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Brain responses to auditory oddball task in children with benign childhood epilepsy with centrotemporal spikes: Quantitative analysis and correlation with neuropsychological assessment scores

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ABSTRACT

Objective: Variable degrees of cognitive dysfunction have been reported in children with benign childhood epilepsy with centrotemporal spikes (BCECTS). Our aim was to perform quantitative analyses of the brain responses to cognitive tasks using event-related desynchronization (ERD) and event-related synchronization (ERS) and correlating the results with the scores of neuropsychological tests in patients with BCECTS.
Methods: This case control study included 30 patients with BCECTS and 20 controls. Clinical assessment, neuropsychological tests, the Positive wave at 300 msec (P300) parameters recording, and quantitative electroencephalography (EEG) analysis were carried out for both groups. Alpha power ERD and ERS were measured in six different brain regions during an auditory oddball paradigm.
Results: Children with epilepsy showed a statistically significant poorer performance in verbal intelligence quotient (IQ), performance IQ, and total scale IQ and lower number of correct responses. Moreover, both groups showed diffuse alpha power attenuation in response to the target tones. After summation of the alpha power ERD over all brain regions to get the net diffuse ERD, the patients' group showed a statistically significant smaller net alpha ERD compared with that of the control group ($P = 0.001$). No significant correlations between the alpha ERD percentage, recorded P300 parameters, and neuropsychological tests scores were found.
Conclusions: Children with BCECTS have subtle cognitive dysfunction proved by significantly lower scores of verbal IQ and performance IQ subtests. The significantly smaller net diffuse alpha power ERD detected in children with epilepsy may be an electrophysiological indicator of disruptive brain activation in relation to cognitive attentional tasks; however, its correlation with neuropsychological tests was insignificant.

1. Introduction

Benign childhood epilepsy with centrotemporal spikes (BCECTS) is the most prevalent epileptic syndrome among pediatric age group and accounts for 15%–24% of all childhood epilepsy [1]. In general, those patients have average intellect and excellent prognosis (patients usually achieve seizures cessation by 15–16 years of age) [2]. However, the association between epilepsy and cognitive deficits has been recognized by earlier investigators [3]. The degree of cognitive dysfunction reported in this age group varies from mild learning problems to profound mental deterioration, and it often reflects the impact of epilepsy on developing cognitive abilities in children compared with adults [4]. Nevertheless, cognitive impairment and seizures may also be independent effects of dysfunctional mechanisms characterizing many neurodevelopmental disorders [5].

Reliable methods to verify the cognitive decline among children are few. Although neuropsychological testing was largely adopted for this purpose, this tool is subjective, time consuming, and influenced by the conditions of testing and cooperation of the child. This emphasizes the importance of exploring other objective methods of cognitive assessment.

Many authors have reconsidered the role of the electroencephalography (EEG) in studying cerebral processing. The EEG can tell us much about the cerebral state but cannot explain all of the brain's activity [6]. The responses of the alpha frequency band have been found to reflect alertness, expectancy, and attentional demands (8–10 Hz), as well as semantic processing (10–12 Hz) [7]. Furthermore, the event-related oscillatory EEG responses can be quantified by the event-related desynchronization/synchronization method. A relative reduction in the power of a given frequency band during stimulus processing (either external or internal) is called event-related desynchronization (ERD), and a relative increase in the EEG power is

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called event-related synchronization (ERS) [8]. As ERD has been documented during cognitive and attentional tasks [9] and ERD mapping has been suitable for studying dynamic- and time-related cognitive processes [10], the ERD is expected to be a useful neurophysiological indicator reflecting cognitive disturbances specific to neurological and psychiatric disorders [11–12].

The aim of the current study was to perform quantitative analyses of the brain responses (alpha waves) to attentional tasks (auditory oddball paradigm) using ERD and ERS and correlating the results with the scores of neuropsychological tests in patients with BCECTS.

2. Subjects and methods

This case control study was carried out between June 2015 and June 2016 at the Department of Clinical Neurophysiology, Beni Suef University Hospitals.

2.1. Subjects

Thirty children with epilepsy were compared with 20 healthy children without epilepsy. Both groups were age- and sex-matched.

For the purposes of the study, the following inclusion criteria were defined:

- Age between 5 and 16 years.
- Normal physical examination.
- Ability to cooperate and understand the instructions. Intelligence quotient (IQ) was above 70 as determined by the Wechsler Intelligence Scale for Children Third Edition (WISC-III).
- Regarding the patients, diagnosis of BCECTS based on both reported seizure manifestations, inter-ictal typical EEG with high-voltage centrotemporal spikes, and normal neuroimaging.

Participants were excluded if they had other medical, neurological, or psychiatric disorders or had profound visual or auditory dysfunction.

Informed consent was obtained from the parents, and the study protocol was approved by the local ethics committee.

2.2. Methods

Both groups underwent the following evaluations:

2.2.1. Clinical assessment

It included history taking and thorough medical and neurological examinations. It was carried out for all subjects. For patients with epilepsy, data regarding disease and treatment characteristics were collected.

2.2.2. Neuropsychological assessment

The tests were administered to individual examinees by trained examiners in a comfortable, well-illuminated, and well-aerated place. For patients, the tests were performed at least 1 week after the last seizure. Session time was approximately 45 min.

The following tests were carried out:

2.2.2.1. Tests for global intellectual function. Four subtests were adopted, two verbal subsets and two performance subsets. They were derived from the WISC-III to assess the I.Q. and the global intellectual task [13]. The Arabic language version translated by Ismaiel and Melika [14] was used.

- **Verbal subtests** included **similarity test** (a measure of abstract, logical thinking, reasoning, and categorization abilities) and **digit span test** (a measure of short-term verbal memory and attention).
- **Performance subtests** included **block design test** (it measures spatial and abstract visual problem solving) and **coding test** (measures visual–motor coordination, associative nonverbal learning, and nonverbal short-term memory).

For all children included in this study, the total scale I.Q. was obtained – according to Ismaiel and Melika charts – by calculating the algebraic summation of the scores of both verbal and performance subtests.

2.2.2.2. Tests for specific cognitive functions

- Spatial memory test

This test was used to measure the visuospatial memory and simultaneous processing. In this test, the child is asked to recall the locations of marks (either in the right, left, or middle) on pages previously presented to him/her for 5 s. The score is the number of pictures recalled properly.

- Trail making test [15]

This test was used to assess the speed of information processing, visuomotor perception, perceptual mental strategies, and planning.

- Letter cancelation test

This test was used to measure the visual attention function. In this test, the child was asked to cancel certain letters on a page with different letters. The score is the time taken for finishing this cancelation properly.

2.3. EEG recording

Nineteen Ag/Ag Cl electrodes were placed on the subject's scalp using electrode paste; according to the international 10/20 system of electrode placement at electrode locations, FP1, FP2, F7, F3, FZ, F4, F8, T3, C3, CZ, C4, T4, T5, P3, PZ, P4, T6, O1, and O2 with reference and ground electrodes were placed over the forehead. The impedances of the electrodes were always below 5 kΩ.

Raw EEG signals were recorded using Galileo Series preamplifiers acquisition system (EBN, Florence, Italy) with a frequency band of 1–70 Hz. The data were recorded using a sampling rate of 1024 Hz.

During EEG recording, the children were seated in a comfortable arm chair. They were guided to assume a comfortable position and avoid eye and head movements in order to reduce muscle artifacts. All participants underwent auditory oddball paradigm task testing.

2.3.1. Experimental design

The auditory oddball paradigm task was explained to the child who was instructed to listen to the series of tones with his/her eyes closed. The auditory stimuli were pure tones presented binaurally at random intervals ranging between 3 and 4 s. All tones were 100 ms in duration with a rise–fall time of 10 ms and were adjusted in intensity to a 70-dB sound pressure level.

The pitches of frequent (standard) and infrequent (target) tones were 1000 Hz and 3000 Hz, respectively, with a total number of 200 tones and a presentation probability for the infrequent tones of (0.2). The subjects were asked to press a button accurately with the thumb of the dominant hand in response to the infrequent tones as targets during 15-minute session.

2.3.2. Event-related potentials (ERPs)

The ERP data were averaged with the sweep beginning 100 ms before the stimuli and lasting until 900 ms after stimulus onset in a common average montage containing 3 channels of midline electrode locations Fz, Cz, and Pz according to the international 10-20 system of EEG electrode placement.

The P300 was examined as the maximum positive deflection between 250 and 700 ms. The maximum amplitudes and peak latencies of the auditory P300 ERP component were measured. Latencies were measured from the onset of the stimulus to the peak, and amplitudes

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