

Cognitive Outcomes in Patients with Frontal Lobe Epilepsy

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Summary: A typical "cognitive profile" or defining behavioral syndrome for patients with frontal lobe epilepsy (FLE) has not been described. While there have been numerous reports of impaired "executive functions" in this population, the nature and severity of these deficits is highly variable, ranging from impaired attention to difficulty with the more complex behaviors involved in planning, selecting goals, anticipating outcomes, and initiating action. These findings have been more difficult to demonstrate in children, in part due to the later appearance of these abilities in normal development. When a clear focal seizure onset is identified, or in cases of a structural lesion, cognitive impairment may be specific to the side, size, and localization of the abnormal cortex. Children who have undergone surgical resec-

tion of the dominant frontal lobe frequently show declines in verbal fluency, and sometimes verbal IQ, visual confrontation naming, and conceptual reasoning. Adult surgical cases have shown the most specific frontal lobe findings, including reduced word fluency with relatively small lesions of the dominant dorso-lateral frontal cortex, the analogous finding of impaired nonverbal fluency with nondominant frontal lesions, and other executive deficits following large resections of prefrontal cortex bilaterally. These reports support the likelihood that it may not be possible to identify a specific cognitive syndrome associated with FLE in the absence of a structural lesion. **Key Words:** Frontal lobe epilepsy-Lesional frontal lobe epilepsy-Cognitive outcome.

Defining a cognitive profile for patients diagnosed with frontal lobe epilepsy (FLE) has proved to be a difficult challenge for the neuropsychologist. Unlike the qualitative behavioral syndromes associated with frontal lobe disease in the broader population of people with neurological problems, patients with seizures of frontal lobe origin may appear to be relatively normal and may have largely unremarkable neuropsychological profiles. Alternatively, they may demonstrate specific cognitive deficits corresponding to the anatomical site of seizure onset, with the type and degree of difficulty showing significant variability, based on the hemisphere involved and the size of the epileptogenic region. Some studies have suggested that it may be difficult to demonstrate these findings in the absence of significant structural lesions involving frontal cortex (e.g., surgical resections or primary brain tumors). In addition, when cognitive deficits are identified, they are usually not associated with behavioral symptoms and syndromes thought to be diagnostic of gross bifrontal pathology. More subtle behavioral changes or personality features associated with FLE have not been adequately researched. Rather, published studies have focused on interruption of "executive functions" which can be more objectively evaluated.

The term "executive functions" is generic and encompasses a category of cognitive processes ranging from basic attentional skills to more complex behaviors such as the ability to anticipate outcomes, select appropriate goals, plan and organize complex responses, and demonstrate higher-level reasoning and conceptualization. The ability to use feedback to monitor and modify complex behavioral responses is also a critical component. A number of neuropsychological tests (both standardized and experimental) have been designed to evaluate these functions and are in widespread use with both pediatric and adult epilepsy populations.

NEUROPSYCHOLOGICAL FINDINGS IN CHILDREN WITH FLE

In normal development, executive functions emerge gradually between birth and adolescence, with evidence of attentional control first appearing in the preschool years, while complete integration of executive functions does not occur until age 11-13. Some recent studies have evaluated these abilities in children with epilepsy. Culhane-Shelburne and colleagues (1) reported that children with FLE showed deficits in planning and executive functions, while memory was intact. A control group of children with temporal lobe epilepsy (TLE) showed an opposite pattern, with deficits in memory but intact executive abilities. Children in this study were not divided by side of

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seizure onset, however, and this may possibly have diminished the differences noted between the groups. Another report compared the performances of children with FLE, TLE, or generalized absence seizures on tasks of attention, memory, and behavior (2). These authors found that FLE children scored lower than the other groups on measures of continuous performance, performance speed, interference during list acquisition, copy and recall of a complex figure, and behavior ratings of attention.

Cognitive performance has also been reported in children undergoing tailored resection of frontal cortex in the language dominant hemisphere for the treatment of seizures or tumor (3). In this series of eight patients, the most significant cognitive declines were noted on measures of verbal fluency, particularly in children with large resections of prefrontal and orbitofrontal cortex, extending to the midline. For some patients, declines were also noted in verbal IQ, visual confrontation naming, and conceptual reasoning. It is notable that six of these children had a concomitant diagnosis of Attention Deficit Hyperactivity Disorder. In general, cognitive outcomes tend to be highly individual in the pediatric epilepsy population and declines in one or more cognitive areas are not invariably associated with frontal lobe resection (Hempel, personal communication).

NEUROPSYCHOLOGICAL FINDINGS IN ADULTS WITH FLE

There are few published studies of adult FLE patients that describe distinctive patterns of cognitive impairment in the absence of a structural lesion. Helmstaedter and colleagues reported that their limited group of FLE patients ($n = 23$) tended to score lower on a wide range of cognitive measures, compared to a group of patients diagnosed with TLE (4). This included measures of psychomotor speed and attention, and interference tasks. No group differences were found based on the lateralization of the epileptic focus or the presence of cerebral lesions. These authors concluded that impaired motor programming and coordination as well as impaired response inhibition in complex tasks characterized about two-thirds of their patients with FLE. In a similar study, Upton and Thompson (5) reported relative impairment on a number of cognitive tasks in patients with FLE compared to TLE, including measures of manual motor skill as well as tests of executive function (e.g., Wisconsin Card Sorting Test, Stroop Interference, Trail Making, Verbal Fluency, and Twenty Questions). The results suggested that many of these measures are sensitive to frontal lobe dysfunction secondary to epilepsy when compared to performance of control subjects, and that overall, greater impairment is noted in the left frontal lobe group compared to the right. However, some of the measures used did not effectively differentiate the FLE patients from those with TLE.

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Exner and associates (6) also compared performances of FLE and TLE patients and included a small group of patients who had undergone surgical removal of frontal lobe tumors. They concluded that patients with frontal lobe pathology independent of neurological cause, were impaired relative to controls but, again, the measures used often failed to distinguish the FLE patients from those with TLE.

Each of these studies offered some discussion of the possible reasons why a distinctive neuropsychological profile in patients with FLE has not been firmly established. These include the diffuse nature of frontal lobe seizures secondary to rapid propagation, and the need for more specialized tests to detect subtle differences specific to side and site of frontal lobe pathology. None of these reports were able to separate patients into subgroups based on the relative size or location of specific pathology within the frontal lobe.

POSSIBLE EFFECTS OF SIZE AND SIDE OF SURGICAL RESECTION IN FLE

Recent data from frontal lobe seizure patients undergoing epilepsy surgery and/or tumor resection suggest that region and size of cortical excision may be important in distinguishing FLE patients from one another (7). In this study, there were no significant differences preoperatively between left ($n = 27$) and right ($n = 14$) hemisphere cases on measures of IQ, phonemic word fluency, design fluency, and cognitive flexibility. Postoperatively, left frontal patients as a group did perform significantly worse on the word fluency measure, and there was a trend toward greater impairment in design fluency for the right frontal group. No other comparisons approached significance. However, when postoperative data were reevaluated with patients divided by size and region of surgical resection, some very clear trends emerged.

Both the right and left frontal groups were divided into those patients who underwent large resections of prefrontal cortex including the frontal pole and orbitofrontal region, and those with smaller resections of the lateral frontal cortex including both dorsolateral and more central lateral excisions. Resections in the right hemisphere for each lesion group tended to be larger than similar resections in the left hemisphere. For the right frontal group, IQ scores were lower both preoperatively and postoperatively in the larger lesioned patients, whereas left frontal patients showed a similar trend for verbal IQ only.

Word fluency performance declined only for left frontal patients with smaller lateral and dorsolateral lesions, consistent with previous reports (8), whereas patients with larger resections of left prefrontal cortex maintained word fluency scores within the average range postoperatively. Performance on design fluency (9) tended to be lower in right frontal patients, with the lowest scores recorded

for patients in the large resection group both before and after surgery. Jones-Gotman has reported independently that epilepsy surgery patients with centrally located right frontal excisions may show the most dramatic deficits postoperatively on this task (10). Finally, on a measure of cognitive flexibility (Wisconsin Card Sorting Test), postoperative decline was greatest in patients who underwent large resections of the right frontal pole and prefrontal cortex (7). Perseverative responses in this group increased from 27% at baseline to 48% postoperatively, while the average number of categories achieved decreased from 5.2 to 3.8.

While these numbers are limited, they do suggest that previous failed attempts to define subtle deficits in frontal lobe functioning among patients with epilepsy may, in part, be explained by a lack of appropriately sensitive measures and limited efforts to subdivide frontal patient populations based on lateralization, localization, and size of pathological region. Whether the presence of epileptogenic cortex alone, independent of focal structural lesions from other causes, contributes any unique features to these focal cognitive deficits remains to be determined.

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