Original Article

Effectiveness of Neuropsychological Protocol with Video Electroencephalography in Diagnosis of Epilepsy

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Abstract

Background: Epilepsy is one of the most frequent brain diseases. Epilepsy usually affects over 70 million people globally with the majority of people who suffer from it living in low- and middle-income countries, and the prevalence in Iraq from 2000 to 2016 nearly 21.74/1000. Neuropsychological protocol, certain protocols that proposed to cause cortical activation to induce the epileptiform abnormalities, by procedures such as reading, talking, writing, and solving mathematical tasks are all incorporated to activate the cortical neurons and then epileptic discharges. **Objectives:** Our aim is to study the effectiveness of neuropsychological activation protocols in inducing epileptiform discharges during video electroencephalography (EEG) recording. **Materials and Methods:** This is a cross-sectional study conducted in neurology ward/video EEG room in Al-Sadeq teaching hospital in Al-Hillah city, through the period from September 2022 till April 2023. The study included 47 patients with age distribution between 12 and 52 years and gender 25 men and 22 women. Patients are recruited from video EEG room in neurology ward after being diagnosed to have epilepsy by experienced neurologist. In addition to the diagnosis, type of epilepsy is stated also in the referral form. All the patients were evaluated with a thorough history and physical examination before being submitted to video electroencephalographic recording in an awake state with activation stages. **Results:** The study results revealed the percent of interictal epileptiform discharges (IEDs) that induces by neuropsychological activation protocol is 72.3%, and the mathematics (written calculation), is considered the higher activity that induced IEDs. **Conclusions:** Neuropsychological activation protocol is a useful tool in inducing interictal discharges.

Keywords: Epilepsy, interictal discharges, neuropsychological activation protocol, video-EEG

Introduction

Epilepsy, is a significant neurological disorder that affects the brain's electrical system, estimated that over 70 million people globally suffer from epilepsy, that makes it one of the most common neurological conditions globally. Approximately 80% of people with epilepsy live in middle- and low-income countries, and more than 75% of the people with active epilepsy in these countries are untreated or on irregular treatment.[1] Epilepsy can affect people of all ages, genders, ethnic backgrounds, and cultures, regardless of their geographical location. Up to one-third of epileptics patients complain drug resistant nature of this disease.[2] It is characterized by unusual electrical activity in the brain that leads to abnormal motor activity, sensation, consciousness, or behavior. It is regarded as one of the most common neurological illnesses that can affect the life adjustment. It affects physical and psychological functions of the person.[3] Epilepsy is estimated to affect approximately seven out of every 1000 people worldwide and rates in Asia were reported to be between 1.5 and 14.0 per 1000,[4] and the prevalence in Iraq from 2000 to 2016 nearly 21.74/1000.[5]

Video electroencephalography (EEG) monitoring is considered the gold standard for the assessment of behavioral and EEG change of seizures,[6] because routine EEG continuous 20–30 min, usually without video,

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often fails to show epileptiform activity, because the manifestations of epilepsy are brief and intermittent.[7]

Neuropsychological activation protocol is certain protocols that proposed to cause cortical activation to induce the epilpetiform abnormalities, by procedures such as reading, talking, writing, and solving mathematical tasks are all incorporated to activate the cortical neurons, and then epileptic discharges,[8] neuropsychological activation is methods used during EEG recording have been used by groups from Japan, Germany, Italy, and Greece, as supporting procedure to detect specific seizure patterns in different epileptic syndromes,[9] Because of methodological differences, the provocative rates of the neuropsychological protocol ranged from 7.9% to 84% and neuropsychological activation may require extended time ranging from 40 min to 6 h.[10]

Aim

Investigate the effectiveness of neuropsychological activation protocols in inducing epileptiform discharges through video EEG recording.

Materials and Methods

The study was cross-sectional and conducted in a neurology ward/video EEG room in Al-Sadeq teaching hospital in Al-Hillah city, through the period from September 2022 till April 2023.

The study included 47 patients with age distribution between 12 and 52 years and gender 25 men and 22 women). Patients are recruited from video EEG room in neurology ward after being diagnosed to have epilepsy by experienced neurologist.

Exclusion criteria

1 Patients with diseases known to cause EEG abnormalities such as migraine and degenerative disease of brain.
2 Patients with brain surgery or head trauma.

All the patients in this study were assessed by full history including physical examination, and then they undergo video electroencephalographic recording.

Electroencephalogram recording

The EEG recording was submitted 4- to 6-hr for video EEG monitoring, eyes opened for 10 min and eye closed, hyperventilation, intermittent photic stimulation, neuropsychological activation followed by sleep EEG recording.

The video EEG was recorded using 22-electrode EEG machine Nihon Khoden, with arranging electrode according standard 10–20 international system.

Electroencephalographic analysis

The EEG technical details are high cut filter 70 Hz, low cut filter 1 Hz, time constant 0.3, impedance <5000 ohms. The sensitivity of EEG is kept between 7 and 15 μV (microvolt)/s. The EEG record was displayed as waveforms of varying morphologies and frequencies, and analysis for presence of interictal discharge, frequency, and type of ictal EEG change that observed together with video record.

Analysis of EEG records along with video recording is done by experienced clinical neurophysiologist who was blind to the patient's history or initial diagnosis proposed by the neurologist. The data obtained from video EEG are then incorporated along with the patient's history and other clinical and imaging data and discussed with the neurologist to have final diagnosis and classification of epilepsy syndrome.

In bipolar montages, "phase reversal," a deflection of the two channels within a chain pointing in opposing directions, is typically used to localize normal or abnormal brain waves.

In a "referential montage," in general, the electrode with the largest upward deflection represents the maximal negative activity.

After ensuring that the EEG is free of artifact, impedance is below 5 Kohms, stable baseline and all electrodes are well conducted, yet we will start EEG recording. The EEG record consists of different stages or phases as follows.

Recording non-activation stages

(Eye closure phase and eye open phase), each stage record for 15 min.

Recording activation stages

Hyperventilation stage

This phase will continue from 3 to 5 min, and will be repeated 2-3 times with periods of 2 min apart. During hyperventilation, close monitoring of the patient condition and EEG is needed due to potential development of ictal event.

Intermittent photic stimulation

Photic stimulation for 3 min with repeated intermittent photic stimulation 2 or 3 times throughout recording.

Neuropsychological activation protocols

Neuropsychological activation protocol was usually done after photic stimulation. It took for 30-45 min, and consisted of achieving multiple tasks or answering certain questions by the patient.

The details of neuropsychological activation protocols are shown in Table 1.

Statistical analysis

All statistical analyses were performed using scientific package for social sciences (SPSS) software (version 23; IBM Statistics, California, USA). For continuous data, *t*

Table 1: Neuropsychological activation stages

"Reading an Arabic text (patients read the same sentences aloud that they had read silently); this was a medical text describing seizures
ten min silently
ten min aloud
Reading an English text if possible
ten min silently
ten min aloud
Speaking aloud for 5 min (patients described their seizures, their lives, and the impact of epilepsy)
Writing for 5 min (patients were asked to write about their seizures)
Mental calculation: subjects responded aloud with answers to four arithmetic problems (18 − 8 + 46, 15 6,5, 100 , 5); when calculation was difficult, an easier problem was presented
Written calculation: patients responded in writing to one arithmetic problem (12 ri23 3i21 1i48)
Drawing: patients were instructed to draw a family, a house, and a clock showing quarter to four
Spatial construction:
Patients achieved a sequence of tasks, for 10 min each: Rubik's cube arranging"

Table 2: Number of epileptiform discharges in non-activation and activation stages

Epileptiform discharge	Non-activation stages			Activation stage		
	Eye closed	Eye opened	Sleep	Hyperventilation	Photic	Neuropsychological activation protocol
Number of patients						
Absent	19 (40.42%)	22 (46.80%)	4 (8.5%)	5 (10.63%)	34 (72.34%)	13 (27.7%)
Present	28 (59.57%)	25 (53.19%)	43 (91.48%)	42 (89.36%)	13 (27.65%)	34 (72.34%)
Total percent	47 (100%)	47 (100%)	47 (100%)	47 (100%)	47 (100%)	47 (100%)

Results are shown as number (percentage)

test was used and represent as mean ± standard deviation (SD), for categorical data use Chi square test and represent as number and percentage. *P* value < 0.05 was considered significant.[11]

Ethical approval

This study was approved by the committee of publication ethics at Babylon university/college of medicine, document number 675 at July 21, 2022, and verbal consent of participation was obtained from patients.

Results

The epileptiform discharge during non-activation and activation stages of video EEG recording

The epileptiform discharges have been detected in different stages of EEG recording including non-activation stages (eye closed, eye opened), activation stages (hyperventilation, photic stimulation, neuropsychological activation stages), and sleep as shown in Table 2. The table clearly shows that most interictal epileptiform discharges (IEDs) are induced by activation procedures, with hyperventilation being the most important activation procedure.

Effect of neuropsychological in inducing IEDs in each seizure type

The number of epileptiform discharges induced in each type of epilepsy through neuropsychological activation protocol are shown in Table 3.

Difference between focal and generalization according neuropsychological activation

Focal seizure associated with IEDs in neuropsychological activation stage 9 from 11 patients (81.8%), whereas general epilepsy that associated with IEDs 69.9%, as shown in Table 4.

Provocative effects of different tasks of neuropsychological activation protocol on epileptiform discharges

Mathematics (written calculation), consider the higher activity that induced IEDs followed by reading (aloud) activity, as shown in Table 5.

Discussion

Effect of neuropsychological in induce IEDs in each seizure type

IEDs induced by neuropsychological activation protocol are shown in Table 3. neuropsychological activation protocol (NPA) induced IEDs in 72.3% of total patients enrolled in the study. This is similar to the study of,[12] who expressed the cognitive tasks provoked IEDs in 84% of patients.

In contrast to study[13] who found that 7.9% of all patients with various epilepsy types experienced IEDs in response to neuropsychological activities.

In this study, the most effective outcome of NPA appeared in focal to bilateral tonic-clonic and frontal lobe epilepsy,

Table 3: Effect of neuropsychological in induce IEDs in each seizure type

Classification of seizure			Number of patient with epileptiform discharge in neuropsychological activation	Percent of NPA effect in each type	Percent of NPA effect of each type from total patients
Focal seizure	Impaired awareness		0	0%	0%
	Focal to bilateral tonic clonic.		4	100%	-8.51%
	Aware	Temporal lobe epilepsy	2	66.60%	-4.25%
		Frontal lobe epilepsy	3	100%	-6.38%
Generalized seizure	Motor	Tonic-clonic	14	66.60%	-29.78%
		Juvenile myoclonic epilepsy	7	70%	-14.89%
	Non-motor (absence)	Childhood absence epilepsy	2	100%	-4.25%
		Juvenile absence epilepsy	2	66.60%	-4.25%
Total percent					72.30%

IEDs: interictal epileptiform discharges, NPA: neuropsychological activation protocol
Results are shown as number (percentage)

Table 4: Different in focal and generalized epilepsy according to effect of neuropsychological activation

Number of epileptiform discharge in neuropsychological activation	Focal seizure	Generalized seizure	Total
	(number of patients)		
0	2 (18.18%)	11 (30.1%)	13
1	2	7	9
2	4	9	13
3	1	3	4
4	1	5	6
5	1	1	2
Total	11	36	47

Results are shown as number (percentage)

Table 5: Effects of different tasks of neuropsychological activation protocol on epileptiform discharges

Neuropsychological activation protocol		Number of epileptiform discharges
Reading	Silent	5 (7.46%)
	Aloud	15 (22.38%)
Speaking	Silent	7 (10.44%)
	Aloud	4 (5.9%)
Writing		1 (1.49%)
Mathematics	Mental calculation	3 (4.4%)
	Written calculation	16 (23.8%)
Drawing		9 (13.43%)
Rubik's cube		7 (10.44%)
Total		67 (100%)

Results are shown as number (percentage)

and childhood absence epilepsy (CAE) as the effect accounts for 100% of each type.

Also, the percentage of inducing IEDs in this study is different according to the type of epileptic disorder like in patients with juvenile myoclonic epilepsy (JME) 70%, of them developed IEDs during NPA, whereas in temporal lobe epilepsy, generalized tonic-clonic, and juvenile absence epilepsy (JAE) are 66.6%. Other study[13] showed markedly different results in different epileptic disorders like JME (46.7%) of patients, followed by JAE (16.7%), general tonic-clonic (15.8%), CAE (7.1%).

On the other hand, controversial results are seen regarding focal onset seizure, some authors demonstrated that NPA may cause inhibitory effect on focal onset seizure except

temporal lobe seizure,[13] and precipitating effect on general onset epilepsy.

Even though,[14] showed NPA test provoked EEG discharges in 23.3% of patients.

In our study, all three patients with frontal lobe epilepsy showed frontal lobe spike and spike wave abnormalities during NPA, with one of them showing completely normal video EEG except at NPA.

NPA had little precipitating effects on higher mental activities that can provoke generalized IEDs, NPA may be attended by myoclonic or absence seizures, seizures precipitated by specific trigger would be a subtype of JME, this essentially to reveals that JME are highly responded to provocative effects of NPA. Epileptic discharges induced in generalized epilepsy by NPA were relatively similar to those that appeared spontaneously, but they consisted of diffuse and symmetric spike-wave or polyspike-wave complexes, also seizure susceptibility to higher mental activities in generalized epilepsy syndromes suggests a pathophysiological similarity between syndromes.[13]

Also, cognitive functions can have different effects on IEDs, depending on the specific neural pathways involved. The parietal cortex is an important region involved in many cognitive functions, and when it is activated, this can lead to the propagation of neural signals to other areas of the brain, including the frontal cortex. This activation can trigger IEDs. Written calculation that may involve activation of the parietal and frontal cortices, which can trigger IEDs in individuals with epilepsy, or if the activation of the parietal cortex occurs without motor involvement, the effect on IEDs can be inhibitory.[9]

In this study we used group of activation procedure for cortical activation, to induce epileptiform discharge, as shown in Table 5.

The mathematics (written calculation) is considered the most common technique that induces IEDs in a rate of 23.8% followed by reading loud in rate of 22.38%.

In this study, both written calculation and reading loud induced staring attack in patients with JAE, despite thereference[15] had offered myoclonic seizure was triggered by mental calculation.

Likewise, in this study, Rubik's cube arranging activity provoked IEDs in 10.44% and one patient (JAE) was had staring attack through this activation procedure.

Unlike the study[9] revealed that action-programming tasks may be more effective than thinking tasks in provoking IEDs in individuals with epilepsy, action-programming task induced IEDs in 84.2% of patients and thinking induced IEDs of 10.5% patients only.

However, the study[10] showed verbal tasks and arithmetic tasks provoked IEDs in 11.4% and 5.7% of patients, respectively, also all activated patients were had generalized epilepsy, and mental calculation increased the yields of IEDs between 5.1% and 7.9%.

In contrast to study,reference[8] revealed less than one-fifth of patients with generalized epilepsy experienced IEDs in response to neuropsychological activation tasks, all of the neuropsychological activation tasks had similar provocative effects, indicating that different types of cognitive tasks may have similar effects on IEDs in some individuals with epilepsy; however, there was a tendency for tasks that required both planning and purposive hand movement to have more prominent provocative effects. This may be related to the activation of motor regions of the brain that can be involved in both planning and executing purposive hand movements whereas mental reading did not provoke EEG discharges.

Although, study[12] exhibited that 39.8% of IEDs triggers by neuropsychological activation tasks related to praxis, language, and flashing lights were found to be provocative in some patients with epilepsy, Among those, the provocative effect was confirmed in 53.3% patients during neuropsychological activation (10 patients had induction by praxis; eight photosensitivity; four praxis and language; one language; and one praxis and photosensitivity).

In this study, the proven use of NPA for induction IEDs, especially uses of written calculation, reading aloud, and arranging Rubik's cube, also associated with provocation ictal attack (especially staring) in addition to IEDs.

Finally, neuropsychological activation protocol had a significant role in the evaluation of patients with epilepsy, because it could support the diagnosis and classification of seizure, and identify precipitating factors, so help in choosing appropriate treatment and to improve prognosis.

Conclusions

1. Neuropsychological activation protocol is a useful tool in inducing interictal discharges, that have important implication in the diagnosis and classification epilepsy syndromes.
2. Neuropsychological activation protocol is considered an important part in provoking IEDs especially in focal seizure like frontal lobe epilepsy, and it may induce seizure attack during recording, especially absence epilepsy.

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Conflicts of interest

There are no conflicts of interest.

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