Development of a Computerized EEG Imaging System with a Personal Computer

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The authors developed a computerized electroencephalography imaging system with an IBM PC AT. The EEG signals amplified with a 16 channel EEG machine were digitized at 51.2 Hz (512 samples per epoch). The shifted DC potential and 60Hz artifacts were removed by a high pass filter and 60Hz notch filter. A window function consisting of a 10% cosine taper was obtained by weighting the points at either end of the epoch by a cosine bell. A fast Fourier transform was applied to every epoch and the power spectrum estimates were computed in 0.39 Hz steps. The activity estimates for the delta, theta, alpha and beta bands were computed by summing adjacent values. The outline of the top-down maps was formed from a series of sagittal cuts, then 32 electrodes were placed on the map. A file was created which contained a table of weighting parameters for calculating the interpolated values for every point within the outline. Each weight was in inverse linear proportion to the distance of the pixel to the nearest four electrodes. The map was finally generated with computation of the spectral EEG in each pixel according to the weighting parameter. The functioning of this system was tested with a functional generator and a human subject.

Key Words: Computer, power spectrum, EEG mapping

Electroencephalography has greatly contributed to the development of clinical neuroscience ever since its development by Hans Berger (Berger 1929). Studies of electroencephalography in the past depended mainly on a qualitative inspection and subjective interpretation. The introduction of a new method of electroencephalogram (EEG) analysis by computer, however, has greatly expanded the areas of EEG application. Even in neuropsychiatric and mental disorders where little abnormality is found with a conventional EEG, some significant findings have been reported with computerized analysis (Number 1985; Duffy et al. 1984; Morhisa et al. 1983; Buchsbaum et al. 1985). Recently, brain imaging system has been developed using quantitative data produced by multi-lead EEG (Duffy et al. 1979; Coppolar et al. 1982). It is possible to see a spatiotemporal change in electrophysiological distribution of the brain with an EEG imaging system.

Although clinical and basic research using this system is required, elaborately designed research is limited when a commercial imaging system is used because of its closed software. The authors have attempted to develop a brain mapping system of EEG with an inexpensive personal computer. We report on the recently completed procedure of its development and the result of experiments testing this system's function.

MATERIALS AND METHODS

Hardware

The personal computer produced by Korea Televideo company which is compatible with the IBM PC AT was used as the main computer (640 KB memory, 1.2 MB FDD, 30 MB HDD). Peripheral devices consisted of a printer and a color monitor driven by an Enhanced Graphic Adaptor (EGA) board. The A/D converter and analog input module were a DTX 2806 and a DTX 311 16 SE/8DI (12 bit) produced by the Data Translation company of the United States. A 16 channel EEG machine was used (Nihon Kodhen,
EEG-4313F) as an amplifier. The configuration of the system is shown in Fig. 1.

Software

There were two main procedures in the development of the software. The first was the computation of the power spectrum. The second was to generate the EEG map. Software was written mainly in the C-language with some assembly language routines and FORTRAN.

Fig. 2. shows the logistical flow of the steps required to compute the power spectrum of the EEG. Amplified EEG signals at gain 2000 were converted to digital EEG at 200 samples per second. Prior to spectral analysis, raw EEG data were inspected on the monitor in 2.56 sec epochs. Any segment containing artifacts was eliminated. Also, shifted DC potentials were removed by a high pass filter. A window function consisting of a 10% cosine taper was obtained by weighting the points at either end of the epoch by a cosine bell. A fast Fourier transform was then applied to every epoch and the power spectrum estimates computed in 0.39 Hz steps. For smoothing, adjacent estimates were summed to yield 1-Hz resolution (square root of power). The activity estimates for
each band were computed by summing adjacent values; delta, 0.8-4.3 cps; theta, 4.7-7.8 cps; alpha, 8.2-12.9 cps; beta 1, 13.3-19.9 cps and beta2, 20.3-31.6 cps.

The map was generated through the steps shown in Fig. 3. First, the outline of the man was determined by the method that Buchsbaum et al. (1986) suggested. A series of sagittal sections of the whole head cut at 1-cm intervals was made, then the outline of the top-down map was formed from these cuts (Fig. 4). The 19 electrodes were placed on the map according to the International 10-20 system. Additionally, 3 midline leads (Fp and Fc and 10% steps and Oz), 2 temporal leads at 5% between T3 and T5, and 8 leads at the centers of squares formed by the other electrodes were added to provide better spatial resolution (Fig. 4).

The map was also generated on the basis of the method that Buchsbaum et al. (1982) and Coppola et al. (1982) suggested. The geometric representation of the brain consisted of an outline and the x-y coordinates of the electrodes within it. A file was created which contains a table of weighting parameters for calculation of the interpolated values for every point within the outline. For every pixel within the outline, the four nearest electrodes were identified. Four corresponding weights were then calculated, where each weight was in inverse linear proportion to the distance of the pixel to the four electrodes. The outline, electrode coordinates, and the interpolation weights were stored together in one file for reference at the time of map generation. In order to provide a gray scale display, the screen was considered as a 128×128 arrangement of pixels where each pixel was a 4×4 dot matrix. The number of dots turned on in this pixel matrix then encoded the gray level by dot intensity. The normal display divided the 0-255 range of the 8 bit data into 9 levels and displayed them accordingly. Additionally, a color image of the same picture file was generated. The 8 bit data range was divided into 11 steps and a color was assigned to each.

Test Procedures

The 10 Hz sine wave of 50μV from a functional generator was used to test the function of data acquisition and spectral analysis. A human subject was also used for inspection of the functioning of this system. The EEG was recorded in resting condition with close eyes. A set of 16 gold disk electrodes was applied separately to the anterior and posterior half of the scalp due to the limitation of the number of

Fig. 5. 16 channel digitized sine wave of 10 Hz.
EEG channels. After recording, both 16 channel EEGs were merged into one 32 channel EEG.

RESULTS

Fig. 5 and Fig. 6 show the 10 Hz sine wave of 50 μV for 2.56 seconds and its power spectrum in 16 channels. Note the peak at 10 Hz of the power spectrum in Fig. 6. The high pass filter and 60 Hz notch filter were tested with one EEG epoch which contained a DC shift and 60 Hz artifacts (Fig. 7). Both artifacts were clearly removed with these filters as seen in Fig. 8. Disappearance of the 60Hz artifacts was also con-

Fig. 6. 16 channel power spectrum of 10 Hz.

Fig. 7. 16 channel EEG which contains a DC shift and 60 Hz artifacts.
Fig. 8. Artifacts which appeared in Fig. 7 were removed with high pass filter and 60 Hz notch filter.

Fig. 9. Power spectrum of the EEG which contains a DC shift and 60 Hz artifacts.

Confirmed with spectral analysis. The 60 Hz spectrum noted in Fig. 9 disappeared when a 60 Hz notch filter was used (Fig. 10). Fig. 11 shows a 16 channel human EEG. The alpha band was the highest in the power spectrum as is usually expected in resting condition with closed eyes (Fig. 12). As the subject was somewhat drowsy at the time of recording, a relatively high power spectrum in the delta band could be seen. The color imagings in four bands; delta, theta, alpha and beta1 were created with a 32 channel EEG in the
same subject. The delta and theta maps (Fig. 13 A,B) showed higher activity in the midline. High activity in the frontal area of the delta map may be caused by the subject’s drowsiness and eye movements. In the
Fig. 12. Power spectrum of EEG of Fig. 11.

Fig. 13. Color EEG maps of four bands, delta (A), theta (B), alpha (C) and beta 1 (D).
alpha map (Fig. 13 C), maximum activity appeared in the occipital area. The distribution of beta activity also showed higher activity in the occipital area similar to the alpha band, except with very high muscle activity in the right temporal area (Fig. 13 D). The overall distributions of electrophysiological activity in the four bands were basically very similar to those of the averaged maps of ten normal persons that Lee and Buchsbaum (1987) reported. In these maps, the scales do not indicate absolute microvolts but rather relative activity.

**DISCUSSION**

There are two main purposes of this research. One is to attempt to have our own model of an EEG imaging system using an inexpensive personal computer because a commercial system is very expensive. The other is to activate psychophysiological research in Korea in the field of clinical neuroscience by this system. With the closed software of a commercial system, it is difficult to design elaborate research.

Also, various forms of statistical analysis with quantitative EEG are necessary for advanced research. Another computer program should be developed to transfer EEG data derived from spectral analysis into the existing statistical packages such as BMDP (Dixon 1981) or SPSS (Norusis 1986). Finally, this statistical information can be displayed as an image. This technique known as significance probability mapping (SPM) was first introduced by Bartels and Subach (1976). Duffy (1981) adapted this technique to the analysis of brain electrical activity and reported its potential value in the localization of anatomical brain lesion and functional brain asymmetries. SPM shows the topographical distribution of the statistical significance of the electrophysiological changes between different conditions or groups.

With a computerized mapping of quantitative EEG, very small changes which cannot be detected on visual inspection of a regular EEG may be revealed in the map due to its high sensitivity. The most important thing in EEG mapping is to obtain a real EEG imaging that does not contain artifacts. In our system, typical artifacts were omitted from quantitative analysis by visual inspection, and a high pass filter and 60 Hz notch filter were attached to removed DC shift and 60 Hz artifacts. We need to apply an additional program which would automatically remove artifacts from the eyes (Elbert and Lutzenberger 1985; Jervis and Nichols 1985). Although we used fast Fourier transform in analyzing EEG, some different methods can be used depending on the characteristics of the activity under study. Fast activity above 20 Hz may sometimes be used, especially in studying cognitive and intellectual functions (Spydell and Sheer 1982). However, brain activity above 20 Hz decreases abruptly (Lee and Buchsbaum 1987) and the activity of muscle starts to appear at 20 Hz (Lindstrom and Petersen 1983). To obtain true fast EEG from a noisy background, statistical method using correlation may be considered (Cooper et al. 1980; Isaksson et al. 1981).

Although alpha and beta activity have been thought to have a different function and origin, their topographic distributions are almost identical. This typical pattern of EEG distribution which shows higher activity in the central and occipital areas no longer appears above 22 Hz (Lee and Buchsbaum 1987). This may imply that the 106 turkey window conventionally used in spectral analysis created some leakage from higher alpha activity to lower beta activity. The leaked activity may greatly influence the distribution of beta activity, since the difference of amplitude between both bands is so large. To solve this problem, a Dolphchebychev window (Harris 1978), which has a minimum effect on leaking, may be introduced.

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Fig. 4. Case 5. (A) Multiple masses with strong contrast enhancement at first admission.

(B) Complete disappearance of tumors after radiotherapy, 3600 cGy in 2 1/2 weeks, under the impression of metastatic brain tumor.

(C) Two years later, newly developed mass on right basal ganglia, proved to be large cell lymphoma by stereotaxic biopsy.

(D) Partial response after re-irradiation.

designated by a variety of terms including “perithelial sarcoma”, “microglioma”, “reticulum cell sarcoma”, and “histiocytic lymphoma”, but has been recently clarified as there are no histologic differences between primary CNS lymphoma and non-Hodgkin’s lymphoma arising in extraneural sites, and the majority are of B cell origin or diffuse histiocytic type by Rapaport classification (Allegranzi et al. 1984; Helle et al.)
Fig. 5. Case 2. (Left) A large lobulating mass on the corpus callosum which completely disappeared after subtotal resection plus radiotherapy. (Right) Follow-up CT scan at 5 years after radiotherapy plus intrathecal methotrexate demonstrated hypodense white matter with hydrocephalus, suggesting necrotizing leukoencephalopathy. There was no evidence of disease. She died at 64 months after treatment.

1984; Henry et al. 1974; Letendre et al. 1982). Before the mid-1970’s, we seldom experienced primary CNS lymphoma cases because of its rarity and difficulty in diagnosis and surgical approach to confirm the diagnosis.

Recently, with the advent of the CT scan, improvement of neurosurgical techniques, and actual increase in frequency, we have gained more experience in the clinical presentation of CNS lymphoma and have confirmed more cases pathologically. Consequently, we are able to perform prompt diagnosis and timely treatment in the management of CNS lymphoma.

As with other brain tumors, most primary CNS lymphomas are suspected by neuroradiologic study including CT scan or MRI imaging. Characteristic CT scan findings of CNS lymphoma are fairly diagnostic, they reveal single or multiple isodensity or high density masses usually on the periventricular region, basal ganglia, thalami and corpus callosum with well defined homogeneous contrast enhancement. It is interesting that transient spontaneous regression of the tumors can be observed. Weingarten et al. (1983) suggested that when initial neuroradiologic study suggests a diagnosis of lymphoma, the subsequent spontaneous resolution of lesions should not be regarded as a benign, self-limiting disease but should be aggressively pursued early in the patient’s clinical course when therapy would be most beneficial. We experienced one case of spontaneous regression, as described above (patient 7). In that case, delayed diagnosis and treatment resulted in bilateral total blindness despite complete disappearance of the tumor after radiotherapy. Besides solitary or multiple discrete intracranial nodules as described above, less frequently, patients with primary CNS lymphoma can present with diffuse meningeal or periventricular lesions, uveal or vitreous deposits, and localized intradural spinal mass. In these patients, brain CT scans often reveal negative findings and CSF study including cytology or myelography is more diagnostic.

When CNS lymphoma is suspected in the CT scan, the next step in the management of CNS lymphoma is surgical intervention for pathologic diagnosis as well as surgical resection of the tumor. However, the role of surgery is very limited because CNS lymphoma is often multiple and extensive surgical resection of these deep seated tumors results in high morbidity and mortality rates. Many authors reported less than 6 months median survival after surgery alone (Henry et al. 1974; Bogdahn et al. 1986). So Surgery alone
has been an abandoned treatment method and, furthermore, the stereotaxic needle biopsy to establish the diagnosis followed by radiotherapy has recently received increased interest because lymphoma is very sensitive to radiation and there is an apparent lack of benefit from subtotal or gross total excision. Trial radiation without biopsy, which is a popular method in pineal tumors, has not been widely accepted in CNS lymphoma. However, we think that it is a reasonable approach in this deep seated, radiosensitive tumor when the patient refuses an operation or in biopsy failed cases. Delayed diagnosis and treatment after pathology confirmation often lose the time when radiation is most beneficial. In this series, we perform-
ed trial radiation without biopsy with 20 Gy in 2 weeks in 3 patients who had multiple tumors or had declined surgery. They showed almost complete response after only 20 Gy which could not be achieved in other pathologies (Fig. 6).

Radiation therapy with or without surgical resection is standard treatment in the management of primary CNS lymphoma. Although the initial response to radiation is very good, long-term results are disappointing. Median survival after radiation was reported as 15.2 months by Henry et al. (1974), 15.3 months by Kawakami et al. (1985), and 18 months by Sagerman et al. (1984). Murray et al. (1986) reported in their extensive literature review including 693 cases that 8% of 3 year survivals and 3% of 5 year survivals, even then half of the 5 year survivors relapsed after 5 years.

Because of unsatisfactory results by operation and radiotherapy, adjuvant systemic and/or intrathecal chemotherapy has been tried by many investigators. Loeffler et al. (1985) observed that the median survival of patients receiving chemotherapy was 44 months compared to 14 months for those patients not receiving chemotherapy and all four long-term survivors received chemotherapy. Kawakami et al. (1985) also suggested that systemic chemotherapy is a meaningful addition in the treatment of primary CNS lymphoma. When he used combined chemotherapy including CHOP (cytoxan, Adriamycin, vincristine and prednisone), VEMP or VEMP (vincristine, cytoxan, procarbazine or 6-mercaptopurine, and prednisolone), or ACNU (1-(4-aminophenyl)-2-methylpyrimidine-5-yl-methylene-acyclo) survival time was prolonged in comparison with that of patients not receiving chemotherapy. Neuwelt et al. (1986) have shown, in three patients with CNS lymphoma, rapid tumor regression after receiving combination chemotherapy (cytoxan, intra-arterial methotrexate, leucovorin rescue, procarbazine, dexamethasone) administered in association with osmotic blood-brain barrier disruption (mannitol). Some authors (Loeffler et al. 1985; Mackintosh et al. 1982) had used intrathecal chemotherapy with methotrexate or Ara-C, and intravenous administration of high dose methotrexate was also tried after the report by Ervin and Canellos (1980). They reported a recurrent CNS lymphoma case who revealed complete response after intravenous high dose methotrexate.

To date, while these reports are encouraging and chemotherapy may theoretically augment irradiation effects and/or eradicate micrometastases within the neuroaxis or beyond the CNS, the use of chemotherapy is still investigational. Furthermore, if combined radiotherapy and chemotherapy is to be considered, the possibility of complications such as leukoencephalopathy must be taken into account. In this regard, the sequence of radiation therapy and chemotherapy may be very important. Bleyer (1981) suggested that intrathecal MTX or high-dose intravenous MTX followed by CNS RT would be the least neurotoxic approach and methotrexate given during or after CNS RT would be much more likely to produce severe neurologic sequelae. Although Loeffler et al. (1985) reported no necrotizing leukoencephalopathy in their 4 patients who received intrathecal methotrexate, the addition of methotrexate to high dose radiotherapy would result in a high rate of necrotizing leukoencephalopathy (Mackintosh et al. 1982; Meadows and Evans 1976). In this series, we tried intrathecal chemotherapy with methotrexate after radiotherapy in 7 cases. In these cases, primary site recurrence was not documented but four patients had suffered from necrotizing leukoencephalopathy, of whom three patients succumbed to that complication. We didn't perform a surgical biopsy or autopsy in these cases to verify this complication, but the diagnosis of necrotizing leukoencephalopathy was possible by CT scan finding and the downhill clinical course. Intrathecal administration of methotrexate after high dose radiotherapy may be the possible cause of the unfortunate high complication rate in our cases. Nowadays we eliminate intrathecal chemotherapy in the management of primary CNS lymphoma. We think that systemic chemotherapy for the control of systemic disease would not be warranted because of the relatively low rate of extra-CNS involvement.

There is no disagreement about the importance of irradiation in increasing the median survival time of CNS lymphoma patients. However, current questions about the dose required for local control as well as the volume of the CNS that should be included within the irradiation fields have not been answered yet. A dose-response relationship has not been established because of the small number of patients, but, many authors agreed that improved survival time could be anticipated with doses greater than 50 Gy to the primary tumor (Berry and Simpson 1981; Littman and Wang 1975; Murray et al. 1986; Sagerman et al. 1983). Littman and Wang (1975) and Sagerman et al. (1983) recommended at least 45 Gy to the whole brain plus a boost dose of 5 to 15 Gy to the primary site. We observed intracranial recurrence in two patients whose recurrent masses occurred in the area receiving irradiation of 30 Gy in 3 weeks and 36 Gy in 2 1/2 weeks. Thus, we also agree with higher dose irradiation of more than 50 Gy with the hope that this
more vigorous regimen will lead to greater longterm survival.

It is difficult to define the volume to be treated, whole brain or local field or craniospinal irradiation by literature review. Although Gonzalez and Schuster-Uitterhoeve (1983) reported slightly improved survival time in patients with local field irradiation (less than whole brain), the nature of multifocal involvement and diffuse infiltration justifies whole brain irradiation rather than local field irradiation. In Yasunaga's review (1986), all 5 patients initially receiving only local irradiation to the primary site relapsed outside the primary field. The role of spinal irradiation or intrathecal chemotherapy for the eradication of the undetected CSF or spinal cord involvement is still investigational. In the literature review by Murray et al. (1986), nine (9.3%) of 92 patients were reported to have a positive CSF finding at diagnosis and 15 (5.6%) of 267 cases showed positive CSF cytology or overt spinal cord disease at disease recurrence. Although some authors recommended craniospinal irradiation because of this risk, and Loeffler et al. (1985) reported that control of CNS lymphoma was seen only in patients receiving craniospinal irradiation or CNS-penetrating chemotherapy, many authors doubt the necessity of spinal irradiation because of the rarity of spinal metastasis and sequelae of spinal irradiation such as bone marrow suppression. Although an increase in local control and survival time may result in an increased recurrence rate within the neuraxis outside the primary tumor, the main problem in the control of CNS lymphoma is currently primary site recurrence. So, we advise spinal irradiation only for patients with positive CSF cytology or overt spinal cord metastasis.

In conclusion, high dose irradiation with a minimum 4000 cGy to the whole brain and more than 5000 cGy to the primary site is a safe and recommendable approach for the treatment of primary CNS lymphoma. To increase tumor control with an acceptable complication rate, the careful and precise combination of irradiation and chemotherapy needs to be studied in a future trial.

REFERENCES
