



Review

Neuropsychology of frontal lobe epilepsy in children and adults: Systematic review and meta-analysis[☆]



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ABSTRACT

Frontal lobe epilepsy (FLE) is associated with cognitive problems, especially in areas related to frontal lobe functioning as executive functions, attention, and motor skills, but with impact on memory and psychosocial adaptation. Deficits are similar in both adults and children with FLE, although no studies have compared adult and pediatric performance in the same study. The aim of this research was to analyze the existing evidence concerning the cognition in adults and children with FLE. A random effect meta-analysis was used using Cohen's *d*, and the confidence interval for each cognitive factor was calculated. The results in the meta-analysis show a general pattern of cognitive dysfunction in FLE, especially in functions related to the frontal lobe, with an influence of the duration and the age at onset of epilepsy, as well as the age of the sample used. In addition, researches in this type of epilepsy are heterogeneous, with too many different sampling and methodological characteristics, which is not a standard format for reporting clinical sample characterization, making it difficult to study FLE in depth.

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1. Introduction

Frontal lobe epilepsy (FLE) is the second most common focal epilepsy behind temporal lobe epilepsy [1], accounting for 15–20% of all focal epilepsies. Frontal lobe epilepsy is characterized by seizures that tend to spread, with a wide variability in behavioral and neuroimaging manifestations and a complex electroencephalographic record, which makes its differential diagnosis difficult [2]. Patients with epilepsy have a high risk of presenting cognitive alterations [3]. However, few studies examine the neuropsychological alterations associated with FLE [1].

The cognitive alterations in FLE are related to dysfunctions in areas related to the functioning of the frontal lobe. In this sense, it has been found that these patients have problems in programming and motor coordination and response inhibition [4], inhibition and cognitive flexibility [5], social cognition [6], and phonetic fluency [7]. The possible amnesic alteration in FLE is not exempted from debate but is not supported by conclusive results [8].

Pediatric patients with FLE show a cognitive alteration pattern equivalent to that of adults [1]. Children with FLE have problems in executive functioning [9], sustained attention [10], motor skills [11], the recovery of information, and the use of recall strategies [12,13].

In general, adults and children with FLE present a series of similar cognitive problems; however, no studies, longitudinal or transversal, compare adult and child performances within the same investigation. The objective of this research is to systematically review and analyze the neuropsychological alterations in child and adult patients with FLE as presented in various studies and to identify the variables that may moderate this performance.

2. Material and methods

The systematic review and meta-analysis were carried out following the MOOSE (Meta-analyses Of Observational Studies in Epidemiology) guide [14] for observational meta-analysis studies in epidemiology.

2.1. Search strategy

The search process for eligible studies was conducted in the Academic Search Complete, ERIC, Medline, Psychinfo, and Psycharticles databases. The search was restricted to articles published between 1989, the publication year of the ILAE=International League Against Epilepsy review of epileptic syndromes, and 2015 to avoid a possible

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change of diagnostic criteria. The search was conducted between May 19, 2015 and June 16, 2015. Articles were screened according to their title and summary, duplicates were eliminated, and then, an additional search was carried out in eligible articles' list of references. Finally, the complete list of eligible articles was obtained on June 19, 2015. The keywords are in [Appendix](#).

2.2. Selection criteria

The studies had to meet the following inclusion criteria:

1. Peer-reviewed publications written in Spanish or English from 1989 to 2015.
2. Studies comparing at least one presurgical group (>2 patients) of patients with FLE with a group of healthy controls and/or another group of patients with epilepsy.
3. Studies with results that include some domain of cognitive functioning measured by neuropsychological instruments with proven validity and reliability.
4. Studies with summary and full text available.

The exclusion criteria were:

1. Studies without a comparison group.
2. Studies in which the results of the group with FLE are different from other forms of epilepsy.
3. Studies for which the article's full text was not available.

2.3. Coding of studies

The moderator variables were coded by age group (children vs. adults), the average frequency of epileptic seizures in the group with FLE, the mean duration in years of epilepsy in the group with FLE, and the average age in years at the onset of epilepsy in the group with FLE.

A coding book was made of each study's moderating variables. The book was initially debugged by a group of experts, and then, to ensure the reliability of the book and the judgments during the coding, two independent researchers coded a random sample of 24% of the studies. The agreement index was calculated using the average Kappa index, which was 0.81. Manifest errors in the coding book were corrected, and inconsistencies were resolved by consensus.

2.4. Summary measures and calculation of effect size

The reviewed studies included a wide variety of cognitive tests. To draw a coherent and valid comparison between them, each neuropsychological test was classified under one of the cognitive factors of the Cattell–Horn–Carroll (CHC) model [15]. This model has been used in other meta-analyses of epilepsy [16] and as a conceptual framework in other pathologies [17–20]. The tests used in the selected studies were classified under six of the CHC model's broad stratum abilities: general cognitive ability (G), comprehensive knowledge (Gc), fluid reasoning (Gf), long-term memory (Glr), cognitive processing speed (Gs), and span and working memory (Gsm). A definition of each factor based on the Woodcock–Johnson III Test of Cognitive Ability [21] is provided in [Table 1](#).

The test results were assigned to one or the other factor according to each test's description as reflected in its manual and in the literature. Because of the studies' variability, not all of them included results for all factors. Also, several studies used different tests for the same factor. In such cases, each test was counted separately, and a standardized mean was calculated between the various tests for the factor. When a study included several results for the same test, only the most representative result was included.

Also, in addition to the CHC factors, and given its theoretical and empirical interest, the executive function factor was added. This classification included results that the manuals, the authors, and the literature define as instruments of evaluation of executive function [22].

Table 1
Description of CHC broad stratum abilities [21].

Factor	Description
General cognitive ability (G)	Aggregate of all cognitive abilities
Comprehensive knowledge (Gc)	Breadth and depth knowledge and verbal comprehension
Fluid reasoning (Gf)	Ability to solve problems, form concepts and reason using novel information
Long-term memory (Glr)	Ability to store and retrieve information efficiently
Cognitive processing speed (Gs)	Speed and efficiency in performing automatic or simple cognitive tasks
Span and working memory (Gsm)	Ability to hold information and use it within several seconds

Using the means and standard deviations of the cognitive tests of each group in the studies, the effect size was calculated from the difference of standardized means between the group with FLE and the comparison group (control or with temporal lobe epilepsy) using Cohen's *d*. If a study compared FLE with TLE and controls, the effect size was calculated with each comparison, and the combined effect was used. The effect size was classified as small, medium, or large according to the values of 0.2, 0.5, and 0.8, respectively [23]. For each *d* value, the 95% confidence interval was calculated to determine when the effect size obtained was statistically different from zero.

2.5. Meta-analysis procedure

The mean sizes and confidence intervals of all the studies for each of the analyzed variables were determined using a random effects statistical model. For each analysis, a forest plot was made, and the *Q* index of homogeneity and I^2 were calculated. The quantitative moderating variables were analyzed through a meta-regression, and the qualitative moderating variables were analyzed by means of an analysis of variance (ANOVA). In addition, the publication bias for each analysis was calculated with a funnel plot and the fail-safe number. Version 3 of the comprehensive meta-analysis program was used.

3. Results

3.1. Selection of studies and characteristics

A total of 21 studies met the inclusion criteria ([Fig. 1](#)). [Table 2](#) shows a summary of the characteristics of the studies considered in the meta-analysis.

3.2. Process

The analysis of all the studies jointly ([Fig. 2](#)) gave an average effect size of 0.32 (95% CI: -0.47 ; -0.17), which was of small-medium magnitude and significant ($Z = -4.19$; $p \leq 0.001$). The heterogeneity is low ($I^2 = 36.48$) and significant ($Q(20) = 31.48$, $p \leq 0.05$). [Table 3](#) shows the overall results of the analyses by factor.

3.3. Summary of the results

In general, there is an effect on the group with FLE in the cognitive profile. In-depth analysis of this effect revealed that it has a medium negative affect on the group with FLE in the factors of Gf, Gs, working memory, and executive function. It oscillates between 0.37–0.63. It has no effect on G, Glr, or Gc. The heterogeneity among all the factors is significant and medium, with values ranging from 54.53% to 66.85%.

3.4. Moderating variables

The analysis of the four moderating variables was conducted for each variable's factor: whether the sample consisted of children (up to

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