Does Hyperventilation Elicit Epileptic Seizures?

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**Summary:** Purpose: Voluntary hyperventilation has been advocated for many decades as an “activating” procedure to provoke clinical seizures and epileptiform discharges in subjects with suspected epilepsy who undergo standard EEG recordings. This study was undertaken to determine the effects of hyperventilation in patients with proven epilepsy.

Methods: We examined the records of 433 consecutive patients with proven epilepsy, as documented by long-term video-EEG studies. The patients underwent 5 min of voluntary hyperventilation during standard EEG recordings. All EEGs were interpreted by board-certified electroencephalographers. The patients ranged in age from 10 to 64 years; 384 (88.7%) had localization-related and 48 (11.3%) generalized epilepsy syndromes.

Results: Hyperventilation was associated with a clinical seizure in two (0.46%) of the subjects (partial seizures in both cases). Interictal epileptiform discharges were interpreted as showing in increase in frequency during hyperventilation in 19 (4.4%) patients, when compared with the baseline EEG.

Conclusions: Voluntary hyperventilation in patients with unequivocal epilepsy is rarely associated with either clinical seizures or an increase in frequency of epileptiform discharges.

**Key Words:** Hyperventilation—Activation procedure—EEG—Epileptic seizures—Hypocapnia.
TABLE 1. Effect of hyperventilation on EEG

<table>
<thead>
<tr>
<th>Epilepsy syndrome</th>
<th>n</th>
<th>No EEG changes</th>
<th>Seizures</th>
<th>Increased IEDs</th>
<th>Seizures and/or increased IEDs</th>
<th>Nonepileptic EEG slowing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localization-related</td>
<td>384</td>
<td>307 (79.9%)</td>
<td>2 (0.52%)</td>
<td>13 (3.4%)</td>
<td>14 (3.6%)</td>
<td>Diffuse: 60 (15.6%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lateralized: 11 (2.9%)</td>
</tr>
<tr>
<td>Generalized</td>
<td>49</td>
<td>35 (71.4%)</td>
<td>0</td>
<td>6 (12.2%)</td>
<td>6 (12.2%)</td>
<td>Diffuse: 10 (20.4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lateralized: 0</td>
</tr>
<tr>
<td>Total</td>
<td>433</td>
<td>342 (79.0%)</td>
<td>2 (0.46%)</td>
<td>19 (4.4%)</td>
<td>20 (4.6%)</td>
<td>81 (18.7%)</td>
</tr>
</tbody>
</table>

IEDs, interictal epileptiform discharges.

during HV, to the frequency of discharges during the remainder of the 30- to 60-min recording; and (d) nonepileptiform changes (i.e., slowing of the background rhythms). Grading of EEGs into one of these four categories was performed without prior knowledge of subjects’ age, gender, or epilepsy syndrome.

RESULTS

In our unselected series of 433 patients with epilepsy, any type of epileptiform EEG changes was observed remarkably rarely, in fewer than 5% of the patients during HV. A clinical seizure did not occur during HV in any patient with a generalized epilepsy syndrome and in 0.52% of patients with localization-related epilepsy. IEDs, in turn, were increased in only 12.2% and 3.4% of the patients with generalized and localization-related epilepsies, respectively. Nonepileptiform slowing of EEG background was observed during HV in about one fifth of all patients. Of the group with HV-related slowing, 13.6% showed lateralized slowing during HV; all of these subjects had a localization-related epilepsy syndrome (see Table 1 for a summary of the findings).

DISCUSSION

Our findings are in sharp contrast to current textbook concepts and the observations previously reported from smaller patient groups. The clinical reports with voluntary HV have been followed by a large number of experimental studies in which severe hyper- or hypocapnic conditions are created to evaluate their effects on seizures (8, 9). Findings from these different types of studies have been merged to formulate the premise that HV-induced hypocapnia is invariably epileptogenic and constitutes the mechanism of action whereby HV provokes epileptic seizures (8).

Several reasons may have existed for the discrepancy between our findings and the earlier clinical studies. Small numbers and selection of patients in previous investigations may have biased the results. Because of the absence of a positive confirmation of epilepsy in the era before long-term EEG-video monitoring, it is probable that at least some previous studies included subjects with nonepileptic seizures. It also is possible that the dramatic slowing of EEG background patterns that occasionally occurs during HV, particularly in children, was misinterpreted by some early investigators as being epileptiform in nature (10). Our report avoids these issues by including, to our knowledge, the largest series of individuals with unequivocal epilepsy who have undergone HV during EEG recordings.

These findings provide compelling evidence that both localization-related and generalized epilepsies are relatively resistant to routine HV activation in adults and adolescents. However, this conclusion may not apply to younger children, especially those with typical absence epilepsy, in whom the evidence for HV provocation of seizures is strongest. We have no data in patients younger than 10 years, and a diagnosis of typical absence epilepsy was distinctly rare in our series. However, it is noteworthy that in none of the 25 older children and adults on our series who had generalized epilepsy that included absence did HV elicit seizures.

Despite the limitations presented here, HV may still have a useful role in clinical practice. The effectiveness of HV in eliciting clinical seizures or interictal epileptiform discharges in young children in general, and those with generalized epilepsy syndromes in particular, remains to be clearly defined. In adults, although we did not find that clinical seizures were provoked by HV in generalized epilepsy, it may be clinically useful nevertheless to find that >10% of subjects with generalized seizures have an increase in interictal discharges during this procedure. Finally, recent evidence suggests that, although HV only rarely provokes seizures or discharges in cases of proven epilepsy, it may be a powerful technique, when used in conjunction with EEG-video monitoring, to elicit events in subjects with psychogenic nonepileptic seizures (11).

In conclusion, our results constitute evidence contrary to the notion that HV is an effective “activating” procedure for the majority of patients with epilepsy. This calls for reexamination of the role of HV in routine clinical EEG studies and the concepts that link hypocapnia to seizure provocation.

REFERENCES


