Interindividual Variability in the Occurrence of Sleep Spindles Induced by Interictal Epileptiform Discharges: an Electrocorticographic Analysis

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Introduction

- Gelinas et al. (Nat Med 2016)1 have reported the following findings: 1) Interictal epileptiform discharges (IEDs) induced "abnormal" sleep spindles in a rat model of temporal lobe epilepsy (TLE); 2) IED-induced spindles were associated with impaired memory in a rat model of TLE; 3) IED-induced spindles were also observed in three TLE and one frontal lobe epilepsy (FLE) patients.
- These findings suggest that the replacement of "normal" sleep spindles by IED-induced spindles may cause impaired memory consolidation observed in the patients with focal epilepsy2, because sleep spindles play a key role in memory consolidation3.
- However, no other studies have confirmed these results yet. Evidence of IED-induced spindles in human patients, especially in patients with extra-TLE, is scarce.
- The aim of this study was to evaluate the incidence of IED-induced spindles in the human patients with FLE.

Methods

- Patients: six FLE patients underwent electrocorticography (ECoG) for seizure localization at Kyushu University Hospital (table 1).
- Data: 44.9 (36.6-50.0) min of ECoG recordings during NREM sleep (stage 2-3). Sampling rate: 1,000 Hz.
- Analysis: sleep spindles were automatically detected using a conservative criteria4. Then, sleep spindle events time-locked to IED were counted. Changes in spindle-band (9-16 Hz) amplitude after IEDs were statistically analyzed. Association between magnitude of IEDs and spindle-band after IEDs were also evaluated.

Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>ID</th>
<th>Age</th>
<th>Sex</th>
<th>Cause of Epilepsy</th>
<th># of IEDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>30</td>
<td>M</td>
<td>Focal cortical dysplasia, type IIa</td>
<td>46</td>
</tr>
<tr>
<td>S2</td>
<td>23</td>
<td>M</td>
<td>Sturge-Weber syndrome</td>
<td>43</td>
</tr>
<tr>
<td>S3</td>
<td>17</td>
<td>F</td>
<td>Focal cortical dysplasia, type IIa</td>
<td>246</td>
</tr>
<tr>
<td>S4</td>
<td>22</td>
<td>F</td>
<td>Focal cortical dysplasia, type Ib</td>
<td>156</td>
</tr>
<tr>
<td>S5</td>
<td>16</td>
<td>M</td>
<td>Desmoplastic infantile ganglioglioma</td>
<td>44</td>
</tr>
<tr>
<td>S6</td>
<td>27</td>
<td>M</td>
<td>Tuberous sclerosis</td>
<td>176</td>
</tr>
</tbody>
</table>

Results

- A clear peak in sleep spindle occurrences 0.5 to 1.0 sec after IEDs was observed in 4 out of 6 patients (S1-S4) (Figure 2).
- These 4 patients showed significant increases in spindle-band amplitude 0.5 to 1.0 sec after IEDs mainly in electrodes located in the middle frontal gyrus (vs 1.0-0.5 s before IEDs, Wilcoxon signed-rank test, p-values were corrected by FDR) (Figure 3).
- Amplitudes of IEDs were significantly correlated with those of spindle-band 0.5 to 1.0 sec after IEDs in 5 out of 6 patients (S1-S5) (Figure 4).

Discussion

- Timing (figure 2) and spatial distribution (figure 3) of IED-induced sleep spindles were consistent with the original report1.
- Spatial extent of IEDs was broader in S1-S4 than in S5-S6 (figure 1), and amplitudes of IEDs were correlated with those of sleep spindles after IEDs (figure 4). These findings suggest that the occurrence of IED-induced sleep spindles depends on the magnitude of IEDs.
- Interindividual variability in the occurrence of IED-induced sleep spindles may be associated with Interindividual differences in the impairment of learning and memory in the patients with frontal lobe epilepsy.

Conclusions

- Sleep spindles induced by IEDs were evident in 4 out of 6 FLE patients (66.6%).
- The occurrence of IED-induced sleep spindles may depend on the magnitude of IEDs.

References


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