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RESEARCH

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Electroencephalographic changes in neurologically free patients with tetralogy of Fallot after surgical repair: a cross section study in Egyptian children

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Abstract

Background Surgical correction of tetralogy of Fallot (TOF) is still one of the most frequently performed intervention in pediatric cardiac surgery. The occurrence of seizures after repair or palliation of congenital heart disease (CHD) is a marker for a central nervous system (CNS) injury and has been associated with adverse neurodevelopmental sequelae. The prognostic value of electroencephalogram (EEG) for outcome prediction is glowing in children with CHD undergoing open-heart surgery who are at risk for subsequent neurodevelopmental deficits. To our knowledge, this is the first study to detect the EEG changes in neurologically free TOF patients after surgical repair

Results Our study included 68 TOF cases and 32 sex- and age-matched control group; they were 66.0% males and 34.0% females. The mean age of the studied children was 11.41 ± 4.23 years. There was statistically significant difference between TOF patients and control group as regards alpha power and Delta% in left occipital region and Alpha% in right occipital region, with dominant alpha waves in patients' right occipital region. None of our patients had epileptic waves. The duration after operation showed negative correlation with Delta% at left occipital region and positive correlation with Alpha% in right occipital region ($p = 0.002$, $p = 0.044$ respectively).

Conclusion TOF cases showed changes in EEG parameters chiefly dominant alpha power and Delta% in left occipital region and dominant Alpha% in right occipital region. Duration after surgery correlated negatively with Delta% at left occipital region, and positively with Alpha% in the right occipital region. Subsequent assessment is recommended to study long-term hazards of these varied dominance of EEG waves in our patients, e.g., evaluation of the cognitive functions.

Keywords TOF, Post-surgical correction, Neurological changes, EEG

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Background

Tetralogy of Fallot (TOF) is the most frequent type of cyanotic congenital heart disease (CHD) with a frequency of 0.34 per 1000 live births [1]. The severity of right ventricular outflow tract (RVOT) stenosis and pulmonary artery architecture affect the degree of cyanosis in patients with TOF. TOF variants like severe Fallot with pulmonary atresia and Fallot type double outlet right ventricle had different anatomical anomalies. Different management and treatment options may be required for these more severe variants [2]. Children with CHD who have corrective surgeries performed during infancy and early childhood have a significant incidence of neurodevelopmental impairment later in life. Prenatal brain injury, preoperative hemodynamic derangements, anesthetic medication exposure, and the atypical physiological states associated with cardiopulmonary bypass, poor perfusion, and profound hypothermic circulatory arrest all contribute to impaired neurocognition [3]. Digital EEG is a precise technology for monitoring brain activity. It is becoming more common in neonatal critical care units to capture both background patterns and electrographic seizures activity, and it may also be used to assess brain function before and after heart surgery [4].

Methods

This is a cross-sectional study that included 68 patients with corrected TOF, aged 3–15 years following up in the post-operative cardiac intervention clinic (PCIC) in Cairo University Pediatric Hospital as well as 32 age- and sex-matched healthy children as controls over a period of 2 years.

Exclusion criteria

Patients with other CHD, or acquired heart diseases, history of convulsions or other neurological problems, or taking antiepileptic drugs.

All patients were subjected to: Full history taking with special attention to cardiac and neurological symptoms, full medical examination including anthropometric measure, cardiac and neural examination, evaluation of heart and respiratory rates with measurement of oxygen saturation using the pulse oximeter.

The patients and controls were referred to Clinical Neurophysiology Department, Kasr Alainy Hospital, Cairo University, to do a complete EEG study.

EEG and brain mapping

A wake EEG was done for all patients using EbNeuro Galileo machine, after revision of patients' history and data with the patients' parents who attended the recording as it was done with the patients fully awake without sedation. Oral consents were taken from the parents. Electrodes were placed according to the 10–20 international system of electrode placement using a cap to which the electrodes are adherent. Mono and bipolar montages with 21 channels were recorded for 30–40 min of recording.

The EEG machine parameters were adjusted before the recording as follows:

- Time constant: 0.3 s for EEG
- Drawing speed: 3.0 cm/s
- Filter: 30 Hz for EEG
- Gain: 70 v/cm.

Then, the EEG tracings were analyzed carefully as regards frequency, amplitude, and symmetry of the background activity, as well as the presence of any epileptic charges and were described as focal, generalized, or focal with secondary generalization. Epileptiform activity was considered lateralized if more than 80% of the discharges originated from one side.

The following EEG parameters were estimated:

- Alpha power, Alpha%
- Theta power, Theta %
- Delta power, Delta%

These are the basic brain waves which occur normally. Alpha waves appear during resting or relaxation and disappear with mental activity or concentration on a specific task, its normal frequency is 8–13 Hz. Theta waves appear temporally during sleep, otherwise they may indicate cerebral dysfunction. Delta waves are low frequency waves with frequency 0.1–3.9 Hz, and they normally appear during deep sleep; otherwise, they indicate damaged area of the brain caused by inflammation, a tumor, or vascular blockage [5].

Statistical analysis

Data were statistically described in terms of mean ± standard deviation (±SD), median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's t test for independent samples. For comparing categorical data, chi-square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity, and specificity. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical

Table 1 Comparison between TOF patients and controls as regards anthropometric measures, O2 saturation and vital signs

Variable	Patients ($n = 68$) Mean ± SD	Control ($n = 32$) Mean ± SD	*p* value
Age (in years)	11.84 ± 3.9	10.50 ± 4.79	0.140
Weight (in kg)	17.19 ± 4.7	28.88 ± 8.74	0.001
Height (in cm)	122.09 ± 18.31	128.96 ± 19.24	0.049
O2 saturation (%)	97.63 ± 1.33	99 ± 0.8	< 0.001
HR (beats/per minute)	81.99 ± 5.43	86.28 ± 7.67	0.002
RR (cycle/minute)	19.93 ± 3	23.72 ± 2.12	< 0.001
Systolic BP (mm/Hg)	112.19 ± 8.35	93.53 ± 11.62	< 0.001
Diastolic BP (mm/Hg)	74.21 ± 5.12	62.5 ± 6.09	< 0.001

Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 21 for Microsoft Windows (2022).

Results

This is a cross section study included 68 TOF cases and 32 sex and age matched control group, they were 66.0% males and 34.0% females, their characteristics were enlisted in Table 1.

The patients had significantly lower anthropometric values, oxygen saturation, HR, and RR than the control group, while the reverse occured as regards systolic, and diastolic BP

We compared the EEG changes between patients and controls in the left occipital region, the results were shown in Table 2.

As shown in Table 2, Alpha power was statistically higher in patients than controls. The Delta waves occurred at slower rate (Delta% is significantly low) but with non-significantly higher amplitude (power).

We compared the EEG changes in both groups in the right occipital region, and the results were enlisted in Table 3.

There was statistically significant difference between TOF patients and control group as regards Alpha% being higher in TOF patients than controls.

However, there was no statistically significant difference between males and females as regards right and left occipital regions EEG parameters with *P* value > 0.05.

None of our patients had epileptic waves or abnormal background activity pointing to epilepsy.

On correlating EEG findings with the duration after operation we found that there were negative correlation between duration after operation and Delta% in left

Table 2 Comparison between TOF patients and control group as regards EEG changes (left occipital region)

O1 (left occipital region)	Group		*P* value	MW test
	Patients ($n = 68$) Median (range)	Controls ($n = 32$) Median (range)		
Alpha power (Uv2)	86.35 (5.36–1012.87)	46.795 (10.26–290.98)	0.023	− 2.3
Theta power (Uv2)	65.67 (9.26–450.57)	66.23 (12.69–762.22)	*0.773*	− 0.3
Delta power (Uv2)	288.3 (15.37–12727.38)	224.38 (43.37–5001.95)	0.935	− 0.1
Alpha%	12.35% (0.50–55.10%)	10.30% (1.50–43.10%)	0.387	− 0.9
Theta%	11.55% (2.20–87.30%)	11.00% (4.30–27.80%)	0.674	− 0.4
Delta%	54.55% (6.40–95.40%)	69.30% (22.40–92.10%)	**0.035**	− 2.1

p value is considered significant if < 0.05, *MW* Mann-Whitney test

Table 3 Comparison between TOF patients and control group as regards EEG changes (right occipital region)

O1 (right occipital region)	Group		*P* value	MW test
	Patients($n = 68$) Median (range)	Controls($n = 32$) Median (range)		
Alpha power (Uv2)	6.94 (4.04–1002.06)	43.85 (8.56–346.53)	0.124	− 1.5
Theta power (Uv2)	58.96 (9.99–2050.98)	77.53 (17.43–508.44)	0.545	− 0.6
Delta power (Uv2)	343.95 (21.51–6659.65)	362.54 (56.96–9710.14)	0.865	− 0.2
Alpha%	18.20% (1.00–59.80%)	10.65% (0.40–37.90%)	0.026	− 2.2
Theta%	10.15% (1.40–69.10%)	14.05% (2.00–33.10%)	0.055	− 1.9
Delta%	58.35% (5.00–97.60%)	63.45% (24.20–97.10%)	0.142	− 1.5

p value is considered significant if < 0.05, *MW* Mann-Whitney test

Table 4 Correlation between duration after operation and EEG in right and left occipital regions

EEG waves	Duration after operation	
	r	*P* value
O1 (Left occipital region)		
Alpha power (Uv2)	0.044	0.727
Theta power (Uv2)	− 0.210	0.096
Delta power (Uv2)	− 0.222	0.078
Alpha%	0.214	0.089
Theta%	− 0.043	0.738
Delta%	− 0.022	0.022
O2 (right occipital region)		
Alpha power (Uv2)	0.026	0.838
Theta power (Uv2)	− 0.234	0.063
Delta power (Uv2)	− 0.240	0.056
Alpha%	− 0.044	0.044
Theta%	− 0.106	0.403
Delta%	− 0.193	0.127

P value > 0.05 non-significant, *P value < 0.05* significant, *P value < 0.01* highly significant, *r* Spearman correlation coefficient

occipital region with p value = 0.022 and positive correlation between duration after operation and Alpha% in right occipital region with p value = 0.044 as presented in Table 4, Figs. 1 and 2.

On correlating EEG findings and age at time of operation, we found that there is no statistically significant correlation between EEG parameters in the right and left occipital regions and age at time of operation as presented in Table 5.

Discussion

One of the most significant successes in congenital cardiac surgery is the repair of tetralogy of Fallot (TOF). The first surgical palliation was performed in 1944, and repair was introduced 10 years later. Since then, remarkable advances have been made in many areas that contribute to good surgical outcomes [6].

Neurodevelopmental delay and complications are one of the most common complications after cardiac surgery especially in neonate and young children, it likely results from a combination of pre- and intraoperative factors. Due to the continuous advancement in the surgical techniques, and pre and post-operative care, the incidence of the immediate complications has decreased but the long-term neurological sequels including the neurodevelopmental compromise is noticeable especially after neonatal surgery [7].

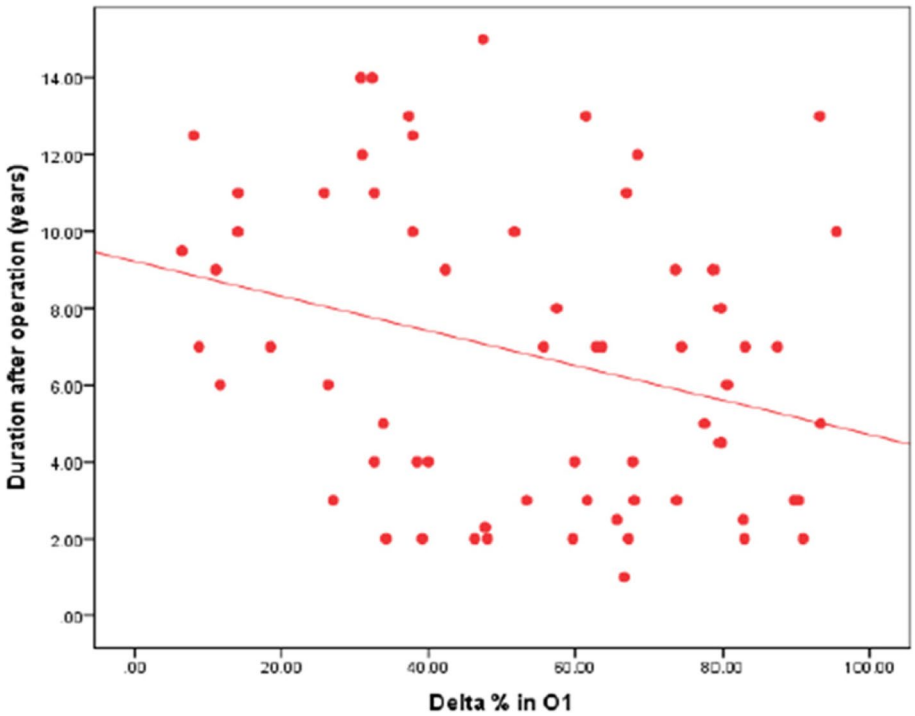

Fig. 1 Correlation between duration after operation and Delta% in left occipital region

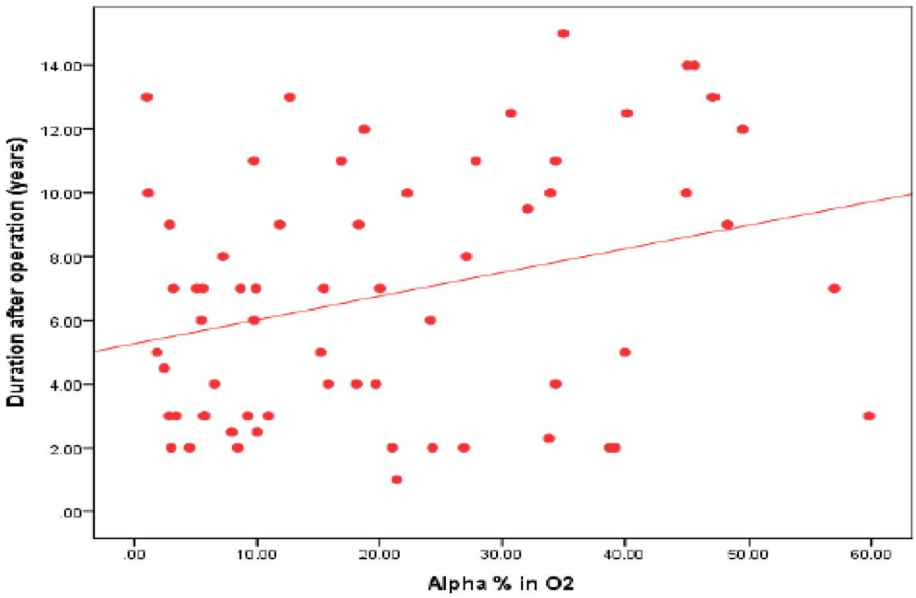

Fig. 2 Correlation between duration after operation and Alpha% in right occipital region

Table 5 Correlation between age at operation and EEG in right and left occipital regions

EEG waves	Age at operation	
	r	*P* value
O1 (Left occipital region)		
Alpha power (Uv2)	− 0.065	0.608
Theta power (Uv2)	− 0.110	0.386
Delta power (Uv2)	− 0.056	0.660
Alpha%	0.045	0.722
Theta%	− 0.057	0.657
Delta%	0.046	0.718
O2 (Right occipital region)		
Alpha power (Uv2)	− 0.106	0.404
Theta power (Uv2)	− 0.130	0.306
Delta power (Uv2)	− 0.071	0.578
Alpha%	− 0.026	0.839
Theta%	− 0.028	0.827
Delta%	0.071	0.577

P value > *0.05* non-significant, *P value* < *0.05* significant, *P* value < 0.01 highly significant. *r* Spearman correlation coefficient

That is why prompt follow up for these patients including monitoring the brain activity and anticipating any abnormality are noteworthy to assure smooth and near normal long-term survival.

In this cross-section study, we aimed to detect EEG changes in patients with TOF after surgical repair using digital EEG and quantitative EEG. The study was held in Cairo University Pediatric Hospital, the study included 100 subjects, 68 TOF cases after surgical repair and 32 age and sex matched controls, with no history of convulsions or other neurological problems in both groups.

In the current study, we found that there is highly statistically significant difference between TOF patients and control group as regards weight, height (p value = 0.000) being lower in TOF patients, this could be explained by the persistent hypoxia in this group of patients, which was parallel to other study where a considerable number of patients had been stunted in height and weight [8]. In our study we found that there was highly statistically significant difference as regards O2 saturation and heart rate between TOF patient and controls ($p = 0.000$, $p = 0.002$ respectively) being lower in TOF patients. This was also reported in research by Butera G et al., who found that heart rate variability (HRV) indices were equal in the two control groups but were considerably lower in patients with TOF [9]. In the current study, we found that there was highly statistically significant difference as regards systolic BP and diastolic BP between TOF patients and control groups with P value = 0.000 and 0.000 respectively being higher in TOF patients than controls, it was parallel to the results of another study that stated higher incidence of hypertension in children with CHD after surgery in comparison with normal control group. This hypertension may be due to neurohormonal stimulation of renin angiotensin system, and sympathetic stimulation due to disturbed cardiac receptors during surgery [10].

As regards EEG parameters, we found that there was significant difference between cases and controls as

regards alpha power, Delta% in the left occipital region ($p = 0.023$, 0.035 respectively) with dominant alpha waves in TOF patients right occipital region ($p = 0.026$). This was partially comparable to the results of a prior study done on 36 children who underwent continuous EEG after congenital heart disease repair, and they reported a substantial increase in delta power in 24 children, including significantly more children without any neurologic deficits than with neurologic deficits at follow-up (86% versus 50%) [11]. Dominant alpha waves may cause difficult focusing, decreased delta waves as in our patients may cause sleep difficulties, inability to revitalize the brain [5]. So far, these waves are not diagnostic nor prognosticators of seizures.

In our study, we did not record electrographic seizures or abnormal background activity, which contrasts the results of our colleagues Hala et al. who found incidence of 3.4% among their patients after cardiac interventions; the higher percentage (11.4%) was after open-heart surgery, but they included the patients with history of neurological abnormalities in the post-operative period [7].

Our results contradict the results of a similar study where they found abnormal EEG findings suggesting epileptic activity in 5/9 (55.6%) patients with previous cardiac surgery, and 3/5 patients with both epileptic changes and background slowing had history of previous cardiac operation [12].

Many factors during the cardiac surgery could affect the brain development. The hypoxic-ischemic injury and systemic inflammatory response, which may arise during the peri-operative period, longer ventilation duration, and longer intensive care stay were associated with a greater risk for an abnormal post-operative background pattern abnormality and epileptic activity [13].

According to our results, we could say despite the several factors that may affect the patients in the operative and early post-operative period, absence of clinical seizures, or other neurological symptoms is associated with absence of EEG epileptic activity.

In our results, we found that no statistically significant difference between males and females as regards right and left occipital regions EEG parameters with P value > 0.05. This was also stated in the study of von Rhein et al., which showed that non-modifiable variables, such as gender, birth weight, Apgar scores, were not associated with the neurodevelopmental outcomes in patients with congenital heart diseases after surgery [14].

We found no significant correlation between EEG parameters in left and right occipital region and age at time of operation, this is partially incomparable with Gaynor et al. who showed that electrographic seizures occurred more in neonates than older infants 14%, 7% respectively [15].

In our study, we found positive correlation between duration after operation and Alpha% in right occipital region with $p = 0.044$, and negative correlation with Delta% in the left occipital region $p = 0.022$, This is different from the results of other study stated that most clinical or electrographic seizures occur within 2 days post-operative [16]. These differences may be because we did not find electrographic seizures and we correlate the changes in the normal waves.

More data are needed regarding the prognostic implications of these EEG changes in children with congenital heart disease after cardiac surgery.

Our study has some limitations including small sample size, lacking the preoperative neurological evaluation and EEG.

Conclusion and recommendations

1. EEG changes are evident post-tetralogy of Fallot total surgical repair especially alpha power and Delta% in left occipital region and dominant alpha waves in right occipital region.
2. Duration after operation may affect some of EEG parameters as Delta% at left occipital region which decreased significantly with more time after the operation, and Alpha% in right occipital region which increased with increasing time after operation.
3. Age at time of operation and gender had no significant effect on EEG parameters.
4. In our patients, absence of clinical seizures or other neurological symptoms is associated with absence of EEG epileptic activity.
5. Subsequent studies investigating cognitive functions in TOF patients are highly recommended to determine long-term significance of these changes in brain waves and its impacts on long-term school performance.

Abbreviations

CHD	Congenital heart disease
CNS	Central nervous system
EEG	Electroencephalogram
HR	Heart rate
NYHA	New York Heart Association
RR	Respiratory rate
RVOTO	Right ventricular outflow tract obstruction
TOF	Tetralogy of Fallot

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Authors' contributions
LAI: manuscript preparation and drafting of the article, review of literature. FAM: concept and design of the study, and final approval of the version to be published. RII: concept and design of study, and review and editing of the manuscript. NME: EEG, analysis, and interpretation of data. BHA: collection of cases. EFE: review and editing of the manuscript. All authors had full access to the data (including statistical results and tables), approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved from the ethical committee of Cairo University Children's Hospital.

Consent for publication
Not applicable

Competing interests
None is declared.

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