either in the speech-dominant ($n$ = 15) or non-speech-dominant ($n$ = 15) frontal lobe. The first 12 of these patients were included in an earlier comprehensive cognitive outcome study from our group [12]. For two of the patients with a left-sided surgery ($n$ = 17), the right hemisphere was speech-dominant (determined by the intracarotidal amobarbital procedure) [15]. Fifteen patients (50%) were seizure free at the two-year follow-up. Seizure freedom was defined as sustained seizure freedom (with or without aura) since surgery (Engel 1A and B) [16]. The patient group was subdivided into four anatomical subgroups: lateral, premotor/SMA, mesial, and orbital as previously described by Helmstaedter et al. [11]. The mesial and orbital resection groups were combined into one group (“mesial/orbital”) due to small sample size (mesial $n$ = 5, orbital $n$ = 4) and since these brain areas mediate functions often described as similar or related to each other [17,18]. Two patients had large resections which did not fit into these categories and were therefore excluded from the subgroup analyses. For medical and demographic variables, see Table 1. Resection size was categorised (by BR who has been on the surgical team for all the patients) as follows: minimal, small, moderate and subtotal frontal lobe resection. For details on medical and demographic data including distribution of etiologies and resection sizes across the subgroups, see supplementary Table S1.

Supplementary Table S1 related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.seizure.2015.05.014.

### 2.2. The control group

The control group consisted of 25 neurologically healthy individuals who did not differ statistically from the patient group concerning age, education or test interval ($z$-values between −1.923 and −.709; $p$-values between .055 and .478), see Table 1. Further details about the control group have been given elsewhere [19].

**Table 1**
Medical and demographic data for patients and controls.

| Variables | FLR ($n$ = 30) | Controls ($n$ = 25) |
|---|---|---|
| Age at baseline (years)[a] | 31.9 (9.6)<br>29.0 (25.0; 37.0) | 35.0 (9.2)<br>36.0 (27.0; 41.0) |
| Education at baseline (years)[a] | 12.1 (2.3)<br>12.0 (11.0; 13.0) | 11.6 (1.9)<br>11.5 (11.0; 12.0) |
| Test interval (years)[a] | 2.5 (0.4)<br>2.3 (2.2; 2.8) | 3.0 (0.2)<br>3.1 (2.9; 3.2) |
| Age at epilepsy onset (years) | 16.0 (9.7)<br>14.0 (8.0; 24.0) | NA |
| Epilepsy duration at baseline (years) | 16.6 (12.0)<br>15.5 (6.5; 22.5) | NA |
| Monthly seizure frequency at baseline | 81.8 (115.9)<br>30.0 (5.5; 134.4) | NA |
| SGTCS (yes/no) at baseline | 17/13 | NA |
| Number of antiepileptic drugs | | NA |
| Baseline | 2.1 (0.9)<br>2.0 (1.5; 3.0) | |
| 2 years | 1.6 (1.2)<br>2.0 (1.0; 2.0) | |
| Laterality (dominant/non-dominant)[b] | 15/15 | NA |
| Aetiology | | NA |
| Cavernomas | 6 | |
| Neurodevelopmental tumours[c] | 5 | |
| Malformations of cortical development | 10 | |
| Unspecified, gliosis | 9 | |
| Site of surgery | | NA |
| Lateral | 8 | |
| Premotor/SMA | 11 | |
| Mesial | 5 | |
| Orbital | 4 | |
| Large | 2 | |
| Seizure outcome | | NA |
| Seizure free | 15 (50%) | |

[a] Mann–Whitney $U$-test, between-group comparisons, FLR vs controls: $p$ > .05.
[b] Speech.
[c] Including dysembryoplastic neuroepithelial tumours (DNET), gangliogliomas, lowgrade astrocytomas.
Mean (SD)/median (Q1; Q3, range from 25th to 75th percentiles); FLR = frontal lobe resection group; SGTCS = secondary generalised tonic clonic seizures; SMA = supplementary motor area; NA = not applicable.

### 2.3. Neuropsychological assessment

All patients underwent a neuropsychological evaluation before (baseline) and two years after surgery (mean test interval 2.5 years). The controls were also assessed at baseline and at a follow-up (mean test interval 3.0 years). Data were collected between 1988 and 2013. During this long time period, some methods were updated and therefore data are missing in some variables for patients tested at later time points. The methods included in the calculations were those which were used in both the patient group and the control group. The following tests were included:

- *WAIS R – The Wechsler Adult Intelligence Scale – Revised version.* The test battery consists of eleven subtests and yields three intelligence scores: global (Full Scale IQ, FSIQ), verbal (VIQ), and performance (PIQ) intelligence score [20,21]. In addition to these IQ scores, eight subtests were included in the study: Digit span forward (FW) and backward (BW), Arithmetic, Comprehension, Similarities, Picture arrangement, Block design, Figure Assembly, and Digit Symbol. The variables measure aspects of working memory, executive functions, verbal reasoning, visual analysis, visuospatial construction ability, and psychomotor speed.