Nonspecific Abnormal EEG Patterns during Hyperventilation Test on the Electroencephalogram of Normal and Epileptic Patients.

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ABSTRACT

Hyperventilation (HV) is being used as an activation/provocative test in clinical EEG laboratories to enhance preexisting abnormalities and/or induce abnormal findings in an otherwise normal electroencephalogram (EEG). The present work was done to compare the incidence of focal or generalized slowing, patterns of uncertain significance using activation methods on the EEG of normal young and adult subjects and the age matched epileptic subjects and also to quantify Changes in different seizure categories like Absent, Focal and Generalized. EEGs were recorded using hyperventilation test as activation procedures in 50 patients, who were proven cases of epilepsy with different seizure categories and compared with 50 age and sex matched normal subjects. Effects of hyperventilation test on EEG were recorded and changes were analyzed statistically. Hyperventilation test showed positive association in activation of non epileptiform background slowing. (P=0.487), even though statistically not very significant. Effect of activation was seen maximally in patients of generalized seizures especially in GTCS (75%). This work suggests that Hyperventilation test provoke Nonspecific Abnormal EEG Patterns in EEGs Of epileptic patients and normal subjects and hence increase the yield of EEG recordings.

INTRODUCTION

Electroencephalography is a noninvasive technique in which the electrical activity of the brain is recorded from the scalp to evaluate the function of the brain. It is thus complementary, rather than an alternative, to neuroimaging techniques. The differences in voltage between electrodes placed in different regions of the scalp are recorded and amplified. The polarity, frequency, amplitude, distribution, and changes with time of this activity are then studied to determine whether the findings are normal or abnormal and whether they suggest any particular type of underlying pathological process [1].

The nonepileptiform slow wave patterns in EEG are nonspecific in etiology, yet the presence of abnormality is often a reflection of the clinical presence and degree of brain dysfunction.

Acuity is unable to be demonstrated by EEG in nonepileptiform abnormalities, although serial tracing may further help to define the trend toward neurological evolution of improvement or deterioration. Therefore, EEG is able objectively to substantiate and quantify to a degree the depth of encephalopathy when diffuse nonepileptiform abnormalities are encountered and lateralize (or even localize) abnormalities...
when focal areas of slowing are evident. Many nonepileptiform and epileptiform abnormalities characterize encephalopathy [2]. Several activation techniques like hyperventilation, intermittent photic stimulation, sleep, and sleep deprivation have been used in clinical EEG laboratories to enhance preexisting abnormalities and / or induce abnormal findings in an otherwise normal EEGs. However, despite being utilized in routine clinical EEGs for decades, a number of differing views on the usefulness and indications for these procedures exist [3,4].

Physiologic Basis of the EEG Response to hyperventilation is the alteration of PCO₂, rather than pH or PO₂, and is the most important factor in producing the EEG response to hyperventilation, where as the most obvious and dramatic physiological effect of hyperventilation is decreased cerebral blood flow [3].

An alternative explanation was proposed by Gibbs and colleagues [11], who believed that cerebral hypoxia sufficient to cause EEG slowing cannot occur because the vasodilatory effects or anoxia should override the constrictive effects of hypocapnia. Instead, they concluded that cerebral hypocapnia is directly responsible for the typical EEG changes. As noted by Patel and Maulsby [12], several observations supports the idea that EEG slowing results from the direct effects of hypocapnia on the brainstem.

There has been considerable variability in the literature reported regarding EEG abnormalities in normal adult and epileptics using “hyperventilation test”. Therefore, the present work was undertaken by using “hyperventilation test” to,

- Compare the incidence of focal or generalized slowing patterns of uncertain significance during hyperventilation test on the EEGs of normal and epileptics.
- Quantification of Changes in different seizure categories like

METHODS

The sample used in this study consisted of 50 epileptic patients and 50 age matched normal subjects. Our study was a comparative study in which 50 Rt handed proven epileptic patients between the age group of 10-30 yrs, attending outpatient departments at M. S. Ramaiah Medical and Teaching Hospital were studied and further compared with age matched normal healthy subjects from the general population.

Ethical clearance was obtained from the M. S. Ramaiah Medical College ethical committee for human research to conduct the study. Patients with a history of Neurological diseases, Head injury ,Migraine, Drug abuse, Severe cardiopulmonary disease, Left handed Men, Uncontrolled hypertension, Sickle cell anemia were excluded from the study.

Data was collected from 50 males with known history of seizures and proven cases were taken as epileptic subjects who satisfied the inclusion and exclusion criteria were recruited from M.S. Ramaiah Medical and Teaching Hospital.

In epileptics, 25 patients had partial seizures and 25 patients had generalized seizures.

Age and sex matched normal volunteers without a history of seizures was taken from the general population. The study extended over a period of two years.

Procedures and Equipment

EEGs were recorded on a 21-channel EEG Nihon Kohden Neurofax Electroencephalograph EEG-1100.

EEGs were recorded from 21scalp sites based on the international 10-20 system (1), using silver/silver chloride electrodes with a ground electrode at the forehead, and use of referential, longitudinal bipolar and transverse bipolar montages.

It was explained that hyperventilation (“deep breathing test”) might bring on attacks. The consent form was signed at this stage.
Before the commencement of HV, the technologist explained and demonstrated the rate and depth of HV effort and asked the patient to hyperventilate continuously with the eyes closed. HV was performed in the supine position for 5 minutes.

Hyperventilation protocol [1] includes for 5 minutes of maximum effort from the subject. EEG activity will be recorded in the baseline condition for 1 minute with eyes closed condition and for 5 minutes during HV when they are asked to breathe deeply with eyes closed.

EEG findings during HV and baseline condition were tabulated as showing:

- No changes.
- Diffuse and lateralized Non epileptiform EEG background slowing.

All EEGs were interpreted by neurolist.

Difference in the 2 groups will be statistically analysed using:

- Analysis of variance
- Chi-Square chart.

Investigations and interventions conducted on patients:

Study involved non-invasive EEG recordings for both cases and controls in the department of neurology as described earlier with no financial liability on them.

RESULTS AND ANALYSIS

This Case control study consisted of 50 normal and 50 epileptic patients were undertaken to study and compare the incidence of non epileptiform background slowing in EEG of normal, and epileptic patients during hyperventilation. Quantification of Changes in different seizure categories like (a) Absent, (b) Focal.

Hyperventilation test showed positive association in activation of non epileptiform background slowing, (P=0.487), even though statistically not very significant.

In our selected series of 50 epileptic patients with different categories,

Non epileptiform EEG background slowing was seen in 12% in both generalized and partial epilepsies. Diffuse slowing was seen in 12% of patients with generalized epilepsy and in 4% of patients with partial epilepsy. Lateralised slowing was seen only in 8% of patients with partial epilepsy. In normal controls only finding was non epileptiform EEG background slowing which was seen in 6% of subjects.

Statistical Methods

Chi-square and Fisher exact test have been used to test the significance of changes in non epileptiform background slowing in different tests comparing between Epileptic and Normal. The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Table 1: Effect of Hyperventilation on non-epileptic slowing in Epileptic patients and Normal

<table>
<thead>
<tr>
<th>Non-epileptic Slowing</th>
<th>Epileptic (N=50)</th>
<th>Normal (N=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperventilation</td>
<td>6 (12.0%)</td>
<td>3 (6.0%)</td>
<td>0.487</td>
</tr>
</tbody>
</table>

Table 2: Type of Non-epileptic slowing in Epileptic patients and Normal

<table>
<thead>
<tr>
<th>Non-epileptic Slowing</th>
<th>Epileptic (N=6)</th>
<th>Normal (N=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse</td>
<td>4 (66.7%)</td>
<td>3 (100.0%)</td>
</tr>
<tr>
<td>Lateralised</td>
<td>2 (33.3%)</td>
<td>-</td>
</tr>
</tbody>
</table>
DISCUSSION

This study was done to test the hypothesis that the activation test such as hyperventilation enhance preexisting abnormalities and / or induce abnormal findings in otherwise normal EEGs [1]. However, hyperventilation test, despite being utilized in routine clinical EEGs for decades, a number of differing views on the usefulness and indications for these procedures exist [4,5,6].

In this study, we gathered evidence suggesting that HV is useful activation method, which increase the yield of EEGs in EEG units.

The typical normal hyperventilation response consists of a buildup of medium to high-amplitude, bisynchronous delta and theta waves and an increase in amplitude of theta and alpha waveforms. The distribution of delta and theta activity is typically anterior dominant in adolescents and adults but can be either anterior or posterior dominant in children. The hyperventilation response often includes frontal intermittent rhythmic delta activity (FIRDA) or particularly in children, occipital intermittent rhythmic delta activity (ORIDA). Although spontaneously occurring FIRDA or OIRDA indicates the presence of a diffuse cerebral dysfunction, their isolated appearance in hyperventilation is considered normal. Similarly, occasional sharply contoured components may be intermixed with FIRDA and OIRDA patterns (particularly if the EEG contains prominent alpha and beta waveforms) that can be misinterpreted as generalized epileptiform activity. Moreover, the alpha rhythm may first appear clearly in the recording only after hyperventilation, perhaps because of its relaxing effects. In normal individuals, the record usually returns to baseline less than 1 minute after hyperventilation ends. The magnitude of the hyperventilation response depends on several factors, including effort, age, posture, and blood sugar. Younger individuals tend to produce the largest responses, whereas elderly individuals often fail to show any EEG change [7].

Non epileptic diffuse slowing seen in normal subject during hyperventilation.
A comparison of more recent quantitative studies suggests that the older the subject is, the more likely hyperventilation will produce an overall increase in EEG amplitude without decreasing the mean frequency \[8,9\]. This may be partly due to the overall greater magnitude of response that occurs in children compared to adults. In a study of 37 normal children ages 6-17 years in which ventilation, partial pressure of oxygen (PO2), and partial pressure of carbon dioxide (PCO2) were measured, Konishi found a nearly inverse relationship between EEG slowing and age using a standardized hyperventilation protocol\[9\]. The effect of hyperventilation on the EEG begins earlier in children than adults and is apparent in 50% of cases within the first minute and 90% within the first 2 minutes \[10\].

Our findings are consistent with the previous studies, where hyperventilation has showed a very good provocative effect in generalized seizure patients \[4\].

In contrary to above findings, a study done by Holmes et al \[5\], to assess the effectiveness of voluntary hyperventilation (HV) in patients with proven epilepsy concluded that, their findings “provide compelling evidence that both localization-related and generalized epilepsies are relatively resistant to routine HV activation in adults and adolescents.

Our data clearly supported the hypothesis that the hyperventilation test enhance preexisting abnormalities and / or induce abnormal findings in otherwise normal EEGs.

The limitations in our current study was that the effects of hyperventilation tests can be assessed more accurately using sub dural depth electrode EEG recordings taken in conjunction with Brain imaging techniques like f MRI scan, SPECT scan, PET scan.

With study done after discontinuing antiepileptic drugs and standardization of hyperventilation using blood gas monitoring, results could have been more accurate.

We could not withdraw the antiepileptic drugs because of fear of recurrence of seizures among the epileptic patients and the also because of ethical constraints.

**CONCLUSION**

With this study it can be concluded that the hyperventilation test does precipitate the non epileptiform changes in EEGs and thus avoid missing abnormalities in EEG recordings and increase the yield of EEGs.

The presence of nonspecific EEG abnormalities when a diagnosis of non-epileptic and epileptic seizures is missed, it may lead to failure to implement appropriate treatment and also unnecessary use of anti-epileptic drugs etc., carry significant risks.

Correct diagnosis of non-epileptic seizures and epileptic seizures using hyperventilation test is associated with a reduction in health care costs and invasive procedures to diagnose epilepsy can be avoided.

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**REFERENCES**


