EEG Recordings in the Course of Recovery From Stroke
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Background and Purpose This study was designed to assess the value of quantified electroencephalography (EEG) in the follow-up of stroke and its possible correlation with other measures of recovery.

Methods EEGs were recorded over a period of 6 months in 34 patients with ischemic stroke in the middle cerebral artery territory who underwent spectral analysis. Two groups were formed: (1) 28 patients with a Barthel Index score of less than 60 at admission and (2) 6 patients with a Barthel score of over 60 and therefore with a much better prognosis. Ten recordings were made in each patient in the first group and at least three in the second group. Motor functions and activities of daily living (ADL) were assessed three times, on admission to the study and after 3 and 6 months.

Results Quantified EEG was significantly abnormal in the unaffected hemisphere of the first group. Side and site were not relevant. Longitudinal recordings showed a significant improvement of the power spectrum in the first 3 months. Alpha band's mean weighted frequency of the injured hemisphere was always slower than that of the contralateral side. All patients improved in motor performance and ADL, with the greatest improvement of the power spectrum in the first 3 months. However, no correlation between quantified EEG and clinical testing was found. By looking at individual profiles, a frequent and unpredictable instability was seen in the "unaffected" hemisphere. In those who made the best recovery, the EEG spectrum became more symmetrical over the left and right hemispheres, an aspect that continued beyond the point of a good motor and ADL recovery.

Conclusions Quantified EEG undergoes early and subtle changes in the follow-up of stroke that can outlast clinical recovery. Routine evaluation unable to anticipate prognosis is not recommended because motor and ADL scales provide earlier and more accurate indicators. In contrast, quantified EEG can be useful for individual patients undergoing rehabilitation to monitor mechanisms of local repair and also to detect changes in the so-called normal hemisphere. It may reveal focal abnormalities that are undetected by coarse clinical evaluation and that call for appropriate neuropsychological testing.

Key Words • cerebral ischemia • electroencephalography • prognosis • rehabilitation

The EEG has been studied in stroke patients chiefly during the acute phase. Its features appear to be weakly correlated with the clinical state and therefore to recovery. Nevertheless, it has been suggested that background reactivity and the possibility of revealing hidden asymmetries by spectral EEG analysis in the acute stage may be useful. It has also been suggested that the EEG could be used to reveal cortical involvement undetected by computed tomographic (CT) scan and to monitor the outcome of endarterectomy. Few studies have investigated the usefulness of serial EEG recordings in the postacute phase, and the coming of the CT era diminished the interest in such EEG studies. Moreover, the EEG recorded in the weeks immediately after a stroke was not predictive of either patients' clinical status or follow-up EEG of patients assessed 3 months or 3 years later. In other studies, although no correlation was found between the magnitude of clinical signs and the magnitude of EEG changes, both measures improved differently from CT scan images.

The present study had three objectives: (1) to describe the time course of quantified EEG (qEEG) in the first 3 months after stroke as a function of either the site of lesion or the severity of the clinical pattern, (2) to compare the evolution of EEG signs with that of motor functions and activities of daily living (ADL), and (3) to assess the value of longitudinal EEG studies in patients in a rehabilitation program.

Methods

Subjects
Forty-three patients with ischemic stroke in the middle cerebral artery were enrolled. There were 39 men and 4 women. The mean age was 63.74 years (SD, 9.8 years). The mean interval between the stroke onset and the first EEG recording was 28.16 days (SD, 7.15 days). This interval was due to the need to wait until the patient was free from complications and emergency therapy, to obtain his consent and cooperation, and to rule out the possibility of a reversible ischemic attack. The average length of hospitalization was 147 days (SD, 47 days). Four patients died of heart attack 4 months after the stroke. Another patient had a relapse after 3 months. Four patients refused or were unable to continue. Thirty-four patients were therefore included in the study.

EEG Recordings
Recordings were made fortnightly at the same time of day (after breakfast) with patients in both "eyes-closed" and "eyes-open" conditions. After the third month (ie, after the seventh recording session), the EEG was recorded once a month for 3 more months. Altogether, each patient was recorded 10 times in 6 months. Four patients with favorable
outcomes were recorded only three times in the first month. Patients who were discharged before the fourth month because of good recovery were assessed as outpatients.

Equipment
Silver-silver chloride cups were pasted to the scalp, in accordance with the international 10-20 system, to form the following channels: F3-C3, F4-C4, C3-T3, C4-T4, T3-T5, T4-T6, T5-O1, and T6-O2. The electrical signal was amplified and filtered with a pass band between 0.2 and 32 Hz. A 50+100-Hz notch filter was also used. The signal was digitized at a sampling frequency of 128 samples per second. Resistances were checked both before and after recording to ensure that they were below 3 kΩ. All the digital operations were performed on an AT-IBM computer. Digitized EEG signals were stored on hard disk. Subsequently, the stored EEG was inspected on a slow-running display to select artifact-free epochs of 4 seconds each. Between 16 and 30 epochs were chosen for analysis for each subject.

Spectral Analysis
The eight-channel EEG signals were sampled at a rate of 128 samples per second and then underwent spectral analysis with the fast Fourier transform. For each channel the coefficients of five frequency bands were calculated: delta, 0.2 to 4 Hz; theta, 4 to 7.75; alpha, 7.75 to 12; beta-1, 12 to 22 Hz; and beta-2, 22 to 32 Hz. For each channel and each band the following parameters were calculated: (1) absolute power, ie, the total mean power; (2) relative power, ie, the ratio between the absolute power of the band and the absolute power of the total spectrum; (3) mean weighted frequency; (4) asymmetry index, represented by the ratio between the absolute power on the uninjured hemisphere and the absolute power on the injured one; (5) reactivity index of the alpha band, ie, the ratio between the absolute power at “eyes open” and the absolute power at “eyes closed.” More technical details on spectral analysis as used by us have been published elsewhere. Based on the above-mentioned parameters (duration and number of EEG epochs), the spectral resolution is equal to 0.25 Hz, and the normalized standard error lies in the range of 0.18 to 0.25.

Clinical Testing
Clinical examination, neuropsychological assessment, routine blood evaluation, and CT scan were performed for every patient. Scales administered to the patients were the Albert Motor Scale, Northwestern University Disability Scale, Rankin Scale, and Barthel Index for ADL. Unnecessary medication was withheld. In some cases, insulin and hypotensive, antiplatelet, and cardiological drugs could not be safely discontinued. All but 3 patients used no tranquillizers. However, in the 3 patients who could not sleep without medication and for whom those drugs were prescribed, the dosage was kept low for the whole course of the investigation. All the patients underwent a rehabilitation plan. On the basis of initial Barthel scores, we had one group of 28 patients scoring less than 60 with a complete longitudinal recording. The other group was formed by 6 patients presenting with milder conditions. According to Granger et al. and Wade and Hewer, a Barthel score of less than 40 means a severe condition, a score of 40 to 60 denotes intermediate conditions, and a score of greater than 60 indicates good prognosis. In the present study, the first two groups were pooled together. In the first group, left lesions had occurred in 13 patients, and right lesions had occurred in 15 patients. Three groups were arbitrarily formed according to the site of lesion: (1) superficial lesion leaving deep nuclei unaffected (n=9); (2) lesion confined to internal capsule with nuclear involvement to a variable extent (n=8); and (3) extensive lesion, being a combination of groups 1 and 2 (n=11).

Statistics
Statistical analysis was performed on clinical scale scores as well as on EEG data collected at baseline and after 3 and 6 months on centro-temporal and temporo-temporal leads. To assess statistical significance, ANOVA for repeated measures, paired-samples t test, the Wilcoxon and Wilcox comparison test, and the Mann-Whitney U test were used. The level of significance was set at α = 0.05, and two-tailed critical regions were taken into account. When simultaneous univariate k tests were necessary to evaluate differences at the different times of analysis, the Bonferroni-adjusted risk was used (α = α/k).

Results
In the temporo-temporal leads of the group of disabled patients (Barthel score <60), relative and absolute EEG powers in the delta, theta, alpha, and beta bands show changes over 6 months of recording. Over the injured hemisphere, delta relative power was significantly lower at 3 and at 6 months compared with baseline. No statistically significant difference was found between the third and the sixth month. Theta and alpha relative powers were significantly higher at 3 and at 6 months compared with baseline. Again, no statistically significant differences were found between the third and the sixth month. Beta frequencies showed no significant differences during the 6 months of observation. All frequencies showed no significant differences during the 6 months of observation in the noninjured hemisphere.

The mean delta relative power of the injured hemisphere decreased by 19% and 21% compared with baseline at 3- and at 6-month recordings. Theta relative power increased by 48% and 53%, alpha relative power increased by 60% and 69%, and finally beta-1 increased by 20% and 23%. In the same group, from the temporo-temporal leads of the noninjured hemisphere, we found that delta relative power decreased by 14% and 6% compared with baseline at 3 and at 6 months. Theta relative power increased by 7%, alpha relative power increased by 31%, and beta-1 remained quite stable. Comparable results were obtained from the centro-temporal leads in this group of patients. The evolution of these events over 6 months is illustrated in Fig 1.

The mean values of delta and theta relative power were higher on the injured hemisphere than on the noninjured hemisphere. The opposite pattern was observed for alpha and beta relative power. The difference was highly significant (P<.0001).

Mean weighted frequency was quite stable over the 6-month interval; differences between successive recordings were not significant for all bands. By contrast, alpha mean weighted frequency on the injured hemisphere was always lower than that on the noninjured hemisphere. On the average, the difference was 0.349 Hz at the baseline and 0.413 Hz after 6 months on the centro-temporal leads. On the temporo-temporal leads the values were, respectively, 0.314 Hz and 0.271 Hz. Six of 28 patients displayed a difference as great as 1 Hz.

The change in absolute power at alpha frequencies between eyes-open and eyes-closed conditions was an index of reactivity. It did not change over time; however, reactivity was higher on the uninjured hemisphere (Table 1). The variance was also high.
FIG 1. Bar graphs show centro-temporal leads: delta, theta, and alpha electroencephalographic bands undergo significant changes during the first 4 months after stroke. Delta relative power is always higher on the affected hemisphere. Alpha relative power is always higher on the unaffected hemisphere. Alpha relative power appears to improve in the unaffected hemisphere as well.

The baseline alpha power was higher on the unaffected hemisphere but became more symmetrically distributed over a 6-month period (Table 2).

By applying Bonferroni 95% confidence intervals to the data from the injured hemisphere, delta relative power was found to be significantly higher and alpha relative power lower in the group of disabled patients, in both centro-temporal leads and temporo-temporal leads. On the noninjured hemisphere both delta and alpha relative power discriminated severe from mild cases in recordings from temporo-temporal leads, whereas in centro-temporal leads only delta relative power did so.

In our observations there was no difference in the modification of qEEG with time that was due to the site of the lesion (deep, superficial, or complete). Side was not significant.

The motor and ADL values recorded over the period of observation are presented in Table 3 (mean and SD). The Kendall correlation matrix applied to Albert, Northwestern University Disability Scale, and Barthel scores was 0.863 (P<.001), 0.956 (P<.001), and 0.944 (P<.001), respectively, at baseline and after 3 and 6 months.

Relative EEG power in the delta, theta, alpha, and beta bands tended to increase with improvement in motor performance and ADL (Fig 2), but Pearson product-moment correlations did not reach significance at any measure.

By looking at individual profiles, a frequent and unpredictable instability was seen in the unaffected hemisphere (Fig 3). In the most favorable cases, delta and alpha powers continued to become more symmetrical beyond the point of a good motor and ADL recovery (Fig 4). In other words, EEG improvement was still taking place after the clinical recovery.

Discussion

The issues of recovery and plasticity are gaining increasing interest. As yet, there is very little information concerning the role of biological mechanisms in clinical recovery after brain damage. Few EEG studies have been devoted to the long-term recovery from stroke; the majority of investigations in this field have been concerned with the acute phase.

Radiological methods, such as CT, are unsuitable for monitoring recovery because there is no correlation between the quality of clinical improvement and radiographically demonstrated changes in the density of the brain, except in the resolution of brain swelling. Positron emission tomography (PET) has given us new insights into the problems of brain metabolism, but nuclear radiation at frequent intervals cannot be safely administered to a patient. On the other hand, evaluation of cortical electrical activity is a relatively inexpensive, absolutely safe method that lends itself to quantitative and statistical analysis.

On clinical grounds, serial qEEG analysis has been reported to have some use in monitoring but no prognostic value. Unlike the study of De Weerd et al, in which three examinations were carried out over a period of 3 years, our protocol included patients who were referred to us for rehabilitation soon after stroke, and our recordings were made during the first 7 months. Recovery and behavioral compensation are supposed to be greatest during this period. Indeed, although slight
TABLE 3. Scales Used for Monitoring Clinical Outcome of 28 Patients With Barthel Scores <60 on Admission

<table>
<thead>
<tr>
<th>Scale</th>
<th>Best Possible Score</th>
<th>Baseline 3 Months</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rankin</td>
<td>1</td>
<td>4.22 (1.11)</td>
<td>3.12 (0.95)</td>
</tr>
<tr>
<td>NUDS</td>
<td>50</td>
<td>17.38 (10.66)</td>
<td>30.06 (13.54)</td>
</tr>
<tr>
<td>Barthel</td>
<td>100</td>
<td>28.33 (25.43)</td>
<td>59.66 (35.33)</td>
</tr>
<tr>
<td>Albert</td>
<td>160</td>
<td>27.88 (27.67)</td>
<td>65.68 (44.85)</td>
</tr>
</tbody>
</table>

NUDS indicates Northwestern University Disability Scale. Data are expressed as mean values (SD).

Changes were seen clinically after 6 months,\textsuperscript{18,19} most of the recovery occurred in the first 3 months.\textsuperscript{13,20,21} The present study has no control group, but the reliability of test-retest procedures in EEG already has been demonstrated.\textsuperscript{22,23}

Our observations agree with those of De Weerd et al\textsuperscript{13} to the extent that the greatest improvement in the EEG occurred in the first months after stroke. Our observations of a decrease of slow activity and improvement of alpha band in the first 3 months after stroke also fit with those of Jonkman et al,\textsuperscript{24} whose observations ended after the 90th day. In our study, patients with severe clinical impairment on admission had much more delta and less alpha relative power than patients with milder impairment. However, the contribution of EEG to the clinical prognosis field is not impressive because motor and ADL scales are more easily applied and are more accurate; they provide information at an earlier stage and have been more extensively studied in the literature. Although we found the same trends in EEG as in motor and ADL scales, ie, more improvement in the first 3 months, we failed to see a clear-cut correlation between them.

Faught\textsuperscript{25} is skeptical about the usefulness of EEG for either prognosis or localization in stroke. We agree with him in these respects, but we think that the time course of EEG normalization and changes in the opposite hemisphere can make an important contribution to the understanding of pathophysiological mechanisms in the field of plasticity. This term is widely used to describe the ability of the central nervous system to cope with injury in some forms of repair. Mechanisms of repair are considered to be involved during this period. At least in the human, the operations of these mechanisms are still unclear, and several are probably far-fetched.\textsuperscript{26} Our data indicate that physiological changes continue after the clinical picture has stabilized, suggesting that processes of neural plasticity are continuing to modify neurological function. Patients with a Barthel Index score of 100 at 4 months after stroke continued to show signs of "electrical repair," such as the increased symmetry of the EEG spectrum. As a consequence, the use of neuropsychological tests that have been especially tailored for a certain lesion is likely to result in much better monitoring of the recovery process than that of the usual behavioral scales.

An interesting finding is the fluctuating changes of the EEG on the unaffected hemisphere during the course of recovery. These effects are not due to chance

\begin{figure}[h]
  \centering
  \includegraphics[width=0.5\textwidth]{fig2.png}
  \caption{Graph shows similarity between the improvement of alpha relative power and the Barthel Index score during the first 7 months after stroke.}
\end{figure}

\begin{figure}[h]
  \centering
  \includegraphics[width=0.5\textwidth]{fig3.png}
  \caption{Graphs show percentages of relative activity in left hemisphere stroke in a 66-year-old patient. E.C. indicates eyes closed. T5-T3 is on the injured side (*). Alpha relative activity is unstable on the so-called normal hemisphere along the recording interval.}
\end{figure}
investigations, in providing better monitoring and more informed clinical decisions. Indeed, qEEG can indicate brain areas that display pathological activity and yet show signs of improving activity in longitudinal recordings. Thus, qEEG can monitor mechanisms of local repair and also detect changes in the so-called normal hemisphere. It may reveal focal abnormalities that are undetected by coarse clinical evaluation and that call for appropriate neuropsychological testing.

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References


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