Continuous Quantitative EEG Monitoring in Hemispheric Stroke Patients Using the Brain Symmetry Index

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Background and Purpose—There is increased awareness that continuous brain monitoring might benefit neurological patients, because it may allow detection of derangement of brain function in a possible reversible state, allowing early intervention. Here, we explore if quantitative continuous electroencephalography (cEEG) monitoring is technically feasible and possibly clinically relevant in patients with acute ischemic hemispheric stroke.

Materials—Twenty-one consecutive patients with an acute hemispheric stroke were monitored in our stroke unit, using cEEG for 12 to 24 hours on the day of admission. EEGs were quantified using a particular measure for symmetry, the brain symmetry index (BSI). This measure was subsequently correlated with the clinical condition of the patient using the National Institute of Health Stroke Scale (NIHSS).

Results—cEEG was technically feasible. We found a most satisfying positive correlation between the BSI and the NIHSS, with \( r=0.86 \) (\( P<0.01 \)).

Conclusions—Technically, cEEG monitoring posed no major problems. It was found that the BSI correlates satisfactorily with the clinical neurological condition of our stroke patients. This suggests that the BSI can be used as a measure to monitor possible changes of brain function in this patient category. (Stroke. 2004;35:2489-2492.)

Key Words: brain symmetry index ■ electroencephalography ■ monitoring ■ stroke

There is increased awareness that continuous brain monitoring might be beneficial to neurological patients, because it may allow detection of derangement of brain function in a possible reversible state. Given the fact that the period during which this reversible state may exist varies from only minutes to sometimes hours, repeated clinical examination, typically performed 1 to 4 times per day, will often fail to detect derangement in this reversible period.

Early detection of derangement of brain function provides the clinician with a window of opportunity during which action can be taken. Possible derangements include systemic hypotension with insufficient brain perfusion, leading to ischemia, postoperative rebleeding, or symptomatic seizures, which occur in \( \approx 6\% \) of stroke patients in the first week. In most of these cases, relevant therapeutic intervention is possible.

Various techniques may assist in the monitoring of the brain. Examples include continuous transcranial Doppler, near infrared spectroscopy, measurement of tissue oxygen, somatosensory-evoked potentials, and continuous electroencephalography (cEEG). Given the clinical setting and the a priori knowledge about possible derangement, particular choices of these various monitoring techniques can be made. Clearly, in the application of these techniques there is often a need for subsequent computer analysis to assist in the interpretation of the signals. The raw EEG signal, for instance, is rather difficult to interpret by nontrained personnel. In addition, computer analysis could provide warning signals for particular events.

We explored if cEEG monitoring, with quantification using a particular measure for symmetry, is technically feasible and possibly clinically relevant in acute ischemic stroke. Application of cEEG monitoring may allow detection of adverse events in a reversible stage, providing an opportunity for early intervention. Because the number of stroke patients is very large, even relatively small improvements in clinical outcome will be beneficial for a large (absolute) number of patients.

Patients and Methods

Patients
Twenty-one patients who were referred to our stroke unit from the end of 2002 to the beginning of 2003 with a 1-sided supratentorial stroke were included. No patient had experienced previous stroke. In all patients, cEEG monitoring was performed within 24 hours of admission and continued for typically 12 to 24 hours. In addition, neurological function was quantitatively assessed on the day of admission using the National Institute of Health Stroke Scale (NIHSS), which is a standard procedure in our stroke unit.

EEG Recording
EEGs were recorded according to the International 10–20 system with Ag/AgCl electrodes, using a bipolar 8-channel subset, using derivations F4-C4, F3-C3, C4-P4, C3-P3, P4-O2, P3-O1, F4-T4, and...
F3-T3. Impedance was kept <5 Kohm to avoid polarization effects. Recording was performed using a BrainLab EEG recorder. The sampling frequency was set to 250 Hz and filter settings were 0.16 to 70 Hz.

The Brain Symmetry Index
As a measure for the amount of ischemic damage, we used the Brain Symmetry Index (BSI) that was recently introduced for monitoring possible brain ischemia in carotid surgery. This measure is defined as the mean of the absolute value of the difference in mean hemispheric power in the frequency range from 1 to 25 Hz.

Because the power spectral density is estimated by fast Fourier transform, we write for the power of the signal obtained from a particular hemispheric bipolar channel pair i (with i = 1, 2, . . . , N) at frequency j (or Fourier coefficient, with index j = 1, 2, . . . , M), $R_{ij}(t)$ and $L_{ij}(t)$ for the right and left hemisphere, respectively. We now define the BSI as:

$$BSI(t) = \frac{1}{M} \sum_{j=1}^{M} \left\| \sum_{i=1}^{N} \frac{R_{ij}(t) - L_{ij}(t)}{R_{ij}(t) + L_{ij}(t)} \right\|$$

with N being the number of channel pairs and M being the number of Fourier coefficients. Note that the lower bound for the BSI is zero (perfect symmetry for all channels), whereas for the upper bound we find that BSI equals 1, which implies maximal asymmetry. For healthy controls, the BSI is 0.042 ± 0.005 (from data from our own digital EEG database).

Data Analysis
For the current study, 5-minute epochs of the EEG were analyzed. Subsequent epochs overlapped by 2.5 minutes. All routines were implemented in MatLab (The Mathworks Inc). The power was estimated using Welch averaged periodogram method. The signal from each bipolar derivation, containing the 5 minutes of data, was estimated using Welch averaged periodogram method. The signal was detrended and windowed. The magnitude of NFFT discrete FFTs of the sections was averaged to form the spectral density. Subsequently, the BSI was calculated for the first 2 to 4 hours of cEEG monitoring (depending of the number of artifacts present). All data were analyzed offline using software developed in our own department. The source code (in MatLab) is available on request from the first author. The analysis was performed after all patients were discharged from the stroke unit.

Results
Twenty-one patients were monitored (10 men, 11 women), with a mean age of 62 (range, 55 to 89) and 69 (range, 63 to 92) years for men and women, respectively. All patients had an infarction in the territory of the middle (n = 19) or posterior (n = 1) cerebral artery or anterior choroidal artery, which supplies the putamen (n = 1).

The NIHSS was between 0 and 23. Typically, twice daily the technician had to check the electrode impedances for adequate recordings. There were no significant technical problems, and there was no interference with the care of the patients by the nurses.

Two examples of a part of a recording with the corresponding BSI trend curve are shown in Figure 1. The left EEG recording is from a patient with a large right hemispheric infarction (NIHSS = 13), showing a mean BSI = 0.18, that remained essentially unchanged during the first 24 hours. The right EEG is from a patient with a mild right-side hemiparesis (NIHSS = 3; BSI = 0.06) and in whom, after several hours, subtle symptomatic focal seizures (rhythmic muscle contractions of the right facial muscles) developed. At this time, the EEG shows seizure activity on the left side, with a BSI approx 0.20. When the seizure stops, the BSI decreases to the preseizure level, illustrating its value in detecting focal seizure activity.

The relationship between the BSI and the NIHSS score for all 21 patients is presented in Figure 2. The data point labeled with an asterisk (*), which tends to be an outlier, is from a patient with an infarction in the putamen, supplied by the anterior choroidal artery; all the other data points are from patients with infarctions in the territory of the middle or posterior cerebral artery.

There is a most satisfactory correlation described by $BYSI = NIHSS \times 0.0077 + 0.044$. The correlation coefficient between the BSI and the NIHSS score is $r = 0.86 (P < 0.01)$.

Discussion
There is increasing awareness that continuous EEG monitoring is relevant in neurological patients. Given the improved therapeutic possibilities and techniques available, quantitative cEEG may assist in the detection of derangement in brain function in a still-reversible state. The current study aimed to explore the technical feasibility and possible clinical relevance of cEEG monitoring in hemispheric stroke patients using the BSI as a quantitative EEG measure.

Technically, we encountered no relevant problems. Typically, the technicians checked electrode resistances twice per day, which seemed sufficient. We remark that the primary motivation for using a limited set of recording electrodes was reduction of the time needed for application and the belief that a relatively small set of recording positions would suffice to monitor the relevant changes in the EEG. Therefore, the overhead was limited, and no interference occurred with the standard care in our clinical neurophysiology department. In addition, the EEG could be viewed not only at the stroke unit but also at the Department of Neurophysiology using the intranet.

As a clinical measure for the neurological condition of our stroke patients, we used the NIHSS. This scale aims to assess neurologic outcome and degree of recovery for stroke patients. In our application, we primarily used the NIHSS as a measure for the clinical condition of the patient, providing a detailed inventory of various levels of neurological deficit.

Various parameters have been proposed to quantify EEG changes in cerebral ischemia, varying from spectral EEG measures and changes in delta power to nonlinear approaches, for instance, the time-dependent entropy. Recently, we have introduced the BSI, which is shown to be very sensitive to detect EEG asymmetry, as may occur during carotid surgery. In this work, we apply this measure to patients with an acute hemispheric stroke. Characteristics of this index are that it provides a normalized single number, ranging from 0 (perfect symmetry) to 1 (maximal asymmetry), which is straightforward to interpret by personnel without a background in EEG reading. In the estimation of the BSI, the patients serve as their own controls, and the BSI provides a normalized measure for symmetry.

Our results show a satisfactory positive correlation between the NIHSS and the BSI. This implies that the BSI can be used as a measure for the neurological deficit in acute
hemispheric stroke patients and strongly suggests that changes in the BSI warrant clinical re-examination of the patient. Causes of BSI changes include ischemia, focal seizures, and hemorrhage, because all these changes will typically disturb the preserved symmetry in the brain. In one patient, focal seizures occurred, with a concomitant increase in the BSI, illustrating the sensitivity of this method to capture these changes (Figure 1). Clearly, these characteristics of the BSI indicate that it is not specific for ischemia. However, this is of no concern in this patient group, because any event that induces changes in EEG symmetry may warrant clinical re-examination.

Because the BSI primarily measures changes in symmetry, its sensitivity may be limited if applied to stroke patients in general. However, in its application to hemispheric stroke patients, as in this study, its sensitivity is most satisfactory. In this respect, we are aware that one could encounter a patient with a previous stroke (or any other unilateral hemispheric process) with a (new) stroke on the contralateral side. This could, theoretically, reduce this patient’s baseline BSI that was present before this (second) stroke occurred. This unlikely event might, in these unfortunate patients, additionally reduce the sensitivity of the technique. The likelihood, however, that “recent stroke-induced” EEG changes yield similar, symmetrical, spectral characteristics as the already existing contralateral EEG changes from the previous injury is very small. Therefore, previous contralateral hemispheric injury from any cause, including stroke, will most likely not significantly reduce the applicability or the sensitivity of the proposed method. Clearly, additional data could further substantiate these considerations.

The clinical potential of the proposed method should be further validated with the availability of the real-time BSI. At the time of this study, the BSI was not available in real-time, and our analysis was performed after all patients were discharged from the stroke unit. Currently, real-time implementation has been realized. This allows further investigation of whether the BSI will detect a change in a patient’s
condition at least as sensitively as in repeated (in our stroke unit, typically once per hour) clinical examination.

In this study, all stroke patients referred to our stroke unit were potential candidates for cEEG monitoring. Most likely, however, a particular subgroup of hemispheric stroke patients could benefit most, with an acceptable “number needed to monitor.” At this time, additional data are needed to define, if possible, this subgroup, which could perhaps be limited to those patients with a particular NIHSS, e.g., NIHSS ≥ 6.

Although our results should be viewed as a first step, and the application of cEEG in stroke patients is currently still rather limited and a topic of debate, we believe that in several stroke patients, cEEG with additional BSI estimation may be clinically relevant. When novel therapeutic approaches in stroke patients may become more standard, such as (mild) sedation or hypothermia, the need for quantitative cEEG may further increase.

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References
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