Epilepsy Research 133 (2017) 22–27

Contents lists available at ScienceDirect

Epilepsy Research

journal homepage: www.elsevier.com/locate/epilepsyres

Evaluating executive function in patients with temporal lobe epilepsy using the frontal assessment battery

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ARTICLE INFO

Keywords:
Temporal lobe epilepsy
Executive function
Frontal assessment battery

ABSTRACT

Previous studies have demonstrated executive dysfunction in patients with temporal lobe epilepsy (TLE). Frontal assessment battery (FAB) is a short neuropsychological tool that was developed for assessment of frontal lobe function in a clinical setting. The aim of the present study is to evaluate the clinical utility of FAB for detection of executive dysfunction in TLE patients.

Forty-eight TLE patients and 48 sex and age-matched healthy controls participated in this study. Compared to healthy participants, the total FAB score was significantly lower among the TLE patients. TLE patients performed significantly worse at the mental flexibility, motor programming, sensitivity to interference and inhibitory control tasks. The duration of time has been passed since the last seizure was the only significant predictor of FAB score and patients who had a seizure less than a week before the evaluation time, had significantly lower FAB scores. The number of antiepileptic drugs (AEDs) did not influence the executive function in this study; however, sodium valproate was found to affect the mental flexibility.

In conclusion, impaired executive function is common in TLE patients, and we suggest that FAB is a clinically applicable tool to monitor it. Moreover, we found that the time of the last seizure is a significant predictor of executive functioning and patients' performance may become worse up to seven days after a seizure. We also recommend that clinicians evaluate the cognitive adverse effects of AEDs especially sodium valproate, which was found to affect the mental flexibility in this study.

1. Introduction

Executive function or cognitive control is the ability to manage complex, goal-oriented thoughts and behaviors. A wide range of cognitive domains including attention, concept formation, inhibition control, mental flexibility, working memory, problem-solving and planning is required to attain this purpose (Diamond, 2013). Executive function is considered as a higher level of cognitive processing which is mainly dependent on frontal lobe function (Diamond, 2013).

Temporal lobe epilepsy (TLE), the most common type of focal epilepsy, is sometimes accompanied by cognitive deficit particularly memory impairment. Recent studies have demonstrated a wider domain of deficits, including executive dysfunction in these patients (Oyegbile et al., 2004; Stretton and Thompson, 2012).

The exact underlying mechanism of impaired frontal lobe function in TLE is not well defined (Stretton and Thompson, 2012). However, neuroimaging studies have documented certain functional and anatomical brain abnormalities in TLE, including gray and white matter atrophy in frontotemporal regions, hypometabolism of temporal and extra-temporal areas in 18-fluorodeoxyglucose positron emission tomography (FDG-PET) studies and abnormal white matter integrity that is evident in diffusion tensor imaging (DTI) (Diao et al., 2015; Keller et al., 2009; Kucukboyaci et al., 2012; Stretton and Thompson, 2012), suggesting organic causes for cognitive dysfunctions.

Frontal assessment battery (FAB), developed by Dubois et al. in 2000 (Dubois et al., 2000), is a short standard neuropsychological test for evaluation of the executive function. It consists of six subtests, each evaluating an aspect of frontal lobe function (conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy). In recent years, FAB has become a popular and applicable tool for detection of executive dysfunction in a variety of neurodegenerative and non-neurodegenera-

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http://dx.doi.org/10.1016/j.eplepsyres.2017.03.011
Received 19 September 2016; Received in revised form 6 March 2017; Accepted 21 March 2017
Available online 05 April 2017
0920-1211/

tive diseases (Cunha et al., 2010; Kopp et al., 2013; Lima et al., 2008; Rodrigues et al., 2009). Here, we applied FAB to a group of TLE patients to assess the executive function among them. To our knowledge, this is the first study to report the clinical utility of this tool in TLE patients.

2. Material and methods

2.1. Participants

This study has been conducted in two referral teaching hospitals of the Tehran University of Medical Sciences (TUMS). Definite medial TLE patients (with or without mesial temporal sclerosis) were included in this study. The diagnosis was made by an experienced neurologist based on clinical presentation and video-EEG monitoring for confirmation. Exclusion criteria were: (1) any concurrent neurologic condition other than epilepsy (e.g., dementia, Parkinson's disease, stroke,…); (2) any history of psychiatric diseases (e.g., bipolar mood disorder, schizophrenia,…); (3) any history of intellectual disability; (4) any history of alcohol or substance abuse (5) any other drugs or medical conditions that compromise the cognition. In order to compare the study results, age and sex-matched healthy volunteers were also included.

The study protocol was approved by the ethical committee of Tehran University of Medical Sciences (the ethics code: IR.TUMS.VCR.REC.1395.521). All participants signed an informed consent before inclusion in the study.

2.2. Material

All included patients were first interviewed by a neurologist and demographic details and seizure-related variables (age of epilepsy onset, duration of epilepsy, days since the last seizure, number and type of antiepileptic drugs (AEDs)) were recorded. Then, FAB was administered by a trained medical student. FAB was previously validated in Persian language (Asaadi et al., 2016). The six subtests of this instrument were evaluated in this study as below:

a) Conceptualization (similarity): Patients were asked to determine the category of two or more objects from the same semantic group. For example, apple, peach, and banana belong to which category?.
b) Mental flexibility (fluency): For this task, patients were asked to name as many words as they can that begin with the sound "B" except for proper nouns, within the 60 s.
c) Motor programming (Luria motor series): to evaluate the ability of programming, patients were first trained how to play the Luria series 'fist, edge, palm' and then, they were asked to do it repetitively by themselves for six times.
d) Sensitivity to interference (conflicting instructions): In this task, patients were asked to tap on the table twice, if the examiner tapped once and to tap once if the examiner tapped twice.
e) Inhibitory control (Go-No-Go Task): This time, the patients were asked to tap on the table once, if the examiner tapped once and to tap twice as the examiner tapped twice.
f) Environmental autonomy (prehension behavior): While the patients' hands were placed palms up on their knees; the examiner touched the patients' palms without saying anything. Examiner tried this again and said "Do not take my hands" if the patient had grabbed her hands in the first time.

According to the FAB scoring system, the minimum and maximum score for each task are 0 and 3 respectively. Calculated scores for the six subtests of this battery were summed up and reported as the "total FAB score".

2.3. Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 23, was used to perform the statistical analysis of this study. The distribution of variables was evaluated by the Shapiro–Wilk test. Categorical variables were compared by chi-square test. Mann– Whitney *U* test was applied to compare the means of non-normally distributed variables. Bivariate correlation analysis was performed for the study variables, and Pearson's or Spearman's correlation coefficients are reported. $P < 0.05$ was considered significant.

Table 1
Clinical characteristics of the study participants.

	Patients (n = 48)	Controls (n = 48)	P-value
Age (Mean ± SD)	33.16 ± 13.73	30.22 ± 11.98	0.259[b]
Sex (Male/Female)	22/26	12/36	0.054[c]
Age of epilepsy onset (median (IQR))[a]	13.5 (7–22)		
Duration of epilepsy (median (IQR))[a]	15 (4.5–25.75)		
Days since the last seizure (median (IQR))	20 (4–180)		
AEDs (n, %):	31 (64.6%)		
Carbamazepine	16 (33.3%)		
Lamotrigine	11 (22.9%)		
Sodium Valproate	11 (22.9%)		
Levetiracetam	4 (8.3%)		
Phenobarbital	2 (4.2%)		
Topiramate	2 (4.2%)		
Phenytoin			
AED Therapy (n, %):	27 (56.3%)		
Monotherapy	21 (43.8%)		
Polytherapy			
Total FAB score (median (IQR))	14 (14–16)	17 (17–18)	< 0.001[b]

SD = Standard Deviation; IQR = Interquartile Range; FAB = Frontal Assessment Battery; AEDs = Antiepileptic Drugs.
[a] Data are shown in years.
[b] Mann–Whitney U.
[c] χ^2 test.

3. Results

Forty-eight TLE patients and 48 healthy controls participated in this study. Clinical and demographic characteristics of the patients are shown in Table 1. There were no differences between the two groups regarding the age and gender of the patients.

3.1. FAB scores differences between groups

The total FAB scores were significantly lower in TLE patients (median (IQR); 14 (14–16)) in comparison to healthy controls (median (IQR); 17 (17–18)) ($P < 0.001$). As is demonstrated in Fig. 1., significantly lower scores were obtained from TLE patients in mental flexibility, motor programming, sensitivity to interference and inhibitory control subtests ($P < 0.001$; $P < 0.001$; $P = 0.002$ and $P < 0.001$ respectively).

Correlation analysis revealed that the total FAB score is significantly correlated with age in healthy controls (Pearson's $r = -0.403$, $P = 0.004$). In the TLE group, a significant correlation was found between the total FAB score and the variable "days since the last seizure" (Pearson's $r = -0.336$, $P = 0.019$). Further correlation analysis was performed in the TLE group, and the results are summarized in Table 2.

In order to control the effects of age on FAB scores, analysis of covariance (ANCOVA) was done. The total FAB score was significantly lower in the TLE group even after it was adjusted for age ($P < 0.001$).

3.2. FAB scores within TLE group

TLE patients were further divided into two groups based on the time