EFFICACY OF ACTIVATION PROCEDURES TO ILLUSTRATE EEG CHANGES IN EPILEPSY

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ABSTRACT

BACKGROUND
EEG or Electroencephalogram, which is the most important diagnostic procedure to evaluate Epilepsy patients, may sometimes fall short of accurate sensitivity and may require few Activation Procedures such as ‘Hyperventilation’ and ‘Sleep’ to bring out the active changes of an Epileptic brain. The present study was done with the aim of knowing the efficacy of such Activation Procedures like ‘Hyperventilation’ and ‘Sleep’ in illustrating the EEG wave pattern changes of an Epileptic brain during the interictal period.

MATERIALS AND METHODS
The present study was done in the Department of Physiology in association with the Department of Neurology, Assam Medical College & Hospital, Dibrugarh, Assam from June 2014 to May 2015. ‘113’ clinically diagnosed cases of Epilepsy were studied and analysed through Electroencephalogram using the internationally accepted 10-20 electrode placement method. Hyperventilation was used in 28 Epilepsy cases and Sleep was used in 14 Epilepsy cases. History & Physical examination findings were recorded in a Proforma. Chi-square analysis was done through GraphPad Prism 6 software to assess the significance of the activation procedures used.

RESULTS
Our study found that EEG of 42 cases out of the total 113 cases required Activation Procedures to elicit the wave pattern changes of the Epileptic brain. Hyperventilation was helpful in adult age group and sleep was useful in children age group. Hyperventilation had overall 53.57% sensitivity in detecting Epilepsy, and Sleep had 64.29% sensitivity in detecting Epilepsy. Hyperventilation was specifically helpful to elicit absence seizures where it had 75% sensitivity.

CONCLUSION
The sensitivity of EEG in detecting Epilepsy can thus be increased by using activation procedures like sleep & Hyperventilation to ensure that no epilepsy cases are missed out in diagnosis & treatment.

KEYWORDS
Epilepsy, EEG, Interictal Period, Activation Procedures.

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BACKGROUND
Activation procedures play a vital role in illustrating EEG changes in Epilepsy. The characteristic wave pattern changes that appear in an EEG i.e. an Electroencephalogram of an Epilepsy patient may sometimes remain hidden in a normal routine EEG, unless activation procedures like Sleep or Hyperventilation are used. In a routine EEG recording in an epileptic patient, various activation procedures are thus used to visualise an IED i.e. an Interictal Epileptiform Discharge, if not apparent in a normal awake EEG, so that a proper diagnosis can be made.

Hyperventilation is routinely performed for 3 to 5 minutes in most EEG laboratories. The purpose is to create cerebral vasoconstriction through respiratory means promoting systemic hypocarbia. Hyperventilation normally produces a bilateral increase in theta and delta frequencies (build-up) that is frontally predominant, and often of high amplitude. Activation, or the generation of epileptiform discharges, is infrequently seen in those with localisation-related epilepsy (<10%); however, this may approach 80% for those with generalised epilepsies that include absence seizures. Hyperventilation may produce focal slowing in patients with an underlying structural lesion.

The neuronal networks that generate wakefulness, NREM, and REM sleep give rise to different physiologic characteristics influencing the likelihood of seizure occurrence in epileptics. NREM sleep is a state of EEG synchronisation and relative preservation of antigravity muscle tone. Synchronous oscillations of cortical neurons that generate sleep spindles, K complexes, and tonic background slow waves during NREM sleep promote seizure
propagation. In contrast, REM sleep is characterised by desynchronisation of the EEG and loss of skeletal muscle tone. Desynchronisation of the EEG impedes seizure propagation during REM sleep and wakefulness. Preservation of antigravity muscle tone during NREM sleep permits expression of seizure-related movements whereas its absence during REM sleep blocks the clinical expression of seizures. Gloor et al. were the first to hypothesise that generalised spike-wave discharges of primary generalised absence epilepsies were generated in the same circuits as sleep spindles. Sleep further activates interictal epileptiform discharges in patients with absence and/or GTC seizures. Typically, spikes increase with sleep onset progressively through NREM3, diminish sharply in REM sleep, and increase again in the morning after awakening. During NREM sleep, generalised spike-wave discharges often become more disorganised, increase in amplitude and slow in frequency, sometimes with the addition of polyspikes, whereas the morphology in REM sleep is similar to wakefulness. The EEG is most abnormal after awakening or nighttime arousals in patients with awakening epilepsy. In contrast, in the sleep epilepsies, the EEG tends to be normal during wakefulness and shows a marked increase in interictal epileptiform discharges during sleep.

Lawrence et al also stated that Hyperventilation increases the rate of generalised discharges in childhood absence epilepsy and other generalised epilepsies. It is less productive in partial epilepsies, increasing the yield of focal IEDs by less than 10 percent.

MATERIALS AND METHODS
The present study was done in the Department of Physiology in association with the Department of Neurology, Assam Medical College & Hospital, Dibrugarh, Assam from June 2014 to May 2015. ‘113’ clinically diagnosed cases of Epilepsy were studied and analysed through Electroencephalogram using the internationally accepted 10-20 electrode placement method. History & Physical examination findings were recorded in a Proforma.

Inclusion Criteria
Clinically diagnosed cases of Epilepsy, of all age groups and of both sexes, attending the Neurology Clinic in AMCH, Dibrugarh for EEG analysis during their interictal period, in the one year of our study period, were included in the study design as cases.

Exclusion Criteria
Patients with Head injury, increased intracranial tension, Uncontrolled hypertension, Acute stroke, Excessive alcohol abuse, Chronic liver disease, Substance abuse, Severe comorbidity, Severe cardiopulmonary disease, Pseudoseizures were excluded from the study.

EEG Equipment used-
24-channel EEG Neuro Page Plus Electroencephalograph NP-3200 P.

If hyperventilation was used as activation procedure, patient was asked to take deep breaths continuously with the eyes closed and in the normal rate for 5 minutes in the supine position. EEG activity was recorded in the baseline for 2 minutes prior to HV with eyes closed and during 5 minutes of HV and then again for 5 minutes post hyperventilation. And Sleep was used mostly for children age group where either medications were used to induce sleep or the EEG was done when the baby spontaneously fell asleep in mother's lap. EEG tracing was taken for a total duration of about 20 minutes and the findings recorded. Chi-square analysis was done through GraphPad Prism 6 software to assess the significance of the activation procedures used.

RESULTS AND OBSERVATIONS
The study population during the one year period of the study comprised of 113 diagnosed cases of Epilepsy of different age groups and both the sexes, as shown in table 1.

The study population had the predominance of ‘the children age group’ (45.13%) during the one year period of study. This was followed by the ‘younger adult age group’ (25.66%). (Table 1). The mean age of presentation was 16.61 years (±SD 12.35 years). The sex distribution was almost equal in both the sexes with the males (50.44%) slightly greater than females (49.56%). (Figure 1).

Of the total number of 113 cases that were clinically diagnosed as Epilepsy, EEG could detect only 63 cases as Epilepsy with positive IEDs (Interictal epileptiform discharges). Thus, out of the total 113 cases, EEG detected 63 cases with positive IEDs and 50 cases had no IEDs in their EEG recording. (Figure 2). The EEG detection of IEDs were greater in the younger adult age group and in the female sex.

Of the total 113 cases, 102 cases were diagnosed clinically as generalised epilepsy and 11 cases were diagnosed clinically as focal epilepsy cases.

Of the 102 generalised epilepsy cases, EEG could detect 56 cases with positive IEDs (Table 2). And of the 11 cases of focal epilepsy, EEG could detect 7 cases with positive IEDs (Table 3). EEG classified the epilepsy cases into different types with the help of IEDs; whether there were Intermittent Generalised IEDs coming from all the channels in the montage chosen; or there were Intermittent Focal IEDs coming from only particular channels in the montage chosen.

Two kinds of Activation Procedures were used in our study in some cases; if a normal awake EEG could not record any IEDs in a clinically diagnosed case. Those were ‘Hyperventilation’ and Sleep records. Of the 113 cases, 14 cases used sleep as the activation procedure and 99 cases were awake records. Hyperventilation was used in 28 selected cases of the awake records. (Table 4).

Sleep was mostly used for children and hyperventilation was mostly used in the adolescents and adults who had no complications, using the exclusion criteria.

It was found that although both sleep and hyperventilation were successful in detecting IEDs in many
cases; in our study, use of sleep as activation procedure was found to be more effective. (Table 4, Figure 3). It was also found that in Generalised epilepsy cases, hyperventilation was very successful in producing IEDs in case of Absence seizures. (Figure 4). IEDs seen in Focal epilepsy cases did not require the use of Activation procedures in our study group (Table 6).

<table>
<thead>
<tr>
<th>Category</th>
<th>Age Group</th>
<th>Male Patients</th>
<th>Female Patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Neonates &amp; Infants</td>
<td>1 yr.</td>
<td>3 (5.26%)</td>
<td>0 (0.00%)</td>
<td>3 (2.65%)</td>
</tr>
<tr>
<td>2. Children</td>
<td>&gt;1 yr. to 12 yrs.</td>
<td>24 (42.11%)</td>
<td>27 (48.21%)</td>
<td>51 (45.13%)</td>
</tr>
<tr>
<td>3. Adolescents</td>
<td>&gt;12 yrs. to 18 yrs.</td>
<td>6 (10.53%)</td>
<td>15 (26.79%)</td>
<td>21 (18.58%)</td>
</tr>
<tr>
<td>4. Younger Adults</td>
<td>&gt;18 yrs. to 35 yrs.</td>
<td>16 (28.07%)</td>
<td>13 (23.21%)</td>
<td>29 (25.66%)</td>
</tr>
<tr>
<td>5. Older Adults</td>
<td>&gt;35 yrs.</td>
<td>8 (14.04%)</td>
<td>1 (1.79%)</td>
<td>9 (7.96%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>57 (50.44%)</td>
<td>56 (49.56%)</td>
<td>113</td>
</tr>
</tbody>
</table>

**Table 1. Showing Distribution of the Study Population**

<table>
<thead>
<tr>
<th>Generalised Epilepsy</th>
<th>Number of Cases</th>
<th>Percentage</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTCS</td>
<td>51</td>
<td>91.07</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Absence Seizures</td>
<td>1</td>
<td>1.79</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. Shows Classification of Generalised Epilepsy by EEG**

<table>
<thead>
<tr>
<th>Focal Epilepsy Detected</th>
<th>Number of Cases</th>
<th>Percentage</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPS</td>
<td>3</td>
<td>42.85</td>
<td>0.4</td>
</tr>
<tr>
<td>CPS</td>
<td>3</td>
<td>42.85</td>
<td></td>
</tr>
<tr>
<td>PSSG</td>
<td>1</td>
<td>14.29</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Shows Classification of Focal Epilepsy By EEG**
DISCUSSION

Angeleri in 1975, Niedermeyer & Rocca in 1972 and Sato et al in 1973 said that the adoption of several methods can increase the chance of detecting IEDs. Sleep effectively improves detection of both generalised and focal IEDs.\textsuperscript{4,5,6} Sato et al in 1983, Miley & Forster in 1977 and Wolf & Goosses in 1986 said that hyperventilation and photic stimulation also induces IEDs in many patients, especially in generalised seizures (Sato et al 1983; Miley & Forster 1977; Wolf & Goosses 1986).\textsuperscript{6,7,8}

In our present study, 99 cases of the total 113 cases showed IEDs in an awake EEG recording and in the rest of the 14 cases, sleep was used as the activation procedure to see if IEDs appear. We found that 9 out of 14 cases showed the appearance of IEDs on sleep, accounting to a 64.29% yield, of sleep as the activation procedure.

In a study held in 2008, ‘First seizure: EEG and neuroimaging following an epileptic seizure’, conducted by Pohlmann-Eden B, Newton M, it was found that the yield of EA (epileptiform activity) in routine EEG ranged from 12% to 27% and increased to 23% to 50% in sleep EEG. EA in first EEG was greater in children compared to patients >16 years.\textsuperscript{9}

In our study, the yield of a routine awake EEG was found to be 54.55% and the yield of EEG while using sleep increased to 64.29%. Thus, our study matches with the above study with respect to the fact that a sleep EEG is found to increase yield of EEG in detecting Epilepsy.

Edward B Bromfield in 2012 quoted that most study results agree that sleep recordings increase the sensitivity of EEG, and some suggest that sleep deprivation can increase the yield beyond its effect on promoting sleep. The other commonly used Activation procedures, Hyperventilation (HV) and Intermittent Photic Stimulation (IPS), occasionally elicit IEDs that do not appear at other times. Both HV and IPS are more effective in inducing generalised epileptiform IEDs than focal IEDs.\textsuperscript{10}

In our study, we used hyperventilation in 28 selected cases, out of which 15 cases showed positive IEDs giving a yield of 53.57%. Hyperventilation was found to be very effective in absence seizure. This observation of ours matches with the finding quoted in Sonia Khans that Hyperventilation is a well-known activator of the generalised 3 Hz spike wave discharges.\textsuperscript{11}

The authors of Nigeria, Owolabi et al, in 2013 found 17 (89.5%) out of 19 patients with 3 Hz spike and complex being activated by Hyperventilation. However, they found hyperventilation unremarkable in 76% patients. (Owolabi L. F. et al., 2013).\textsuperscript{12}

This finding too matches with our study in which 3 out of 4 cases of 3 Hz spike and wave complex showed positive IEDs on hyperventilation, accounting to 75% of efficacy of hyperventilation in absence seizures. However, in contrast to their study, overall, we found hyperventilation unremarkable in only 46.42% of patients and remarkable in 53.57% of patients. Lawrence et al in 2010 also stated that hyperventilation increases the rate of generalised discharges in childhood absence epilepsy and other generalised epilepsies. It is less productive in partial epilepsies, increasing the yield of focal IEDs by less than 10 percent.\textsuperscript{2,3}

Pillai et al quoted that Hyperventilation increases generalised spike–wave activity in 50–80% of patients with absence seizures, and frequently precipitates clinical absences, especially in untreated patients. The effect of hyperventilation on focal spikes is less impressive.\textsuperscript{3} In our study, also we did not require the use of hyperventilation in the focal epilepsy cases.

CONCLUSION

The present study thus confirmed the importance of ‘Activation procedures’ in the EEG study of Epilepsy cases. Wave patterns associated with ‘Absence seizures’ are better elicited by ‘Hyperventilation’ while running an EEG. Similarly, ‘Sleep’ in case of children helps in the EEG diagnosis of Epilepsy. Thus, in conclusion, it can be said that Epilepsy cases under strong clinical suspicion, that do not show significant changes in a routine EEG, must undergo activation procedures, unless contraindicated, so that no diagnosis can be missed out and all patients get treatment successfully.

REFERENCES


