Neuropsychological EEG activation in patients with juvenile myoclonic epilepsy

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Summary

We studied the effects of higher mental activity on the EEG, i.e., neuropsychological EEG activation (NPA), in patients with juvenile myoclonic epilepsy (JME). Thirty patients with JME underwent a conventional EEG recording and EEG recording during performance of a battery of twelve neuropsychological tasks, which involved decision making, reading, calculations, constructive activities and drawing.

Twenty-three JME patients (76.6%) responded (i.e., showed EEG activation) to at least one neuropsychological task (p=0.003). Four neuropsychological tasks, two involving the use of the hands and two without manual involvement, were associated with a high frequency of EEG activation (40-60% of JME patients), although statistical analysis did not reveal any one test as the most significant for NPA activation.

Neuropsychological EEG activation, using a variety of tasks both manual and non-manual, is a useful tool in evaluating patients with JME.

KEY WORDS: EEG, juvenile myoclonic epilepsy, neuropsychological tests.

Introduction

Juvenile myoclonic epilepsy (JME) is a well-defined and common idiopathic generalized epileptic syndrome with onset in puberty (1). It is characterized by myoclonic jerks, mainly on awakening, and concurrent generalized tonic-clonic and absence seizures (1). Despite the syndrome’s distinct clinical features and EEG findings, patients may not actually receive a diagnosis of JME, particularly if their presenting symptoms are atypical and their EEG lacks epileptic features (2-7).

Patients with JME are very sensitive to external factors such as sleep deprivation, sudden awakening, fatigue, fever, and flickering lights (2-5). Seizures in these patients may also be precipitated by complex mental tasks e.g., calculations, constructive activities, drawing, or playing complex strategic board games (8-11). The monitoring of neuropsychological EEG activation (NPA), i.e., the presence of EEG activity prompted by the execution of cognitive tasks, has been proposed as an auxiliary method in the diagnosis of various epileptic syndromes (12). Matsuoka et al. (13) found that the NPA tasks used in their protocol provoked epileptic discharges in 7.9% of their patients with different types of epilepsy. The purpose of our study was to explore the effects of cognitive function on the EEG (i.e., NPA) in patients with JME.

Materials and Methods

Patient selection

Thirty de novo JME patients, 13 men and 17 women, were studied. Diagnosis was based on the criteria of the Commission on Classification and Terminology of the International League against Epilepsy (1). The demographic features of our patients are shown in Table I. Conventional EEG and NPA battery were performed as part of their initial laboratory investigation prior to the start of treatment. Only 8 patients reported myoclonic jerks provoked by reading, solving arithmetic problems and playing backgammon. The patients all gave their informed consent to their participation in this study.

Neuropsychological EEG activation (NPA)

On day 1, in the morning, all the patients were submitted to a conventional (awake) EEG with 3-minute hyperventilation and intermittent photic stimulation. The EEG was recorded on paper using a traditional polygraph (ERA 14-21, OTE Biomedica SpA, Florence, Italy, bandpass 0.5-
35 Hz), with silver/silver chloride surface electrodes, placed on the scalp according to the 10-20 International System.

The NPA assessment began on day 2. EEG recordings were made while the patient performed a battery of neuropsychological tasks, such as decision making, reading, calculations, constructive activities, and drawing. The NPA assessment battery lasted approximately 100-110 minutes. Since this activation period was too long for the patient to endure in one session, we decided to divide the battery into three parts, one to be performed on each of three successive days. In order to allow subsequent test-retest analysis, a 5-minute routine EEG was performed on each of these three days before starting the NPA assessment. A task was deemed to have precipitated EEG abnormalities if the frequency of discharges (number of discharges per minute) was at least twofold compared with baseline EEG on the same day (13). Patients who showed NPA in at least one task were classed as responders.

The neuropsychological tasks employed and their relative durations were the following:

1. Tasks involving decision making:
   - Brooks letter-outline task, which tests mental spatial manipulation (duration: 10 min). This task required the patient to describe from memory a route around the outline of an uppercase letter, which he or she had previously seen, specifying the sequence of necessary left and right turns. The Greek letters H, E, K, Π, Z, X, M, T, and Σ were used (11-14).
   - WAIS Similarities subtest (duration: 6 min) (15,16).
   - WAIS Vocabulary subtest (duration: 5 min) (16,17).
   - Word fluency (duration: 3 min). The patient was asked rapidly to name words beginning with the Greek letters Μ, Π, Α. (18).
   - Silent reading (duration 5 min). The patient was asked to read silently the political article of a newspaper (9, 11,17,19).

2. Mathematical calculations. The following tests were performed:
   - WAIS Arithmetic subtest (duration: 10 min), which assesses performance in mental arithmetic (9,11,15-17).
   - Written multiplications of two-digit numbers. (duration: 5 min) (14,17).
   - Written divisions with a remainder (duration: 5 min) (14,17).

3. Constructive activities and drawing. These were examined using:
   - WAIS Block Design subtest (duration: 8 min) (9,11,14,16,19,20).
   - Drawing common objects from memory (duration: 5 min) (e.g., a ship, a bicycle, a toothbrush, a radiator, an elephant) (14,21).
   - Drawing geometric designs from memory (duration: 3 min) (e.g., a trapezoid, an hexagon, a rhomb, a cube, a cylinder) (14,19,21).
   - Doodling figures from memory (duration: 6 min) (e.g., a dragon, a sunny day, a small supermarket viewed from the outside) (14,19,21).

The NPA battery was performed under the supervision of a psychologist and a neurologist. The psychologist asked the patient to perform the various tasks and wrote down the patient’s answers. The neurologist monitored the EEG and recorded the beginning and the end of each test.

Statistical analysis

The NPA data are presented as one-sample proportions (percentages) with confidence intervals (22). The association between clinical characteristics (age, disease duration, seizure frequency) and NPA was examined by means of eta squared, while family association was tested by means of the phi and contingency coefficients. The chi square test was employed for comparisons between NPA responders and non responders. Comparisons between NPA tests were performed using the McNemar’s test. Finally, comparisons between clinical characteristics of the disease in the responder and non-responder groups were performed by means of Student’s t-test. Data were analysed using the SPSS for Windows, version 10.0, statistical software.

Results

All patients had epileptiform discharges, consisting of sharp waves, spikes and polyspike-wave complexes in the conventional EEG. The median number of discharges per minute was 0.8 (range 0.1-1.8). Application of the NPA battery resulted in an at least twofold increase in the number of epileptiform discharges per minute.

Twenty-three patients (76.6%) responded to at least one neuropsychological task and seven failed to show NPA (χ²: 8.53, p=0.003).

Table II presents analytically the percentages of patients

Table II - Neuropsychological EEG activation (NPA) in 30 patients with juvenile myoclonic epilepsy.

<table>
<thead>
<tr>
<th>Tests</th>
<th>Patients showing NPA n. %</th>
<th>95% Confidence Interval [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooks letter-outline task</td>
<td>15 50</td>
<td>33.2-66.8</td>
</tr>
<tr>
<td>WAIS Similarities</td>
<td>8 26.6</td>
<td>14.2-44.4</td>
</tr>
<tr>
<td>WAIS Vocabulary</td>
<td>4 13.3</td>
<td>5.3-29.7</td>
</tr>
<tr>
<td>Word fluency</td>
<td>4 13.3</td>
<td>5.3-29.7</td>
</tr>
<tr>
<td>Silent reading</td>
<td>8 26.6</td>
<td>14.2-44.4</td>
</tr>
<tr>
<td>WAIS Arithmetic (mental arithmetic)</td>
<td>15 50</td>
<td>33.2-66.8</td>
</tr>
<tr>
<td>Written multiplications of two-digit numbers</td>
<td>5 16.6</td>
<td>7.3-33.6</td>
</tr>
<tr>
<td>Written divisions with a remainder</td>
<td>13 43.3</td>
<td>27.4-60.8</td>
</tr>
<tr>
<td>WAIS Block Design</td>
<td>10 33.3</td>
<td>19.2-51.2</td>
</tr>
<tr>
<td>Drawing common objects from memory</td>
<td>3 10</td>
<td>3.5-25.6</td>
</tr>
<tr>
<td>Drawing geometric designs from memory</td>
<td>5 16.6</td>
<td>7.3-33.6</td>
</tr>
<tr>
<td>Doodling figures from memory</td>
<td>18 60</td>
<td>42.5-75.7</td>
</tr>
</tbody>
</table>
showing NPA in each of the tasks used.

Figure 1 shows polyspike-slow wave discharges in the conventional EEG of a 15-year-old patient (male). Figure 2 shows polyspike-slow wave discharges (NPA) induced in the same patient by doodling a figure (a dragon) from memory.

Table III (over) presents the results of comparisons of the four tasks most frequently found to produce EEG activation (Brooks letter-outline task, mental arithmetic, written divisions with a remainder, doodling figures from memory) with those less frequently found to produce EEG activation. These comparisons failed to identify a single test as the most significant for NPA activation. The most frequent provoker of EEG activation, i.e., the doodling figures from memory task, was not found to differ significantly from the other three frequent EEG-activating tasks. However, it was found to differ significantly from all the tasks less frequently found to evoke EEG activity.

No significant correlation emerged between any clinical characteristic (such as age, disease duration and frequency of seizures) and neuropsychological task. Furthermore, patients with a family history of seizures showed greater EEG activation in written multiplications (phi coefficient: 0.539, p=0.003; contingency coefficient: 0.475, p=0.003), written divisions (phi coefficient: 0.385, p=0.035; contingency coefficient: 0.360, p=0.035) and Block Design test (phi coefficient: 0.373, p=0.041; contingency coefficient: 0.350, p=0.041).

Finally, comparisons between the clinical characteristics
of the responders and the non responders did not reveal statistically significant differences.

**Discussion**

It is already known that epileptic seizures can be precipitated by various higher mental activities such as reading, writing, solving arithmetic problems, decision making, and constructive activities (19, 20, 23, 24). The frequency of such precipitation in different types of seizure and epileptic syndromes remains unclear. Matsuoka et al. (9) first reported that an NPA protocol provoked paroxysmal discharges in 84% of patients with JME. The most provocative mental activities were writing, written calculations with figures, and constructive activities, which provoked discharges in 62%, 60% and 32% of their patients respectively. The constructive activities included the Block design test and figure drawing. Senanayake (11) observed in patients with JME that the frequency of epileptiform abnormalities increased during NPA protocol tasks, especially when the patients were solving puzzles requiring spatial manipulation, but not during intelligence tests, reading, writing or memory tests.

In a more recent paper, Matsuoka et al. (13) reported that mental activities mainly associated with the use of the hands, such as writing, written calculations and spatial construction, provoked discharges in 68.4%, 55.3%, and 63.2% of patients with different types of epilepsy, respectively. Mental calculation and reading provoked EEG discharges in only 7.9% and 5.3% of the patients. Among their epileptic patients the precipitating effect of the NPA was most obvious in the group of patients with JME, being observed in 46.7% of these subjects (13).

In our study, EEG activation was induced by at least one neuropsychological task in 76.6% of the JME patients. This finding is comparable with similar reports in the literature (9,13). Although some tests yielded high rates of activation, statistical analysis failed to identify any one of them as the most significant. It is noteworthy that the tasks most frequently activating the EEG included both manual – doodling figures (60%) and performing written calculations (43.3%) – and non-manual activities – solving arithmetic problems mentally (50%) and mental spatial manipulation (50%). Significant activation by non-manual tasks has not been described in other similar studies (9,11,25), which stress the importance of manual tasks in NPA. Nevertheless, our findings suggest that non-manual tasks can induce NPA in a substantial number of JME patients.

Therefore we propose that a combination of manual and non-manual neuropsychological tasks should be employed for NPA procedures in JME patients. The pathopsysiological mechanism underlying the NPA phenomenon is unclear. It has been proposed that the phenomenon may be related to activating mechanisms responsible for the induction of seizures in reflex epilepsies.

Further studies are needed in order to correlate NPA results with successful management of epilepsy and to clarify the possible existence of reflex epileptic traits in JME and the relation between JME and reflex epilepsy.

**References**

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EEG activation in juvenile myoclonic epilepsy

Concerning the document, extract the following:
