EEG spectral analysis in delirium

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SUMMARY Spectral analysis of EEG was conducted for 51 elderly delirious patients meeting the Diagnostic and Statistical Manual of Mental Disorders III (DSM-III) criteria and for 19 controls. As a whole group, and also when subdivided according to the type of delirium, severity of cognitive decline or the type of central nervous system disease, delirious patients showed significant reductions of alpha percentage, increased theta and delta activity and slowing of the peak and mean frequencies and these changes were also obvious in individual recordings. The alpha percentage and various ratio parameters correlated significantly with Mini Mental State score, and delta percentage and mean frequency with the lengths of delirium and hospitalisation. The results indicate an association between spectral EEG changes and severity of cognitive deterioration in delirium.

Delirium is an organic mental disorder characterised by disorganisation of mental functioning due to widespread, temporary derangement of cerebral metabolism appearing symptomatically during the course of an underlying physical illness.1-3 It features concurrent disorders of attention, perception, thinking, memory, psychomotor behaviour, and the sleep-waking cycle with fluctuations in depth, and often with delusions or hallucinations.4 The aetiology of delirium is almost invariably multifactorial, often including a predisposing central nervous system (CNS) disease and one or more possible causative factors.5 6

In demented patients, a number of studies with routine and quantitative EEG have shown slowing of the mean occipital frequency and increased activity in the lower frequency bands with correlation to the degree of dementia, especially in Alzheimer’s disease.7-12 In delirious patients, previous studies using routine EEG have also shown an increase of slow wave activity and slowing and disruption of the normal alpha rhythm.5 13 14 As information concerning the possible correlations between the clinical symptoms (such as severity of cognitive deterioration and type of delirium) and EEG changes in delirious patients is limited, we decided to study the spectral EEG changes in delirious elderly patients meeting the DSM-III criteria15 and to compare them with age-equivalent healthy controls.

Material and methods

Patients and controls: EEG spectral power analysis parallel with routine EEG was conducted for 51 patients with a mean age, SD of 74.3, 6.6 years (range 60-88 years, sex distribution: 24 males and 27 females) as a part of our prospective clinical, neurochemical and neurophysiological study on delirium at Moisio Mental Hospital jointly with the Departments of Neurology and Clinical Neurophysiology, University Central Hospital of Kuopio. Patients with alcohol delirium were excluded because of possible follow-up difficulties. All other delirious patients with informed consent and meeting the DSM-III criteria were included consecutively. EEG with spectral analysis was also performed for 19 optimally healthy controls (6 males and 13 females, mean age, SD 72.4, 8.2 years, range 61-83 years), who used no CNS-active drugs and showed normal mental status in neuropsychological tests. All controls lived at home and participated in the normal ageing study of the University Central Hospital of Kuopio. The sex distribution of the delirious patients and controls was similar (chi square = 1.35; p > 0.05).

The patients and controls were studied thoroughly during the period of hospitalisation. Their previous charts were reviewed, a close relative was interviewed, and medical, neurological and psychiatric examinations were carried out. The diagnostic work-up also included CT of the head, radiography of the chest and laboratory analyses of blood and CSF. Cognitive capacity was assessed using the Mini Mental State (MMS) examination6 during the same day as the EEG recording. The evaluation of the putative central nervous system diseases and aetiological factors in delirious patients was based on the history, clinical examination and

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laboratory results. Seven of the delirious patients (14%) met the DSM-III criteria for primary degenerative or Alzheimer-type (AD) dementia, but owing to the variability of the course of dementia they are rated as possible AD patients according to the NINCDS-ADRDA criteria.7 Thirty patients (59%) met the DSM-III criteria for multi-infant dementia, two patients (4%) had Parkinson’s disease and in 12 (23%) cases some other apparent CNS disease could be found. In AD patients the most common triggering factor for delirium was infection (5 cases), and in patients with multi-infant dementia a new stroke (10 cases) was often implicated as the putative aetiology for delirium. Metabolic disorders included one severe hyperthyroïdism, one hepatic insufficiency and three severe hyperglycaemias with electrolyte disturbances. The individual aetiologies of delirium are listed in table 1.

In order to compare quantitative EEG results in various subgroups of delirium, the patients were also grouped according to their cognitive performance (mild cognitive decline scoring from 21–24 in the MMS, moderate 11–20 and severe 0–10) and the type of delirium (1. the hyperactive variant of delirium, which is characterised by psychomotor overactivity, high alertness and enhanced tendency to psychosis; 2. the silent or hypoactive variant with reduced level of psychomotor activity and alertness and less pronounced psychotic symptoms; and 3. the mixed variant with features of both hypo- and hyperactive variants).18

**Spectral EEG method:** For the delirious patients the EEG was performed on the first day after admission. The EEGs were recorded with 16-channel Siemens-Elema equipment with a time constant of 0.3 s and a high frequency limit of 70 Hz using the international 10–20 electrode placement system.19 Verbal communication was used if necessary to maintain alertness of the subject. EEG reactivity was tested with eyes open—eyes closed procedure immediately before and after the quantitative EEG sampling.

Our method of spectral EEG has been previously described.20 The fast Fourier Transform (FFT) was computed for off-line resting awake EEG sample from the T6-O2 derivation (or T5-O1 if artifacts in T6-O2). The EEG epochs were visually inspected on an oscilloscope screen and epochs with artifacts were manually rejected. Each eight (precisely 8–192) second epoch was digitised with 12-bit multichannel analyser (Tracor Northern 1710), using a sample rate of 125 Hz and resulting therefore 1024 samples per epoch. The digitised EEG samples were then transferred to a Tektronix 4052D computer and stored on a disc. For each epoch the FFT was computed on a series of half-overlapping sections comprising 512 points. To reduce leakage and time truncation errors, the time-domain waveform of each section was multiplied by a cosine (Hanning) window before the FFT operation. The FFTs from a total of twelve sections were averaged to obtain a frequency spectrum of the whole EEG sample of 32,772 seconds.

The relative powers (% of total EEG power) in the delta (1.46–3.91 Hz), theta (4.15–7.32 Hz), alpha (7.57–13.92 Hz) and beta (14.16–20.02 Hz) ranges were calculated. The total range of analysis was 1.46–20.02 Hz. The power ratios in different bands, that is alpha/theta and (alpha + beta)/(theta + delta) were calculated as well as the occipital peak frequency and the mean frequency in the range 1.46–20.02 Hz.

An experienced clinical neurophysiologist estimated the appearance of general disturbance in routine EEG (cf ref 21).

According to the standards of our laboratory the spectral EEG results were considered abnormal if the relative alpha power was less than 50%, the theta or delta percentage was more than 15% or mean frequency value at 1.46–20.02 Hz range was lower than 8 Hz.21 When present, each of these deviations was scored one resulting in a total abnormality score range from 0 to 4.

**Statistical methods:** Means and standard deviations were computed for all parametric data and spectral EEG variables were intercorrelated with the MMS score using the Pearson correlation technique. Comparisons between the delirious patients and controls were made using Student’s two-sample t test or chi-square test for sex distribution. The significance of differences between the subgroup means was estimated by oneway analysis of variance followed by the Student-Newman-Keuls’s range statistic. All calculations were conducted using the Statistical Package for the Social Sciences.

**Results**

There were highly significant differences between the spectral EEG variables of the delirious patients and controls (table 2). The MMS score showed statistically significant correlations with alpha percentage (r = 0.31; p < 0.05) and alpha/theta (r = 0.30; p < 0.05) and (beta + alpha)/(theta + delta) ratios (r = 0.32; p < 0.05). The age had no statistically significant correlations with the spectral EEG variables in either delirious patients or controls, and the t test showed no statistically significant differences between delirious patients using neuroleptics and unmedicated delirious patients. The mean, SD daily neuroleptic dose was 142, 63 mg in chlorpromazine-equivalents. In the delirious patient group, the lengths of delirium and hospitalisation correlated significantly with delta percentages (r = 0.36; p < 0.01 and r = 0.37; p < 0.01) and the mean frequency in the 1.46–20.02 Hz range (r = −0.33; p < 0.01 and r = −0.28; p < 0.05).

When the delirious patients were divided into subgroups according to the severity of cognitive deterioration, a trend for a more profound EEG disorganisation with declining cognition was seen (table 2). Statistically significant subgroup differences
**Table 2** Spectral EEG parameters in controls and delirious patients grouped according to the severity of cognitive decline

<table>
<thead>
<tr>
<th>Severity of cognitive decline</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>All</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>6.8</td>
<td>(1.7)</td>
<td>7.2</td>
<td>(6.1)</td>
<td>5.7</td>
</tr>
<tr>
<td>A</td>
<td>58.7</td>
<td>(24.8) NS</td>
<td>42.2</td>
<td>(20.4)</td>
<td>33.5</td>
</tr>
<tr>
<td>T</td>
<td>20.5</td>
<td>(13.9) NS</td>
<td>25.3</td>
<td>(17.7)</td>
<td>29.9</td>
</tr>
<tr>
<td>D</td>
<td>13.9</td>
<td>(12.3) NS</td>
<td>25.2</td>
<td>(11.9)</td>
<td>31.0</td>
</tr>
<tr>
<td>A/T</td>
<td>5.2</td>
<td>(4.7)</td>
<td>5.2</td>
<td>(2.8)</td>
<td>1.7</td>
</tr>
<tr>
<td>B + A/T + D</td>
<td>3.7</td>
<td>(3.3) NS</td>
<td>1.6</td>
<td>(1.8)</td>
<td>1.0</td>
</tr>
<tr>
<td>fml</td>
<td>8.1</td>
<td>(1.3)</td>
<td>7.4</td>
<td>(1.4)</td>
<td>6.6</td>
</tr>
<tr>
<td>MMS</td>
<td>23.0</td>
<td>(1.4)</td>
<td>14.8</td>
<td>(2.5)</td>
<td>4.5</td>
</tr>
</tbody>
</table>

A = alpha percent (SD); T = theta percent (SD); B = beta percent (SD); D = delta percent (SD); A/T = alpha/theta (SD); B + A/T + D = (beta + alpha)/(theta + delta) (SD); fml = mean frequency in the 1.46–20.02 Hz range (SD); N = number of patients; MMS = Mini Mental State score (SD).

*p < 0.05; †p < 0.01; ‡p < 0.001 (patients vs controls, 2-tailed t test).

Supporting this trend were observed in the ratio parameters as for alpha/theta oneway F was 3.77, df = 2; p = 0.03, and for (beta + alpha)/(theta + delta) F = 4.87, df = 2, p = 0.01 respectively.

When the delirious patients were divided according to the type of the basic CNS disease, notable differences were seen when the subgroup means were compared with the controls (table 3). Although the MMS scores also differed between these subgroups (oneway F = 3.36; df = 3; p = 0.02), statistically significant differences were seen in alpha percentages (F = 4.51; df = 3; p = 0.007), delta percentage (F = 3.03; df = 3; p = 0.04), and alpha/theta (F = 3.90; df = 3; p = 0.01), and (beta + alpha)/(theta + delta) (F = 4.66; df = 3; p = 0.006) ratios and mean frequency in the 1.46–20.02 Hz range (F = 2.40; df = 3; p = 0.07) indicating that patients with AD or multi-infarct dementia had the most conspicuous EEG changes.

The oneway procedure showed no statistically significant differences in the subgroup means of spectral EEG parameters or MMS scores when the patients were divided according to the type of the delirium, but these subgroup means also differed significantly from the controls (table 4).

When the criteria for spectral EEG abnormality were applied, five of 19 controls had one abnormality in EEG. Two had alpha power less than 50% (47.4% and 48.9% respectively), but high beta power values (29.4% and 29.9%). Three controls had delta power more than 15% (17.3% in two cases and 16.3% in one case). In the delirious patients, the abnormalities were obvious as only five patients had normal spectral EEG and 27 patients had maximal abnormality score. This difference is also seen in all subgroups of delirious patients when grouped according to the basic CNS disease (table 5) but it is most conspicuous in the AD and multi-infarct dementia patients.

**Discussion**

The electroencephalogram is widely accepted as a valuable ancillary laboratory procedure for diagnosis and serial evaluation of delirium, as EEG changes virtually always accompany delirium. At present

**Table 3** Spectral EEG parameters in controls and delirious patients grouped according to the type of the basic CNS disease

<table>
<thead>
<tr>
<th>Multi-infarct dementia</th>
<th>No apparent CNS disease</th>
<th>Mb Alzheimer</th>
<th>Mb Parkinson</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>6.7 (5.2)*</td>
<td>6.4 (2.6)*</td>
<td>6.5 (2.9)*</td>
<td>7.1</td>
</tr>
<tr>
<td>A</td>
<td>32.3 (17.4)†</td>
<td>54.9 (20.7)*</td>
<td>29.3 (20.5)*</td>
<td>38.1</td>
</tr>
<tr>
<td>T</td>
<td>30.1 (11.7)*</td>
<td>21.7 (14.6)*</td>
<td>19.9 (13.6)*</td>
<td>30.1</td>
</tr>
<tr>
<td>D</td>
<td>134 (15.4)%</td>
<td>17.0 (11.8)*</td>
<td>13.3 (16.9)%</td>
<td>24.6</td>
</tr>
<tr>
<td>A/T</td>
<td>1.6 (1.9)*</td>
<td>4.4 (3.9)*</td>
<td>1.4 (1.5)†</td>
<td>2.0 (2.4)*</td>
</tr>
<tr>
<td>B + A/T + D</td>
<td>0.9 (1.0)*</td>
<td>2.8 (2.7)*</td>
<td>0.8 (0.8)*</td>
<td>1.5</td>
</tr>
<tr>
<td>fml</td>
<td>7.1 (1.3)*</td>
<td>8.1 (1.4)*</td>
<td>6.7 (2.2)*</td>
<td>7.8</td>
</tr>
<tr>
<td>MMS</td>
<td>9.8 (5.7)†</td>
<td>11.7 (9.3)†</td>
<td>3.3 (3.2)†</td>
<td>6.0</td>
</tr>
<tr>
<td>N</td>
<td>30</td>
<td>12</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

A = alpha percent (SD); T = theta percent (SD); B = beta percent (SD); D = delta percent (SD); A/T = alpha/theta (SD); B + A/T + D = (beta + alpha)/(theta + delta) (SD); fml = peak frequency (SD); MMS = mean frequency in the 1.46–20.02 Hz range (SD); N = number of patients; MMS = Mini Mental State score (SD).

*p < 0.05; †p < 0.01; ‡p < 0.001 (patients vs controls, 2-tailed t test).
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Table 4 Spectral EEG parameters in controls and delirious patients grouped according to the type of delirium

<table>
<thead>
<tr>
<th>Type of the delirium</th>
<th>Silent</th>
<th>Mixed</th>
<th>Hyperactive</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>4·9 (2·4)$^{+}$</td>
<td>6·9 (5·1)$^{+}$</td>
<td>5·9 (3·7)$^{+}$</td>
<td>12·5 (7·9)</td>
</tr>
<tr>
<td>A</td>
<td>42·5 (26·2)$^{+}$</td>
<td>36·3 (20·9)$^{+}$</td>
<td>37·3 (19·7)$^{+}$</td>
<td>70·1 (13·3)</td>
</tr>
<tr>
<td>T</td>
<td>24·9 (11·1)$^{+}$</td>
<td>27·1 (12·8)$^{+}$</td>
<td>31·6 (14·1)$^{+}$</td>
<td>7·9 (3·7)</td>
</tr>
<tr>
<td>D</td>
<td>27·6 (19·1)$^{+}$</td>
<td>29·8 (16·8)$^{+}$</td>
<td>25·2 (12·8)$^{+}$</td>
<td>9·5 (4·7)</td>
</tr>
<tr>
<td>A/T</td>
<td>2·8 (3·4)$^{+}$</td>
<td>2·3 (2·7)$^{+}$</td>
<td>1·9 (2·5)$^{+}$</td>
<td>13·1 (11·0)</td>
</tr>
<tr>
<td>B + A/T + D</td>
<td>1·7 (2·2)$^{+}$</td>
<td>1·4 (1·8)$^{+}$</td>
<td>1·2 (1·5)$^{+}$</td>
<td>6·3 (4·3)</td>
</tr>
<tr>
<td>fp</td>
<td>8·1 (2·2) NS</td>
<td>7·2 (1·5)</td>
<td>7·2 (1·5)</td>
<td>9·7 (1·1)</td>
</tr>
<tr>
<td>fml</td>
<td>6·9 (1·7)$^{+}$</td>
<td>6·9 (1·5)$^{+}$</td>
<td>6·9 (1·5)$^{+}$</td>
<td>9·8 (0·9)</td>
</tr>
<tr>
<td>MMS</td>
<td>4·7 (5·1)</td>
<td>10·5 (7·5)</td>
<td>9·2 (5·7)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>7</td>
<td>28</td>
<td>16</td>
<td>19</td>
</tr>
</tbody>
</table>

$A =$ alpha percent (SD); $T =$ theta percent (SD); $B =$ beta percent (SD); $D =$ delta percent (SD); $A/T =$ alpha/theta (SD); $B + A/T + D =$ (beta + alpha)/(theta + delta) (SD); $fp =$ peak frequency (SD); $fml =$ mean frequency in the 1-46-20·02 Hz range (SD); $N =$ number of patients; $MMS =$ Mini Mental State score (SD).

* $p < 0·05; \; \; \; f p < 0·01; \; \; f p < 0·001$ (patients vs controls, 2-tailed t test).

The spectral analysis of EEG is a valuable technique to quantitate EEG background activity, and power in a frequency band normalised to the total power is a simple method for reducing the variability of the EEG data.26 27

Although normal elderly show some changes in the EEG such as slight background slowing and attenuation of theta activity,11 26-28 the delirious patients differed substantially from the controls. We observed a significant positive correlation between the alpha percentage and the various ratio parameters and cognitive functioning as evaluated by the MMS score, and significant differences in the various ratio parameters among the various subgroups of delirious patients when grouped according to the degree of cognitive deterioration. Our results suggest a relationship between spectral EEG changes and cognitive deterioration in delirium, which is in line with the suggestions of Engel and Romano.1

In patients with mixed or silent delirium, the intensity of confusion and reduced levels of awareness and arousal have in previous studies been found to correlate with slowing of the EEG activity.11 14 31-34 On the other hand, in patients with hyperactive delirium, low voltage fast activity characteristic of intense arousal has also been described.34 In our delirious patients there were no statistically significant differences in the subgroup means of spectral EEG variables or MMS scores when grouped according to the type of delirium, which suggests a profound disturbance of EEG as a common finding in different types of delirium with equal cognitive dysfunction.

All types of somatic treatment in psychiatry influence brain function as evidenced by EEG, and all drugs acting on human psychopathology are capable of producing significant EEG alterations.35 36 However, no statistically significant differences in the EEG variables between the patients using neuroleptics and unmedicated patients were seen, which suggests that medication has not significantly affected our findings. The lack of age-correlations either in the delirious patients or controls is in line with the results of Coben et al.,37 but may be due to the limited age-span of our patients.

Previous clinical and experimental reports suggest that subcortical white matter and thalamic lesions produce localised or lateralised delta activity, and bilateral lesions of the mesencephalic reticular formation produce generalised delta waves.38 39 49 Delta waves in the EEG are the most common sign of either

Table 5 Number of abnormalities in spectral EEG in controls and delirious patients grouped according to the type of basic CNS disease:

<table>
<thead>
<tr>
<th>Type of the basic CNS disease</th>
<th>Multi-infarct dementia</th>
<th>No apparent CNS disease</th>
<th>Mb Alzheimer</th>
<th>Mb Parkinson</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of abnormalities</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

$N =$ number of patients.
structural or metabolic brain pathology,\(^{10-43}\) which was also seen in our material as a conspicuous increase of delta activity particularly in those delirious patients with primary degenerative or multi-infarct dementia suggesting disruption of the reticulo-thalamocortical connections important in the maintenance of normal arousal and attention, which are both severely disturbed in delirious patients.\(^{44-46}\) Delta percentage and the mean frequency in the 1-46–20-02 Hz range also correlated with the lengths of delirium and hospitalisation indicating that patients with the most severe EEG disturbance suffered from the most long-lasting delirium and needed prolonged psychiatric hospitalisation. These findings together with the numerous EEG abnormalities in individual patients further support the central role of structural brain diseases as an important predisposing factor for delirium.\(^{44-46}\)

In summarising our results we conclude that in aetiologically heterogeneous non-alcoholic delirium marked differences existed in the spectral EEG variables between delirious patients and controls, and these changes showed an association with cognitive deterioration. These differences were also seen in most individual cases particularly when our abnormality criteria were applied, suggesting that spectral EEG is of value in the diagnostic work-up of delirious patients.

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