

CHAPTER

6

**Comparison of Language
Profiles and Electrocortical
Dysfunction in Aphasia**

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Anatomoclinical principles in aphasiology are derived from well-documented evidence that aphasia syndromes are correlated with lesions of specific anatomic foci. For the most part, anatomoclinical principles are based on identified relations between *structural* brain lesions and behavioral disturbances. Methods used for identifying structural brain lesions include clinical pathological correlations (CPC) and anatomic brain imaging by computerized tomography (CT) and magnetic resonance imaging (MRI) (Basso, Lecours, Moraschini, and Vanier, 1985; Broca, 1961; Hayward, Naeser, and Zatz, 1977; Kertesz, Harlock, and Coates, 1979; and Wernicke, 1908).

Since brain function may be impaired with or without identified structural abnormalities, questions are being raised regarding relations between *functional* brain lesions and clinical profiles (Ingvar and Schwartz, 1974; Metter, Wasterlain, Kuhl, Hanson, and Phelps, 1981; Nuwer, Jordan, and Ahn, 1978). Aspects of brain function that may be measured include electrocortical activity, regional cerebral blood flow, and cerebral metabolism. Due to new developments in neuroimaging techniques, these aspects of brain function can be studied *in vivo* with minimal risk to the patient. Electrocortical function is measured by electroencephalography (EEG) or more recently by topographic brain mapping (TBM), a computerized approach to analyzing the EEG and long latency cortical evoked potentials. Regional cerebral blood flow can be measured by single photon emitted tomography (SPECT), and cerebral metabolism by positron emission tomography (PET). Regional abnormalities identified by these measures are called "functional" lesions and should not be confused with functional disturbances referring to behavioral disturbances. Brain function measures supplement information provided by structural scanning methods and are being used to redefine the extent of a lesion and recovery of brain and behavior over time.

While the application of functional brain imaging appears promising, the clinical utility is limited until evidence is provided that the procedure can be trusted (Oken and Chiappa, 1986). Validation of new measures entails applying them to large clinical populations in whom the relation between brain and behavior has been well established. Until such validation is complete, skepticism is necessary when applying the measures and interpreting findings in populations with poorly understood neuropathophysiology.

The purpose of this project is to investigate whether TBM, one of the new functional brain imaging measures, is a valid and useful tool in clinical neurophysiology. TBM is a quantitative topographic and statistical approach to EEG and evoked potentials, described separately by Duffy, Burchfiel, and Lambrosa (1979) and John and colleagues (1977). Basically, both groups proposed the statistical analysis of quantitative electrophysi-

ological features from EEG and evoked potentials studies aids in the differential diagnosis of brain dysfunctions.

TBM is the first real advance in EEG in over half a century, providing an objective means of analyzing volumes of data with the aid of a computer. Two assumptions underlie TBM: (1) EEG and evoked potentials contain untapped information valuable to differential diagnosis, and (2) clusters of individuals can be identified with similar electrophysiological profiles that relate to established anatomoclinical principles. Compared to routine EEG, TBM reportedly demonstrates better anatomic definition (Nuwer, Jordan, and Ahn, 1987). While the application of TBM has been reported in Alzheimer's disease (Duffy, Albert, and McAnulty, 1984) dyslexia (Duffy, Denckla, Bartels, and Sandini, 1980), spasmodic dysphonia (Finitzo and Freeman, 1988), seizure disorders (Gregory and Wong, 1984), schizophrenia (Pool, Finitzo, Paulman, Judd, Gregory, and Raese, 1988), and stroke (Jonkman, Nagato, Mizukami, Araki, Kawase, and Hirano, 1982; Nuwer et al., 1987), either sample sizes have been small, validation of lesion identification has been unavailable, or the disorder itself was poorly understood. In this chapter we report on TBM in 100 confirmed stroke patients in an effort to evaluate the above two assumptions which underlie TBM.

METHOD

SUBJECTS

The subjects were 100 stroke patients evaluated consecutively at the Dallas Rehabilitation Institute. Patients were referred with an admitting diagnosis of stroke, confirmed by neurological evaluation on admission. All patients had a complete language assessment and TBM evaluation within 1 month from admission and at least 1 month post-stroke. Patients included 55 males and 45 females, ages 18 to 87 with a mean of 57 years and standard deviation of 14. CT or MRI studies were available for 87 of the 100 patients.

Our patient population represented a heterogeneous group, as they were not selected according to lesion site or aphasia type. The population consisted of patients with unilateral left, right, or bilateral cortical lesions and subcortical lesions. A relative degree of severity homogeneity was inherent in the patients due to the natural selection of patients admitted to a rehabilitation center.

INSTRUMENTATION

TBM was performed using the BEAM system (Nicolet Instrument Corporation). Ten-millimeter gold cup electrodes were attached with collo-

dion to achieve impedances less than 3K ohms. Twenty electrodes were placed according to the International 10-20 system with less than 3 mm error center to center. Six additional electrodes were placed over the zygoma, infraorbitally, and over the nuchal areas bilaterally to assist with artifact detection. All electrodes were referenced to linked ears (A1 and A2). The low-frequency filter was set at 1 Hz and the high-frequency filter at 300 Hz. Filters had a 6 dB per octave roll-off. No notch filtering was used. Gain was 20,000.

The EEG was modified so that the output signal from each amplifier directly connected an analog to digital converter to achieve sampling intervals of 4 ms per channel. Hard-copy production of the input signal was recorded by a digital to analog converter using the same 4 ms per channel sample interval. This analog-reconstituted signal was input into the penwriters of the EEG machine.

Measurement Technique

Each subject was tested in a leather recliner in a dimly lit, sound-insulated room. The EEG was recorded in eyes-open and eyes-closed condition to achieve a minimum of 30 artifact-free, 2-second segments of data for Fourier analysis. In the eyes-closed condition, eyes were taped to minimize eye movement. In the eyes-open condition, subjects focused on a dot and were encouraged to hold the eyes steady. The fixation point was altered frequently to reduce defocusing.

EEG Analysis

Spectral analysis was performed on awake, alert, artifact-free EEG data. Selection of the 2-second segments of EEG for subsequent fast Fourier transformation (FFT) was done by visual inspection to ensure that non-cerebral activity was excluded. Segments were deleted that contained vertical or horizontal eye movements, eye blinks, and muscle or electrode artifacts. Segments were inspected for desired state of arousal. The FFT was obtained for each segment selected and then arithmetically averaged over all selected segments to produce a mean FFT for each electrode in both the eyes-closed and eyes-open condition. From these curves, relative amplitude files were also calculated. The relative files provide information on the percent of total EEG activity represented by a particular frequency.

A topographic map was constructed to display the average amplitude at each frequency band at each electrode. A computer colorgraphic display of 9216 pixels was created. Values from each pixel in the computer display are determined by the three adjacent electrodes by three-point linear

interpolation. In addition to amplitude, statistical maps of t-tests corrected for small sample sizes were also computed.

LANGUAGE ASSESSMENT

Subjects' language performance was assessed by the Boston Diagnostic Aphasia Examination, Boston Naming Test, Reading Comprehension Battery for Aphasia, Selective Reminding Test, and Token Test. Two aphasiologists, blinded to BEAM results, independently rated the patients' behavior along three dimensions: fluency, comprehension, and expression. The rating scale consisted of four levels: normal, mild, moderate, or severe impairment. The subjects were classified into one of two groups, aphasic or nonaphasic.

GROUP COMPARISONS

In this chapter, we report the results of EEG spectral analysis for the delta frequency band (0.5–3.5 Hz). Nuwer and colleagues (1987) found delta frequency bands to be one of the most useful bands in defining areas of cortical impairment using TBM with stroke subjects. Delta activity is also remarkably symmetrical among the normal subjects.

Six group comparisons of the EEG delta frequency band were made (1) aphasic subjects versus normal controls, (2) aphasic versus nonaphasic stroke subjects, (3) global (severe rating on all three dimensions) versus nonglobal aphasic subjects, (4) subjects with normal versus severe non-fluency, (5) subjects with normal versus severe comprehension impairment, and (6) subjects with normal versus severe expression deficits. The normal data, resident in the BEAM system, included 96 healthy, neurologically normal adults, stratified by decade and ranging in age from 40 to 79 years. As stated, multiple-measure and small-sample-corrected t-tests were used to determine statistically significant differences between groups. The t-test values were selected to achieve $p < .01$ level for each analysis, taking differing sample sizes into account to achieve $p < .05$ for the entire study.

RESULTS

APHASIC (46) VERSUS NORMATIVE DATA BASE (96)

The comparison of delta activity between aphasic stroke patients and normals demonstrated statistically significantly increased amplitude at all electrodes for the patient group ($p < .001$).

APHASIC (46) VERSUS NONAPHASIC STROKE (54)

Figure 6-1 demonstrates delta spectral amplitude for aphasic subjects, nonaphasic stroke subjects, and their t-test comparison, respectively. The image is a topographic left lateral view of brain. Note that amplitude scalings for the two groups are the same. Scaling for the t-test map is set so that values with $p < .005$ are shown in white. As seen in the t-test map, statistically significant increase in delta activity is present for aphasic subjects as compared to nonaphasic stroke subjects in the left perisylvian region. No statistically significant differences were found in the right hemisphere for this group or any of the following comparisons.

GLOBAL (20) VERSUS NONGLOBAL APHASIC (26)

Figure 6-2 illustrates the delta activity and the comparisons for the global and nonglobal aphasic subjects. The between-group difference is statistically significant in the left posterior temporoparietal region ($p < .01$).

SEVERE (24) VERSUS NORMAL FLUENCY (59)

The amplitudes and t-test differences between these two groups are shown as maps in Figure 6-3 and 6-4. Severely nonfluent subjects exhibited markedly increased delta activity across the entire left hemisphere ($p < .001$). Figure 6-4 illustrates the same data with the t-test map scaled to demonstrate the maximal regional difference between groups. This difference is localized to the left inferior frontal/anterior temporal region ($p < .0001$).

SEVERE (33) VERSUS NORMAL COMPREHENSION (36)

As shown in Figure 6-5, subjects with severe comprehension deficits (rating of 3) showed a global increase in delta over the left hemisphere when compared to stroke subjects with normal comprehension ($p < .001$). Figure 6-6 shows a maximal difference in left posterior temporoparietal cortex for subjects with severe comprehension deficits ($p < .0001$).

SEVERE (32) VERSUS NORMAL EXPRESSION (40)

Figure 6-7 demonstrates the region of maximal difference between these two groups. A focal increase in delta activity occurred in left posterior temporoparietal cortex in subjects with severe expression deficits compared to those with normal measures of expression ($p < .001$).

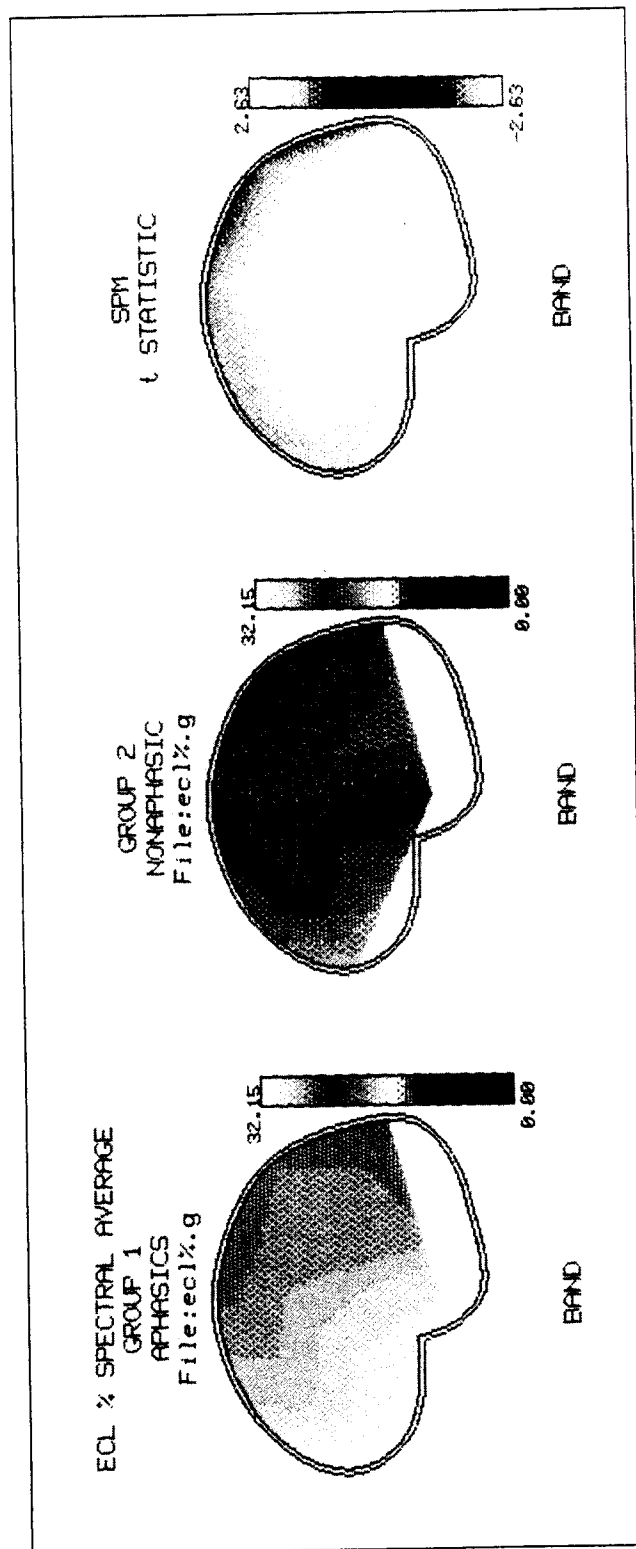


Figure 6-1. TBM for aphasic versus nonaphasic stroke subjects. Left map on Figure 6-1 is amplitude for the aphasic subjects; the middle map is delta amplitude of nonaphasic stroke subjects both scaled to 32.15 uv. The right map is the t-test statistical difference map comparing these two groups at $p < .005$ level. Note that the difference is widespread, although maximal over the left perisylvian cortex. Image is the left lateral view of the cortex.

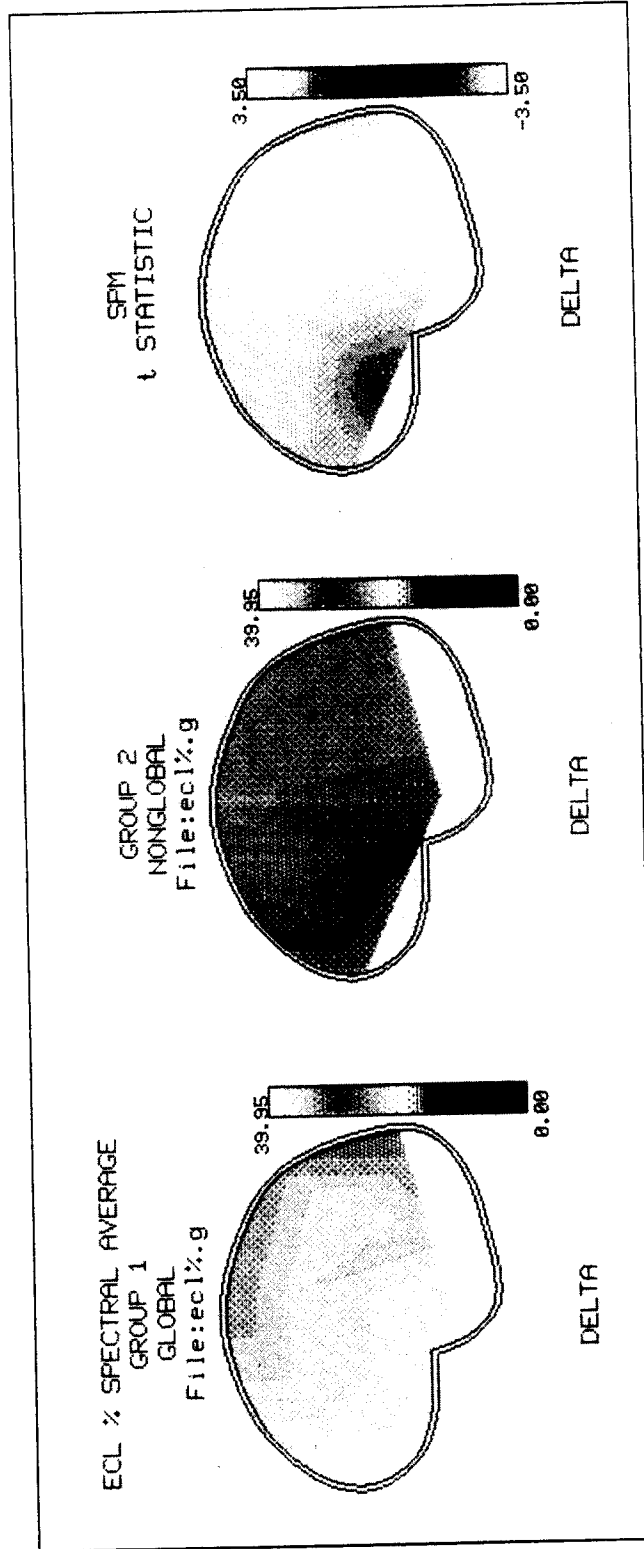


Figure 6-2. TBM of delta amplitude for global versus nonglobal aphasic subjects (similar comparisons as Fig. 6-1). The t-test difference on the right map is over the left perisylvian cortex ($p < .01$).

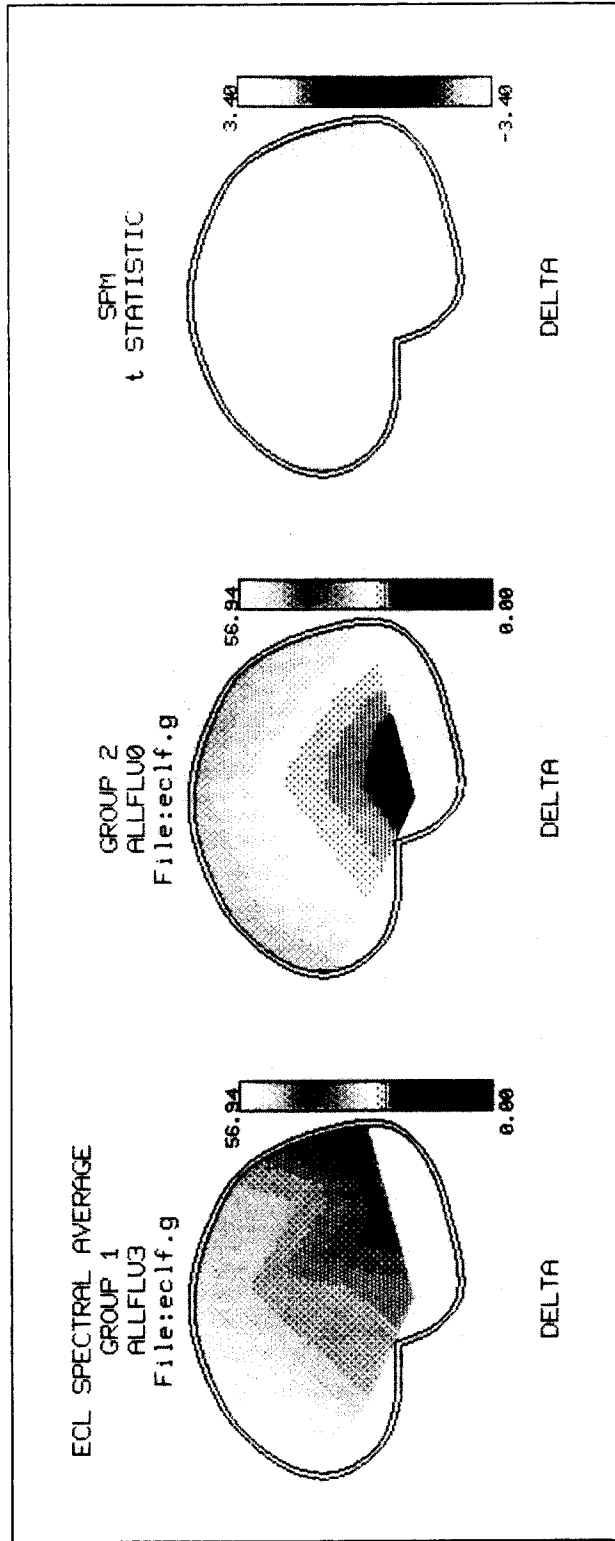


Figure 6-3. TBM of delta amplitude for subjects with severe (left) and normal fluency (middle). The t-test suggests global left-hemisphere differences between the two groups ($p < .001$).

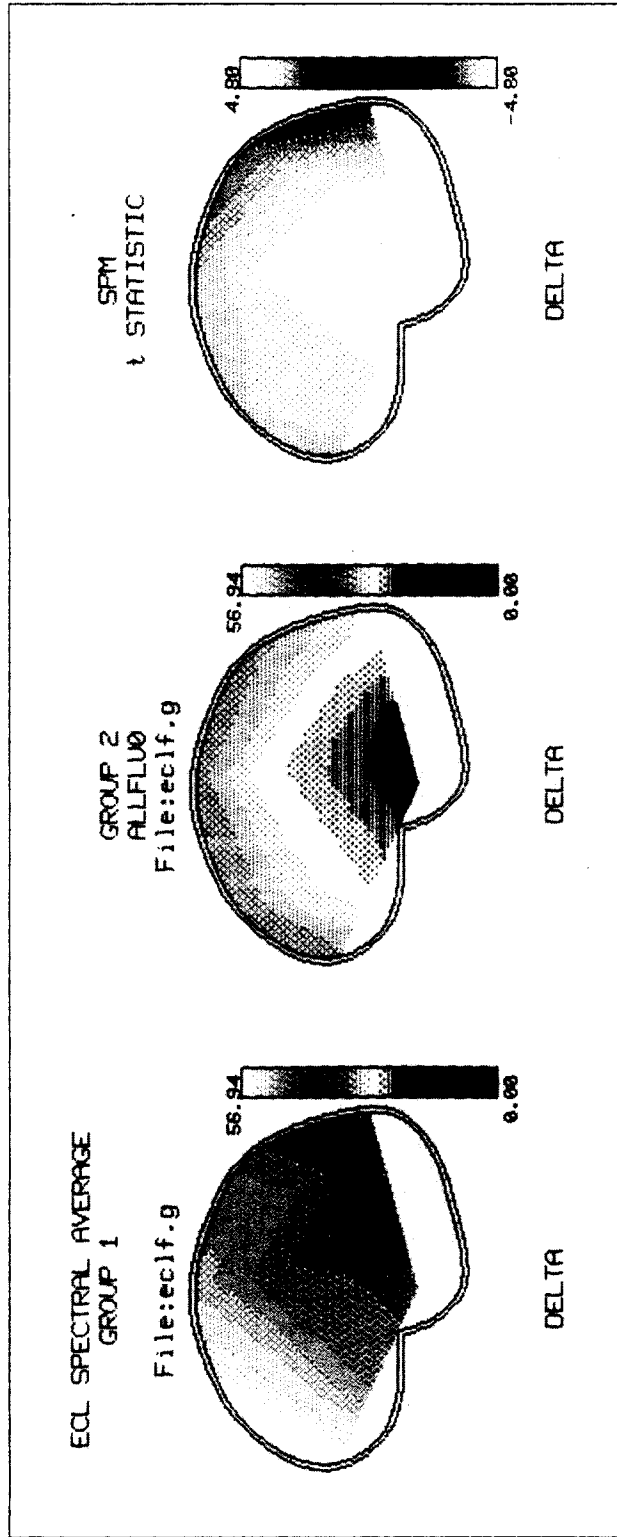


Figure 6-4. TBM showing region of maximal difference between subjects with severe (*left*) and normal (*middle*) fluency. The maximal regional difference is localized to the left inferior frontal/anterior temporal region ($p < .0001$). (Same data as Fig. 6-3, different comparison.)

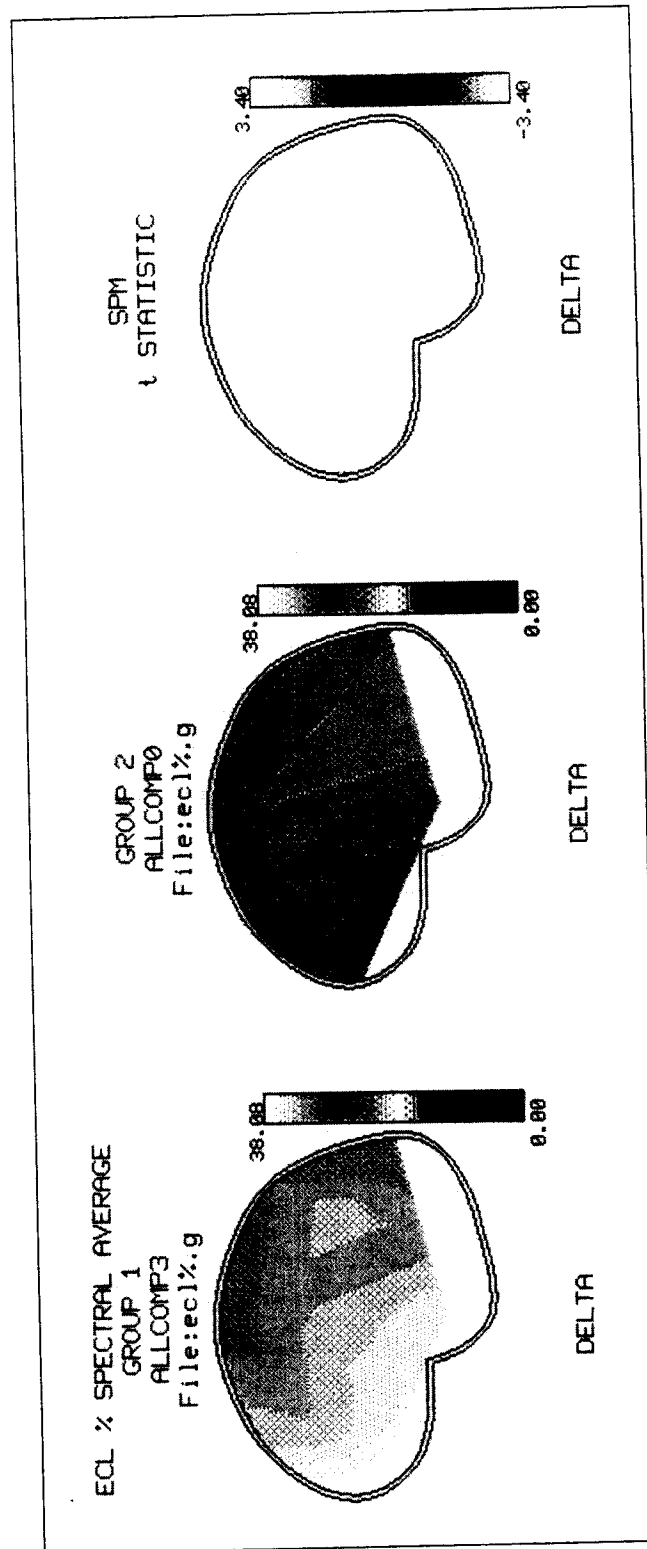


Figure 6-5. TBM of delta amplitude for subjects with severe comprehension (*left*) and normal comprehension (*middle*). The t-test map on the right shows globally increasing amplitude over the left hemisphere ($p < .001$).

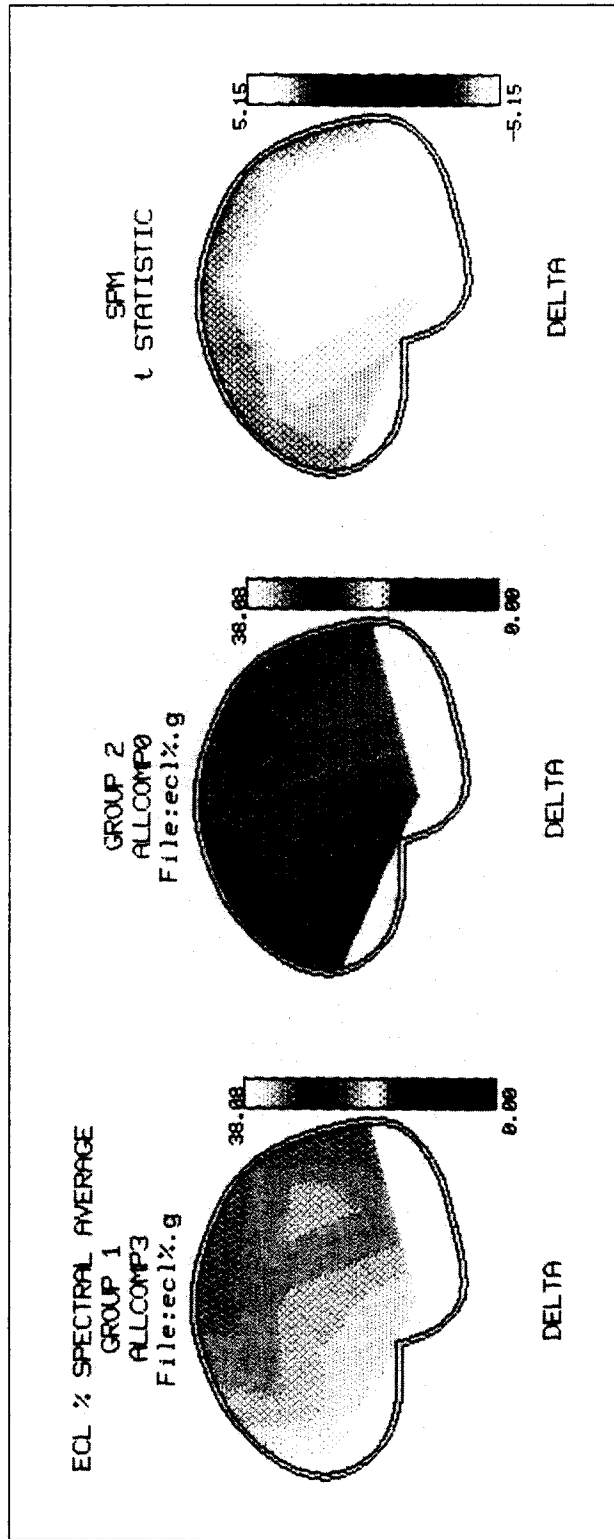


Figure 6-6. TBM showing region of maximal difference between subjects with severe (left) and normal comprehension (middle). Region of maximal difference is the left posterior temporoparietal cortex ($p < .0001$). (Same data as Fig. 6-5, different comparison.)

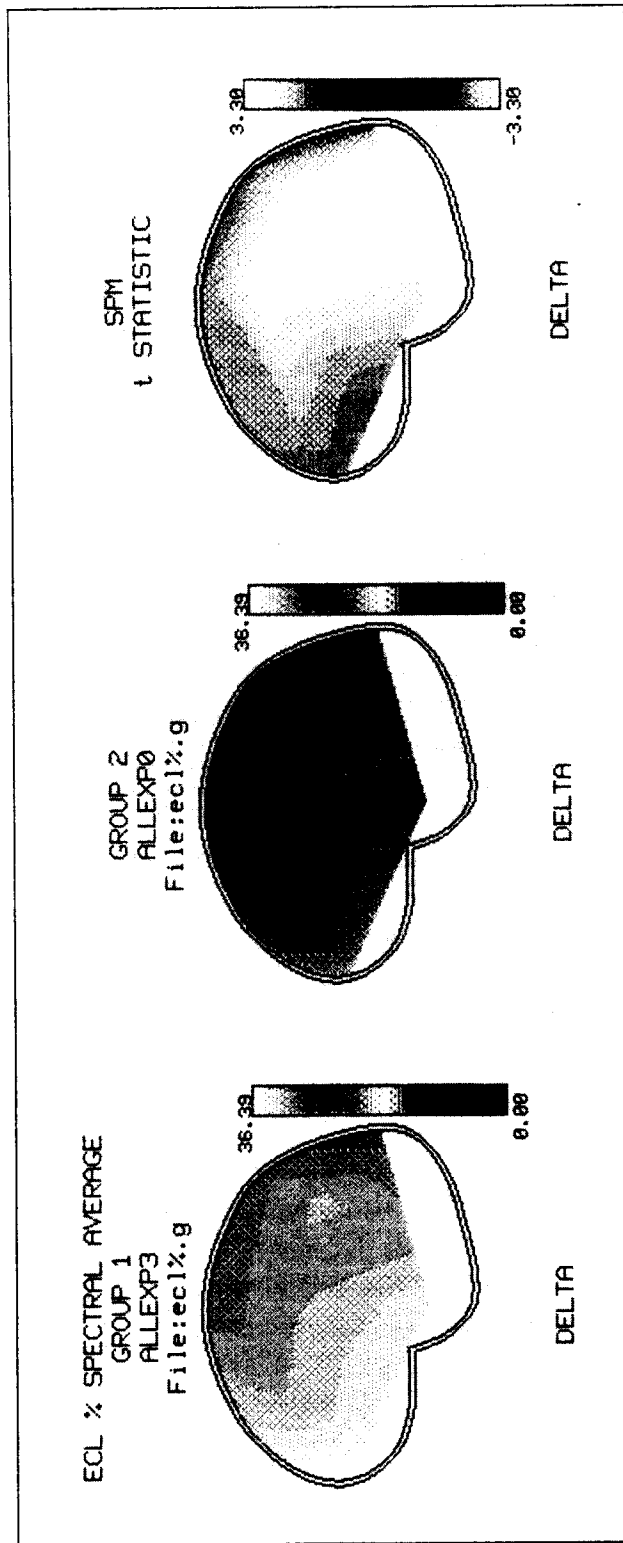


Figure 6-7. TBM showing region of maximal difference between subjects with severe (left) and normal expressive (middle) measures. Region of maximal difference is left posterior temporoparietal cortex ($p < .001$).

DISCUSSION

The primary purpose of this investigation was to evaluate the efficacy of using TBM, a relatively new EEG mapping technique, in identifying cortical pathophysiology. Stroke subjects with and without aphasia were selected for study because focal cortical pathology in aphasia has been well documented (Broca, 1861; Basso et al., 1985; Kertesz, Harlock, and Coates, 1979; Wernicke, 1901).

The major findings suggest that EEG as measured by TBM can provide clinically useful information regarding the basic processes involved in cerebrovascular disease. This is based on evidence described herein of localized electrocortical changes in regions consistent with classic aphasia theory. Specifically, classic aphasia theory has localized aphasia to the left hemisphere, nonfluency to Broca's area or left inferior frontal cortex, and impaired comprehension to left posterior cortex. In the present study, subjects with aphasia subsequent to stroke exhibited electrocortical abnormalities localized to left hemisphere. Changes in electrocortical function in subjects with nonfluency as opposed to fluency occurred primarily over the left inferior frontal/anterior temporal cortex. Furthermore, subjects with severe comprehension deficits demonstrated abnormal EEG spectral content localized to left posterior temporoparietal cortex.

Two findings were somewhat unexpected but not necessarily inconsistent with anatomoclinical principles of aphasia. One was the significant electrocortical difference in aphasic versus normal healthy controls broadly across both hemispheres. Initially, we expected the abnormality to be more localized to the left hemisphere with a specific focus in the perisylvian region for aphasic subjects. Upon reconsideration, we recognized that these groups differed in two ways, that is, presence of cerebrovascular disease *and* aphasia. The aphasic subjects were not selected based on unilateral stroke but rather were selected for the presence of aphasia from a population already selected for the presence of cerebrovascular disease. Therefore, many of the aphasic patients may have had multifocal or bilateral stroke resulting in more diffuse involvement of cortex. Consequently, the differences between aphasic and normal subjects across both hemispheres may be reflecting not only aphasia but cerebrovascular disease as well. The effects of cerebrovascular disease were not seen in the comparison of aphasic versus nonaphasic stroke subjects. In this comparison, the aphasic subjects demonstrated a focal lesion in the left hemisphere, suggesting that cerebrovascular disease was a confounding factor when aphasic subjects were compared to normals.

While we anticipated a left posterior lesion focus for patients with impaired comprehension, we did not expect a similar lesion focus for subjects with severe expression deficits. Both groups showed a maximal elec-

tro cortical difference in the left posterior temporoparietal cortex when compared to subjects with normal comprehension and expression, respectively. Anatomoclinical principles provide limited guidelines for the localization of impaired expression. Whether the topologic similarity arises from nonindependence of the measures or from an anatomically similar neural substrate cannot be determined.

The findings from the present study are supported by recent research (Nagata et al., 1982; Nuwer et al., 1987). These two studies reported on TBM findings of 20 stroke patients each. TBM was shown to be clinically useful in identifying localized electro cortical lesions consistent with brain/behavior theory. In addition, TBM findings correlated with structural lesions on CT and functional lesions on regional cerebral blood flow studies. We are currently analyzing whether any relations exist between behavioral signs and localized structural and functional lesions in our subjects.

The advantage of this relatively large study of stroke is that electro cortical profiles across groups can be compared, making generalizations possible. The findings support the two previously stated assumptions underlying TBM, that is, that EEG contains information valuable to differential diagnosis and that groups with different behavioral profiles have the anticipated differences in electrophysiological profiles.

The disadvantage of a large study is having to group aphasic subjects in order to make comparisons. Grouping is problematic because considerable controversy exists over how aphasic patients should be classified. While classifying patients according to broad linguistic and nonlinguistic parameters such as fluency, comprehension, and expression deficits is a widely accepted schema, three major problems exist. First, the processes of fluency, comprehension, and expression reflect multiple related processes. For example, how can expression be measured independent of comprehension? Second, within each dimension, there is considerable behavioral variability. That is, aphasic subjects with moderate comprehension deficits may exhibit quite different language profiles. Finally, the classification dimensions of fluency, comprehension, and expression are not represented by one specific anatomical brain region, but rather several brain regions underlie most behavioral processes. Another reason group studies are limited is that individual features are lost when subjects are grouped. It is often individual pattern differences that provide a better understanding of organization of language in the brain.

Despite these inherent problems, we were able to address the primary purpose of this study, which was to determine regions of electro cortical dysfunction in well-recognized focal cortical pathology. The evidence leads us to believe that we can trust data provided by TBM. TBM may allow us to investigate both the heterogeneity and homogeneity of our

clinical populations. Future studies of TBM with less well understood aphasia syndromes such as transcortical sensory and motor, conduction, and anomic aphasic patients as well as other neurogenic disorders may provide insights into relations between behavior and brain structure and function. Finally, studies of brain function may be useful in understanding recovery, both cortically and behaviorally.

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DISCUSSION

Q = question; A = answer; C = comments.

- Q. In normals versus aphasics, can we determine what might be a more temporary electrophysiology phenomenon of diaschisis in the classic sense and what might be permanent damage? Would this information be useful to a clinician?

- A. Jonkman has suggested that there is an electrophysiological phenomenon of diaschisis. We are trying to decide whether we can validate that; we believe that there may be some. Electrical measures, in general, do not appear to be quite as vulnerable as metabolic measures to the phenomenon of diaschisis. If a major disassociation between a metabolic and electrical measures of function occurred, it would bias us toward the suspicion that the metabolic measure was diaschisis. At this point, we do not know if electrical diaschisis exists or whether specific markers exist that reflect permanence of injury. The issue is being studied. It is important to the understanding of cerebrovascular disease and ischemia and needs to be clarified.
- Q. I'd like to inquire about the speculation relative to some of the sources of exception that you found and what you're looking for and ask if you know the proportion or breakdown in your subject sample of first stroke versus second and other sequential strokes. Perhaps that might be an explanation to some of the exceptions that you found. Do you have a sense of that and if there is a correlate to it?
- A. I can't give you a specific number off the top of my head, but I can give you a general impression. It depends in great part upon what criteria we judge first stroke. If we take the reported referral by the clinician at the time the patient is referred to the rehab facility, almost all of these patients are first stroke, single stroke, unilateral lesions. If we take the neurological exam, and additional histories acquired upon admission, we find that preexisting transient ischemic attacks (TIAs) or strokes are quite frequent even though they have reportedly presented with their first stroke. Part of the quandary we find ourselves in is trying to report data on pure single lesions. Where do we make that cut?
- Q. Although I realize that the purpose of the study was not to look at comparisons between the metabolic and structural measures, I wonder if you have done that in any patients. I was thinking about the work of the Nagata group in Japan that has looked at metabolic blood flow and BEAM activity and found bilateral delta activity. These are just single case descriptions, as you know, with neuropsychological profiles in patients with very discrete posterior lesions and only posterior hypometabolic profiles. Have you looked at any single cases that you could relate to the CT scan or the MRI and the SPECT?
- A. I think that it is important to realize that we are measuring different animals. We have collaborative studies in SPECT and BEAM in other clinical populations, and while we oftentimes see overlapping or similar anatomical lesions, that is not always the case. The differences are interesting to us. We have a fair number of subjects who have CT

scans showing very small discrete lesions who behaviorally suggest somewhat wider spread lesions and who electrophysiologically show similar widespread lesions — that's very common. On the other hand, we have patients who show essentially normal electroconvulsive physiology who have isolated subcortical lesions on CT scan which fit their clinical picture. Neither structural imaging nor any specific functional imaging at this point gives all the answers. If it did, all the rest of these toys and machines would go away except whichever one worked. They give us different answers and different ways of probing and looking at brain function. In our experience, electrophysiology gives us answers sometimes when other measures don't. So I think it should be used in conjunction with other measures.

- Q. I wonder if you have any interest in longitudinal studies, taking people that have had TIAs and trying to catch them, if you want to call it that, in a normal state, bringing these people back and trying to watch just what kind of changes occur over time.
- A. If you want to write your congressman We are going to be submitting a grant to do a longitudinal prospective study and look at issues like that and we would certainly appreciate your support.
- Q. Just a question about people who have had temporal lobectomies for intractible seizures and the old reports that if you get up to 6.0 cm, you don't have clinical findings, beyond 6.5, you do, and the placement of that electrode. Have you thought about running those kinds of patients to compare to aphasics or moving the electrodes? I realize that that can't be arbitrary.
- A. Yes. We've thought about this in a couple of ways. We don't run an epilepsy center, but there is one in town. We have begun to entertain discussions with them about cross-collaborative efforts to look at lobectomy cases for that reason. The possibility of moving electrodes becomes confounding because if we want to be able to use individual subject data or use some of these data dating back 3 to 5 years, we couldn't. It's tough to throw out 5 years of data, and say whoa, I'm going to move it back half an inch. What is currently in the developing field of electrophysiology is being able to extract three-dimensional localization data out of electrical measurements to produce three-dimensional imaging so we can then infer from the surface recordings what positions data are generated from.