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EEG discriminant analyses of mild head trauma

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Summary Measures of EEG power spectral analyses were obtained from a total of 608 mild head trauma patients and 108 age-matched normal subjects. A training-set discriminant function was first developed from 264 mild head-injured patients and 83 age-matched controls yielding an overall discriminant classification accuracy of 94.8%. The first independent cross-validation of the discriminant function using 130 mild head trauma patients and 21 age-matched normals yielded a discriminant classification accuracy of 96.2% for the trauma patients and 90.5% for the normals. A second independent cross-validation of the discriminant function using 51 patients and measures of test-retest reliability from 93 patients yielded classification accuracies ranging between 77.8% and 92.3%. A third independent cross-validation of 70 mild head-injured patients tested at a different location with a different EEG computer system yielded a discriminant accuracy of 92.8%. The discriminating EEG power spectral analyses indicated 3 classes of neurophysiological variables which are attributable to mechanical head injury: (1) increased coherence and decreased phase in frontal and frontal-temporal regions; (2) decreased power differences between anterior and posterior cortical regions; and (3) reduced alpha power in posterior cortical regions.

Key words: EEG; Power spectral analysis; Mild head trauma; Discriminant analyses

Mild cerebral injury is typically defined by a Glasgow Coma Score between 13 and 15 with either no loss of consciousness or a period of unconsciousness of 20 min or less (Langfitt and Gennarelli 1982). There is a constellation of post-concussion symptoms which may be present in varying degrees in the mildly injured patient, such as memory difficulties, problems with attention and concentration, lassitude, disturbance of sleep, irritability, depression and headache (Kwentus et al. 1985; Gennarelli 1986; Prigatano and Pepping 1987). Although these symptoms typically reach their peak in the weeks following the injury and sometimes persist for 6–12 months, they usually dissipate over time. Several studies (Gronwall and Wrightson 1980; Rimel et al. 1981; Barth et al. 1983; Kwentus et al. 1985), however, suggest that there may be permanent sequelae associated with 'minor' cerebral injury. In contrast, other studies have failed to demonstrate any permanent disability in mild head trauma patients (Gentilini et al. 1985; Levin et al. 1987). The discrepancy in these studies is due, in part, to inconsistencies and difficulties in the detection and quantification of neurological damage. For example, studies by Gennarelli et al. (1982) suggest that structural damage at the microscopic level cannot be detected by CT or MRI in many patients with mild head trauma. This appears to be especially true in the case of diffuse axonal injury (DAI) in which shear-strain forces of rapid acceleration and deceleration result in injury to axons.

A technique that has promise for the detection and quantification of diffuse axonal injury, and thus the detection of mild cerebral injury, is the power spectral analyses of coherence and phase from the human EEG. Coherence is analogous to

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a cross-correlation coefficient in the frequency domain and thus is a metric of the amount of shared activity between two regions, while phase is a measure of the lead or lag of shared rhythms between two regions (Otnes and Enochson 1972; Bendat and Piersol 1980). The relevance of measures of EEG coherence and phase to the issue of mild head trauma was recently demonstrated in studies that have shown EEG coherence and phase to reflect topographic inhomogeneities which correspond to the known features of cortical cytoarchitecture and cortico-cortical axonal fiber systems (Nunez 1981; Thatcher et al. 1986, 1987; Tucker et al. 1986). Consistent with these observations are the results of a prognostic analysis of 162 severe, moderate and mild closed head-injured patients which showed that EEG coherence and phase were among the best predictors of outcome at 1 year following injury (Ducker et al. 1982; Thatcher et al. 1983).

The goal of the present study was to evaluate the ability of power spectral analysis of EEG to discriminate between mild head-injured patients and a group of age-matched normal subjects. Among the questions of interest were: (1) are there anatomical or topographic patterns that are more discriminative than other patterns?, (2) are there particular features of the power spectral analysis of EEG which are more discriminative than others?, and (3) what is the classification accuracy of power spectral analysis of EEG in the mildly head-injured patient?

Methods

Patient population

A total of 608 patients were included in the study (63.5% males). Of these patients 538 were tested either as inpatients or outpatients during the period from 1981 to 1987 at the Maryland Institute for Emergency Medical Systems and Services (MIEMSS). An additional 70 patients were tested as outpatients in the diagnostic laboratories at University Services in Philadelphia, PA. Of the 538 MIEMSS patients, 264 were included in the initial development of a discriminant function, 130 were included in the first independent cross-validation and 144 patients were included in a second independent cross-validation and test-retest reliability evaluation, and the 70 mild head-injured patients tested at University Services were included in a third independent cross-validation. Approximately 60% of the patients were motor vehicle accident victims, another 10% were pedestrians, and the remainder were victims of industrial or home accidents or violent crime. For the inpatients the length of stay in the hospital varied from 24 to 21 days, depending upon the extent of non-head injuries. For the outpatients tested at MIEMSS the interval from injury to EEG test varied from 7 days to 363 days. The third cross-validation group of 70 patients tested at University Services were admitted as outpatients from 3 months to 8 years following injury. All of the patients in this study were diagnosed as having a mild closed head injury.

Mild head trauma was defined by an admission Glasgow Coma Score (GCS) of 13–15 without subsequent deterioration. Of the total number of patients, 37% had a GCS of 15, 38.6% had a GCS of 14 and 24.4% had a GCS of 13. Although there was evidence of head injury such as superficial scalp lacerations, bruises and patient reports, a patient was excluded if there was evidence of skull fracture or evidence of an intracranial mass lesion such as a hematoma or any intracranial surgical procedures or complications such as meningitis. Based on patient and medical personnel interviews, the patients suffered either no loss of consciousness or a loss of consciousness for a duration of 20 min or less.

A range of approximately 14 different categories of medication were administered at various times to some of the inpatients admitted to the emergency medical service. These included, tranquilizers, muscle relaxants, antidiuretics, antibiotics, anti-inflammatories, anti-hypertensives, anti-coagulants, hormones, vitamins and trace elements, etc. Approximately 67% of the patients admitted with Glasgow Coma Scores of 13 and approximately 23% of the patients with GCS of 15 were medicated at the time of the EEG test. However, none of the 214 mild head-injured outpatients were medicated at the time of EEG test. Given the diversity of dosages and types of medication it was impossible to control for the effects of medication on the EEG. As described in the Results and Discussion, the EEG discriminant function was stable and invariant independent of the presence, dosage or type of medication.

Normal control subjects

A total of 108 age-matched normal subjects were included in the study. An initial sample of 104 subjects were staff members working at the University of Maryland, students enrolled at the University of Maryland and research subjects recruited as part of a normative EEG study (Thatcher et al. 1987), and 4 normal subjects were staff members associated with University Services in Philadelphia, PA. Normality was defined by: (1) no history of head injury with cerebral symptoms, (2) no history of central nervous diseases, (3) no history of convulsions of emotional, febrile, or other nature, (4) no obvious mental diseases, and (5) no abnormal deviation with regard to mental and physical functioning.

Electroencephalographic acquisition and analysis

Grass silver disk electrodes were applied to the 19 scalp sites of the international 10/20 system. A transorbital eye channel (electro-oculogram or EOG) was used to measure eye movements and all scalp recordings were referenced to linked ear lobes. Impedance measures for all channels were generally less than 5000 Ω. Amplifier bandwidths were nominally 0.5–30 Hz, the outputs being 3 dB down at these frequencies. The EEG activity was digitized on-line by a PDP 11/03 data acquisition system. An on-line artifact rejection routine was used which excluded segments of EEG if the voltage in any channel exceeded a preset limit determined at the beginning of each session to be typical of the subject's resting EEG and EOG.

One minute of artifact-free EEG was obtained at a digitization rate of 100 Hz. The EEG segments were analyzed off-line by a PDP 11/70 computer and plotted by a Versatec printer/plotter. Each subject's EEG was then visually examined and edited to eliminate any artifacts that may have passed through the on-line artifact rejection process.

A second-order recursive digital filter analysis was used to compute the auto- and cross-spectral power density (Otnes and Enochson 1972) for each channel. This procedure is essentially identical to the Fast Fourier Transform (FFT) method of computing power spectral density. The advantage of the recursive digital filter, when a limited number of bands are analyzed, is increased computational efficiency and a simpler design, since the recursive filters provide a natural form of windowing and leakage suppression. The procedure involved using a first difference pre-whitening filter and a 2-stage (4-pole) Butterworth band-pass filter (Otnes and Enochson 1972). Frequency bands, including the center frequencies and half-power B values were: delta (0.5–3.5 Hz; $fc = 2.0$ Hz and $B = 2.0$ Hz), theta (3.5–7.0 Hz; $fc = 4.25$ Hz and $B = 3.5$ Hz), alpha (7.0–13.0 Hz; $fc = 9.0$ Hz and $B = 6.0$ Hz); beta (13–22 Hz; $fc = 19$ Hz and $B = 14.0$ Hz). Degrees of freedom = 2BwT, where Bw = the bandwidth and T the length of the record (e.g., for 20 sec of EEG there are 160 degrees of freedom) and the start-up and trail-off periods of the filter are 2/Bw sec or 0.5 sec for a 4 Hz bandwidth. The artifacting routines precluded EEG segments less than 0.8 sec in length and the range of EEG epoch lengths over which the power spectrum was computed varied from 16 sec to 60 sec (mean = 46.12 sec and S.D. = 14.23 sec). Relative power was computed by dividing the total power from 0.5 to 22 Hz into the power within each frequency band.

EEG coherence and phase

Coherence and phase were computed for all pairwise combinations of electrodes (Otnes and Enochson 1972; Thatcher et al. 1986). Coherence is defined as

$$\gamma^2_{xy}(f) = \frac{\left(G_{xy}(f)\right)^2}{\left(G_{xx}(f)G_{yy}(f)\right)}$$

where $G_{xy}(f)$ is the cross-power spectral density and $G_{xx}(f)$ and $G_{yy}(f)$ are the respective auto-power spectral densities. Coherence was computed for all pairwise combinations of the following 16 channels (O1, O2, P3, P4, T5, T6, T3, T4, C3, C4, F3, F4, F7, F8, Fp1, Fp2) for each of the 4 frequency bands. The computational procedure to obtain coherence involved first computing the power spectra for x and y and then the normalized cross-spectra. Since complex analyses are involved this produced the cospectrum ('r' for real) and quadspectrum ('q' for imaginary). Then coherence was computed as:

$$\gamma^2 = \frac{\gamma_{xy}^2 + q_{xy}^2}{G_{xx}G_{yy}}$$

and the phase difference, in milliseconds, was computed as: $\text{phase} = 159.1549 \tan -1(q/r)/SC$, where SC is the center frequency.

EEG power differences

Because the recursive filter analysis was performed over specific frequency bands the absolute power of the EEG was computed in μV^2 for each frequency band. Differences in absolute power were computed between the same pairs of electrodes as in coherence described in the previous section (i.e., left and right intrahemispheric and interhemispheric electrode combinations). The formula for power differences was (left − right/left + right) for the inter-hemisphere comparisons and (anterior derivation − posterior derivation/anterior + posterior derivation) for intrahemisphere comparisons.

Comparisons between ANL computers and the Q.S.I. 9000

It is desirable to test the generality and efficacy of the discriminant function by cross-validating with a completely independent sample of patients tested at a different location, by different personnel, and on a different EEG computer system. This was accomplished by testing 70 mild head trauma patients and 4 normals at the laboratories of University Services located in Philadelphia, PA, using a Q.S.I. 9000 EEG acquisition and analysis computer system. In order to insure data compatibility, the amplifier characteristics of the Q.S.I. 9000 were first compared to the amplifier characteristics of the Applied Neuroscience Labs' (ANL) EEG acquisition computers from which the original discriminant function was derived. Differences in frequency and gain characteristics were found to be minor (i.e., $< 5\%$). However, in order to insure exact duplication the 100 Hz digitized EEG data acquired on the Q.S.I. 9000 were multiplied by weighting coefficients that exactly matched the differences in amplifier characteristics between the Q.S.I. 9000 and the Applied Neuroscience Labs' amplifiers. This new set of raw EEG data was then spectrally analyzed using the recursive filter procedure described above.

Statistical procedures

Data screening and transforms

Data analyses involved first double checking all scores before and after entry into the PDP 11/70 computer files. Each measure category was then screened for extreme values (outliers) and for normality of distribution (Wilkinson 1987). Outliers were detected primarily through visual examination of the scattergrams and normal probability plots using Systat (Wilkinson 1987). Because of the effectiveness of the on-line artifact rejection procedures and visual editing, however, the EEG data were very well behaved and only 3 subjects out of the total population were screened from the study because of artifactual extreme values.

Previous work with EEG and evoked potential measures has resulted in the use of standard transforms (John et al. 1977; Gasser et al. 1982; Thatcher et al. 1983) to insure gaussian normality. For relative power and coherence variables the transforms were $\log_{10} X/100 - X$. For the amplitude asymmetry variables the transform was $\log_{10} (200 + X)/(200 - X)$. For absolute phase the transform was $\log_{10}$. After applying the appropriate transform the Lilliefors option in the Wilkinson Systat program (Wilkinson 1987, NPAR-8) was used to test for deviation from a standardized normal distribution. This test uses the Kolmogorov-Smirnov 1-sample test to determine whether the distribution of a variable has the same shape, location and scale as a standardized normal population. Separate analyses were conducted on the normal and mild head trauma patients for each variable and a $P < 0.05$ level of significance was present in only 6.3% of the variables. This level of gaussianity is similar to that reported by Gasser et al. (1982). It should be noted, however, that the 20 variables used in the final discriminant function (see Table III) were all normally distributed.

Homogeneity of variance

One would expect there to be greater variance in the mild head trauma group than in the normal population since neural functioning in the head trauma patients may not have stabilized at the time of EEG sampling and because there is a great variety in the types, location and sources of head injury. However, in the practical world of clinical assessment it is preferable, although not absolutely essential, that discrimination between normals and trauma patients be based upon variables which do not violate the homogeneity of variance assumptions. This is preferable because the best discriminant is one that is reliable independent of the type, source and location of the injury as well as one that is maximally stable and invariant. For this reason the Bartlett test for homogeneity of group variances (Wilkinson 1987) was conducted on each variable for each GCS 13, 14 and 15 group versus the normal group. Only those variables that had equal variances in the 2 groups were selected for entry into the discriminant analysis.

Step-wise development of a discriminant training set

Independent replication of the discriminant function is essential in order to assess its reliability. With this in mind a step-wise procedure was developed in which 3 independent discriminant functions were developed, one for each of the GCS 13, 14 and 15 groupings. In this way the variables that were independently identified as maximally discriminating in the 3 separate analyses could be compared. If they are the same or at least very similar, then this would constitute a replication. Thus the procedure involved breaking the data into variable subsets (i.e., relative power, total power, coherence, amplitude asymmetry, and phase) conducting separate multivariate analyses of variance between the normal versus each GCS grouping and then selecting variables with the highest Fs from these analyses (provided they did not violate the homogeneity of variance assumption). The variables with the highest Fs from each of the variable subgroupings were then combined into a final multivariate analysis of variance. From these analyses 20 variables with the highest F values were entered into the final discriminant function. A maximum of 20 variables were selected since this provided a favorable subject to variable ratio of 17 : 1 (Bartels and Bartels 1986).

Results

Development of the training set

Of the first group of 394 trauma patients, 264 were randomly selected using a normal random number generator (Wilkinson 1987) in order to develop the initial training set discriminant function. The remaining 130 randomly selected trauma patients were not entered into the training set but were later used to cross-validate the discriminant function. The priors option was used in all analyses in order to adjust for differences in sample size between the normals and the trauma patients.

The mean and range of ages in the GCS = 13, 14 and 15 mild head trauma groups were first established and then a group of normal subjects were selected with overlapping age ranges with roughly equal numbers to each of the GCS subgroups. Analyses of variance did not reveal any significant difference in age between the normals and the GCS groupings. The age and number of days between injury and the EEG test are shown in Table I.

TABLE I

Mean days from injury as well as mean age and age range of the normal and mild head trauma patients entered into the discriminant training set and independent cross-validation.

	GCS = 13	GCS = 14	GCS = 15
Age range normals	15–73	14–73	15–73
Age range patients	15–75	13–82	16–71
Mean age normals	22.9	20.2	22.9
Mean age patients	28.6	26.2	29.1
Mean days from injury	7.9	7.7	8.6
Range of days	1–24	0–62	0–298

TABLE II

Computer classification of normal and mild head trauma patients in the training-set discriminant analysis.

Actual group	N	Classification percent as	
		Normal	Mild trauma
Normal	83	89.2 (N = 74)	10.8 (N = 9)
Mild trauma	264	3.4 (N = 9)	96.6 (N = 255)

Overall classification accuracy = 94.81%.

Examination of the 3 independently developed discriminant functions revealed between 90 and 97% classification accuracy but, most importantly, essentially the same variables had been independently selected and entered into the 3 different discriminant equations (i.e., the variables were either identical or similar, such as, alpha frontal coherence versus beta frontal coherence, etc.). Stability and replicability were thus indicated by the fact that identical and/or similar variables were maximally discriminating in the 3 independent analyses. On this basis, these common variables were combined into one discriminant analysis which was capable of accurately discriminating normal subjects from head trauma patients independent of the exact Glasgow Coma Score (i.e., GCS 13–15). Table II shows the classification accuracies for the 264 patients and 83 normals entered into the final 'training-set' discriminant analysis with 89.2% of the normals and 96.6% of the head trauma patients accurately classified yielding an overall classification accuracy of 94.8%.

TABLE III

List of EEG power spectral variables entered into the training-set discriminant function and the pooled-within-groups correlation between each variable and the canonical discriminant function.

Variables	Correlations
Theta frequency coherence between Fp1 and F3	0.3366
Beta frequency coherence between T3 and T5	0.2598
Beta frequency coherence between C3 and P3	0.3915
Beta frequency phase between Fp2 and F4	−0.4658
Beta frequency phase between F3 and F4	−0.4537
Alpha frequency amplitude asymmetry between F4 and T6	0.3298
Alpha frequency amplitude asymmetry between F8 and T6	0.3129
Beta frequency amplitude asymmetry between F4 and T6	0.2886
Beta frequency amplitude asymmetry between F8 and T6	0.2921
Alpha frequency amplitude asymmetry between F3 and O1	0.2939
Alpha frequency amplitude asymmetry between F4 and O2	0.3241
Alpha frequency amplitude asymmetry between O1 and F7	−0.2944
Beta frequency amplitude asymmetry between F4 and O2	0.2722
Alpha frequency relative power for P3	−0.2612
Alpha frequency relative power for P4	−0.2544
Alpha frequency relative power for O1	−0.3532
Alpha frequency relative power for O2	−0.3529
Alpha frequency relative power for T4	−0.2390
Alpha frequency relative power for T5	−0.2851
Alpha frequency relative power for T6	−0.2832

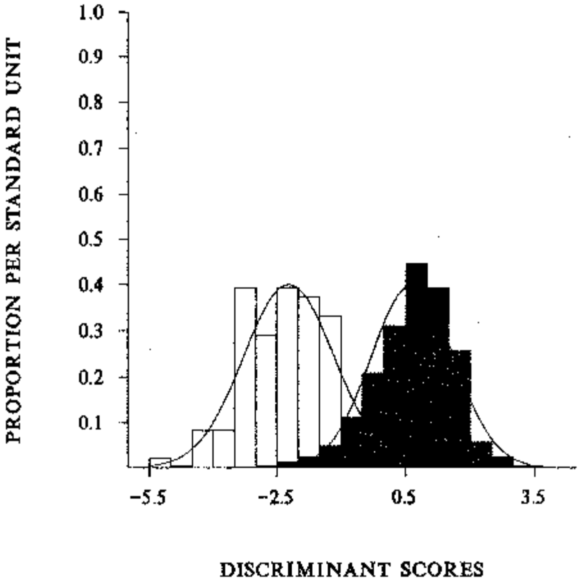

Fig. 1. The distribution of discriminant scores in: normal subjects in the left distribution (open columns) and mild head injured patients in the right distribution (shaded columns) that were entered into the training and first cross-validation discriminant analyses. Proportion of subjects in each population is represented on the left y-axis.

Fig. 1 shows the distribution of the discriminant scores in the 2 groups of subjects (open columns = normals, closed columns = trauma patients). The scales of the axes are the same for the 2 distributions so that the relative proportion of discriminant scores can be compared. It should be noted that the criteria discriminant score where by subjects were classified as members of the mild head-injured population was $\geqslant -1.2101$.

Table III shows a list of the variables that were entered into the final discriminant analysis. Of the discriminating variables 60% were in the alpha frequency band, 35% in the beta frequency band, 5% were in the theta frequency band and none of the variables involved the delta frequency band. An approximately even distribution between left and right hemisphere variables was observed. The most frequent anatomical regions were frontal and frontal temporal (55%), temporal only (20%), parietal and parietal-central (15%) and occipital (10%).

First independent cross-validation of the discriminant function

The first independent cross-validation of the discriminant function involved classifying the 130 randomly selected head trauma patients who had not been members of the initial training set as well as an additional 21 normal subjects based upon the discriminant function coefficients developed through the training procedure. An overall cross-validation (i.e., using the total of 130 patients) as well as the ability to cross-validate the equation for each of the GCS groupings were conducted. The results of the independent cross-validation of the mild head-injured patients and the cross-validation of the 21 additional normals are shown in Table IV. An overall classification accuracy of 95.4% was obtained.

Test-retest reliability of the discriminant function

Of the 394 patients used to develop and cross-validate the discriminant function, the mean time from injury to EEG test was only 8.36 days (see Table I). This represents a relatively short period of time in which a variety of factors specific to the acute phases of injury may have influenced the discriminant function. For example, factors such as medication, diffuse swelling and even unique psychological states. In order to evaluate the stability and reliability of the discriminant function EEG measures, a total of 144 additional outpatients were entered into the discriminant analysis using the discriminant equations developed in the training procedure. Approximately 65% (N = 93) of the patients were given second, third or fourth EEG re-tests at varying times following injury and, thus, were members of the original or cross-validation patient set. The remaining 35% (N = 51) were not in the original discriminant analyses since they were new patients referred to the electrophysiological clinic either as outpatients or as patients with mild head injuries who were tested for the first time several weeks or months following injury. The 144 patients were grouped into 4 different post-injury times. Group I (N = 50) had a mean interval between injury to EEG test of 17.2 days (range from 6 to 21 days), group II (N = 47) had a mean interval from injury to EEG test of 26.47 days (range from 22 days to 32 days), group III (N = 29) had a mean interval from injury to EEG test of 43.28 days (range from 33 days to 60 days) and group IV (N = 18) had a mean interval from injury to EEG test of 223.6 days (range from 62 days to 624 days). Table V shows the results of the discriminant analyses. The

TABLE IV

First independent cross-validation of discriminant function of mild head trauma patients and normals.

Actual group	N	Classification percent as	
		Normal	Mild trauma
Normal	21	90.5 (N = 19)	9.5 (N = 2)
Mild trauma	130	3.8 (N = 5)	96.2 (N = 125)

Overall classification accuracy = 95.4%.

TABLE V

Independent cross-validation and test-retest reliability analyses of the discriminant function using mild head trauma outpatients tested at the University of Maryland at varying times following injury. Mean days from injury are: group I = 17.2 days, group II = 26.47 days, group III = 43.28 days and group IV = 223.6 days post injury.

Actual group	N	Classification percent as	
		Normal	Mild trauma
Group I	50	20.0 (N = 10)	80.0 (N = 40)
Group II	47	10.8 (N = 6)	89.2 (N = 41)
Group III	29	7.7 (N = 3)	92.3 (N = 26)
Group IV	18	22.2 (N = 4)	77.8 (N = 14)

Overall discriminant accuracy = 87.5%.

accuracy of discrimination was relatively constant as a function of post-injury time and varied from 77.8 to 92.3% with an overall classification accuracy of 84% (i.e., 121 out of 144). The stability of the discriminant function was indicated by the fact that 82.17% (i.e., 106 out of 129) of the patients were classified as members of the mild head trauma group in both the first and second EEG test, 92.3% (i.e., 12 out of 13) were consistently classified as mild head-injured in 3 independent EEG tests and 100% (i.e., 2 out of 2) of the patients that were tested 4 times were classified as members of the mild head trauma group on all 4 tests.

Additional independent cross-validations of the discriminant function

Additional independent cross-validation was accomplished by: (1) evaluation of the discriminant analyses from the 51 mild head trauma outpatients who were not part of the development of the discriminant function or the first cross-validation, and (2) by recruiting and testing an additional 70 mild head trauma outpatients and 4 normal subjects under the direction of University Services in Philadelphia, PA. The latter cross-validation test involved the use of a different data acquisition and analysis computer system (i.e., the Q.S.I. 9000) from that used in the University of Maryland sample of subjects. As described in Methods, careful matching of the amplifier frequency and gain characteristics between the Q.S.I. 9000 machine and the Applied Neuroscience Laboratories acquisition and analysis systems was first established to insure data compatibility.

Table VI shows the classification accuracies for these additional cross-validations of the discriminant function. Of the 51 University of Maryland patients, 84.3% (i.e., 43 out of 51) were classified as members of the mild head trauma group. Of the 70 mild head trauma patients tested by University Services, 92.8% (i.e., 65 out of 70) were classified as members of the mild head trauma group and 100% of the normals were classified as members of the normal group. The latter analyses yielded an overall discriminant accuracy of 89.3%.

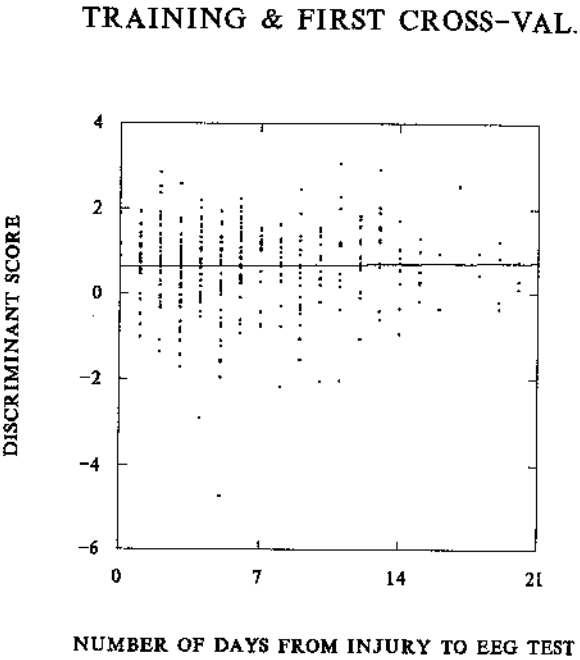

Fig. 2. Scattergram showing the distribution of discriminant scores (y-axis) versus number of days from injury to EEG test (x-axis). Linear regression line shows a slight but non-significant increase in the value of discriminant scores as a function of time from injury.

TABLE VI

Cross-validation accuracy of discriminant function for mild head injury outpatients and normals tested at University Services, Philadelphia, PA.

Actual group	N	Classification percent as	
		Normal	Mild trauma
Outpatients	70	7.2 (N = 5)	92.8 (N = 65)
Normals	4	100 (N = 4)	0.0 (N = 0)

Overall discriminant accuracy = 95.2%.

Post-injury time course of discriminant pattern

The time course for the evolution of the EEG discriminant pattern was evaluated in 2 ways: (1) by evaluation of the time between injury and first EEG test for which a significant mild head injury discriminant score was first present, and (2) by comparisons of the percentage of patients exhibiting a significant mild head injury discriminant score at various test-retest intervals. Fig. 2 shows a scattergram of the percentage of patients with a significant mild head injury discriminant score at

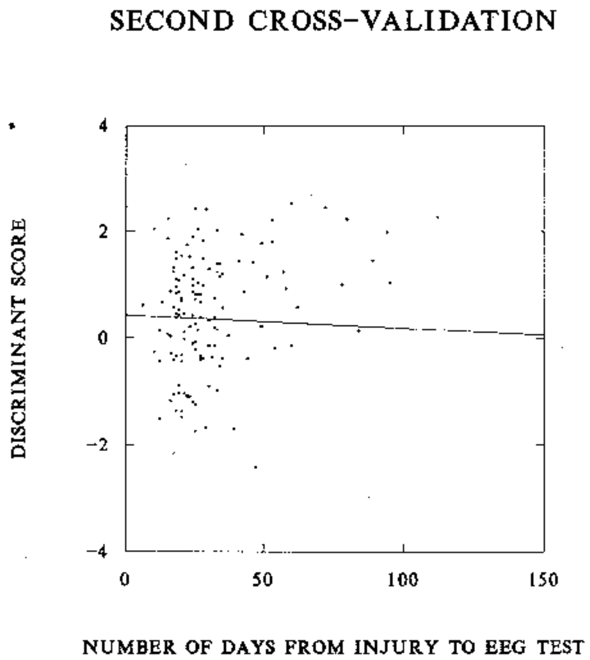

Fig. 3. Scattergram showing the distribution of discriminant scores (y-axis) versus number of days from injury to EEG test (x-axis) in the second cross-validation study. The linear regression line shows a slight but non-significant improvement in discriminant score values (i.e., trend toward normal) as a function of time from injury.

different injury-to-first EEG test times. Information about the exact hour at which a head injury occurred was not available, as a consequence the ordinate was scaled in days with the first column representing a injury-to-EEG test interval of 24 h or less. All of the patients (N = 4) tested within 24 h of their injury and 93.75% (60 out of 64) patients tested within 2 days post injury were classified as members of the mild head trauma group. This level of accuracy remained relatively constant over the 2 week period, although there was a slight but non-significant decline ($R^2 = 29.2\%$, $P < 0.68$) as a function of the interval between injury and EEG test (see Fig. 2).

Fig. 3 shows the change in discriminant scores as a function of post-injury times in the second cross-validation group. A trend toward the normal group was present in this analysis ($R^2 = 48.3\%$, $P < 0.38$).

Discussion

The need to develop an objective, non-invasive and readily available measure capable of identifying and classifying patterns of neurophysiological dysfunction in mild head trauma patients is acute. For example, of the approximately 8 million individuals that suffer head injuries of all types each year in the U.S.A. (Wilder 1976) approximately 80% involve mild head injuries with more than 200,000 patients with mild head injury admitted to hospitals in the United States each year (Caveness 1976; Anderson and McLauring 1980). The public health consequence of these injuries is emphasized by the fact that many of these individuals are unable to return to work, complain of headache and memory problems and exhibit a variety of neuropsychological dysfunctions (Rimel et al. 1981; Langfitt and Gennarelli 1982; Uzell et al. 1987). Improving diagnostic evaluation and furthering our understanding of the neurological consequences of mild head injury will aid in the prevention and treatment of these injuries. The value of a non-invasive diagnostic measure is further emphasized by the fact that several studies have shown measurable recovery in patients who were initially impaired in neuropsychological functioning following mild head injury (Langfitt and Gennarelli 1982). An objective measure of cortical neurophysiological functioning may also aid in the development and evaluation of remediation techniques to optimally promote recovery of function.

Components of EEG discriminant pattern

The results of this study demonstrated that patients admitted to an emergency service with mild head trauma can be discriminated from age-matched normals with high accuracy (> 90%) at various times following injury. A specific electrophysiological pattern was present shortly after injury and persisted in a relatively stable form for an extended period of time (see Table IV and Figs. 2 and 3). There are 2 possible interpretations of these data: (1) that they are the result of some form of systematic bias such as muscle artifact, the effects of medication or EEG acquisition differences, or (2) that they represent a real difference in the spatio-temporal patterning of the EEG between age-matched normals and individuals who have suffered a mild head injury and, correspondingly, reflect a difference in neurological status. Evidence against a systematic bias interpretation is provided by the fact that the discriminant function was independently cross-validated with 3 different samples of subjects some of which were tested by different technicians, at different locations and on different EEG machines. Effects of medication can be ruled out by the fact that only approximately 23% of the GCS 15 patients were medicated at the time of their first EEG test and yet they exhibited nearly identical discriminant variables as the more frequently medicated GCS 13 patients and there were no significant differences in discriminant scores between patients on medication versus those off medication.

Differences due to muscle artifact and/or movement artifact can be ruled out by the fact that each EEG record was visually examined to eliminate such artifact and the discriminant variables are not those that would be expected if there were artifact (e.g., beta activity in T3/4 or diffuse slow waves, etc.). Finally, efforts were taken to minimize systematic bias by insuring gaussianity of the measure set and adherence to basic statistical principals, such as homogeneity of variance.

Given the large sample size and the stability of repeated cross-validation, it is most consistent to conclude that the discriminant EEG pattern reflects a real difference in the neurophysiological organization of the cerebral cortex in normal versus mild head-injured individuals.

Functional interpretation of EEG patterns

The electrophysiological discriminant pattern, which was not obvious in preliminary univariate analyses, was represented by a multivariate discriminant function that was made up of 20 variables that constituted 3 classes of electrophysiological features. Fig. 4 is a diagrammatic representation of the 3 classes of variables. Class I was represented by local frontal, temporal and central-parietal abnormalities in EEG coherence and/or phase which involved short interelectrode distances (e.g., approximately 7 cm, see Thatcher et al. 1986). Class II was represented by long interelectrode distance (e.g., 21 cm), intrahemispheric power differences (i.e., frontal-posterior amplitude differences), and class III was represented by diminished alpha activity in posterior cortical regions (i.e., occipital, parietal and posterior temporal).

The 3 classes of electrophysiological features are consistent with the mechanics of cerebral trauma which involve shear-strain and rotational forces that damage white matter and localized contusions of the grey matter. The frontal and fronto-temporal cortex is especially susceptible to contusion due to the nature of the bony vault upon which the brain rests (Langfitt and Gennarelli 1982). Rapid acceleration and deceleration frequently result in torsion and shearing forces that damage both short and long distant axons (i.e., diffuse axonal injury, Strich 1961) and, finally, contusions to posterior regions through the 'coup-contra-coup' process are commonly observed following cerebral trauma (Langfitt and Gennarelli 1982; Bigler 1987). The localized frontal EEG coherence and phase abnormalities are consistent with localized contusions and axonal injury to frontal regions, the posterior cortical diminished alpha activity is consistent with 'coup-contra-coup' damage to posterior regions and reduced cortical excitability in general, while the diminution of the intrahemispheric power differences may reflect decreased functional differentiation between anterior and posterior cortical regions (Thatcher et al. 1983). The direction of the correlation between the variables and the discriminant function (see Fig. 4) also provides insight into the nature of the neurophysiological dysfunctions. For example, the mild head trauma patients consistently exhibited increased coherence (i.e., positive correlations) and decreased phase (i.e., negative correlations). This direction of correlation has been implicated in normal subjects to reflect reduced functional 'differentiation' or increased functional redundancy between neuronal systems (Thatcher et al. 1983; Tucker et al. 1986). Similarly, decreased power differences between anterior and posterior cortical regions are also consistent with diminished functional differentiation (Thatcher et al. 1983) while reduced power in

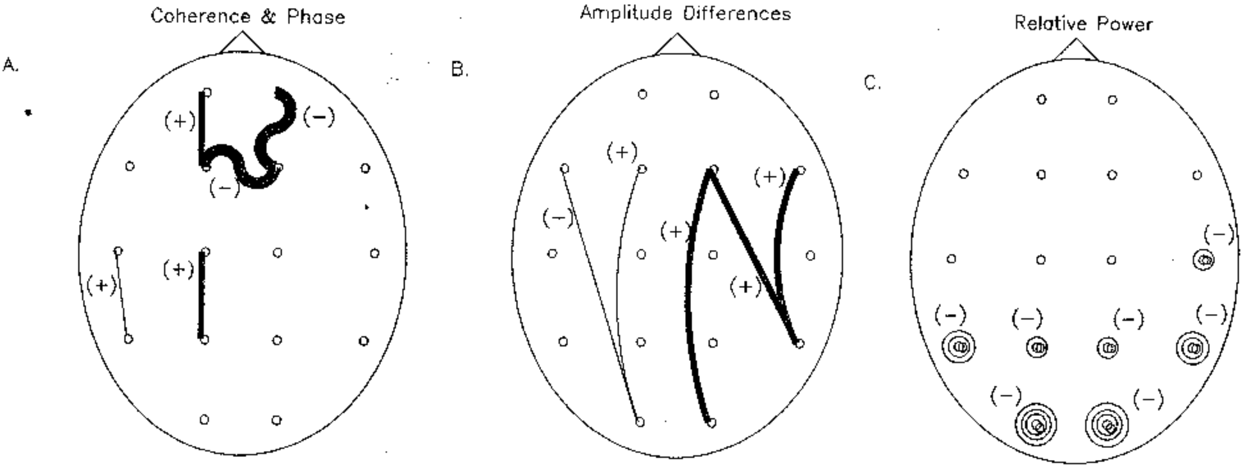

Fig. 4. Head diagrams showing the locations and strength of correlations of the discriminant variables from Table III. A: coherence (straight lines) and phase (curved lines) discriminant variables. B: amplitude difference discriminant variables. C: relative power discriminant variables. In A and B the magnitude of the correlation is represented by the width of the lines, and in C the magnitude of the correlation is represented by the diameter and number of concentric circles. The direction of the correlation between the variable and the discriminant function is represented by + or −. The thin lines in A and B represent correlations from 0.20 to 0.29, the intermediate width lines represent correlations from 0.30 to 0.39 and the thickest lines represent correlations from 0.40 to 0.49. In C, 2 concentric circles correspond to correlations between 0.23 and 0.27, 3 circles correspond to correlations between 0.28 and 0.30 and 4 circles correspond to correlations > 0.35.

the EEG alpha band has been interpreted to reflect reduced cortical excitability (Nunez 1981). When the patterns of the discriminating EEG variables are considered as a whole, then the most consistent interpretation is that the consequences of a mild head injury are the development of a new neurophysiological stable state characterized by a combination of the effects of localized contusion and a diminution of the total magnitude of functional cerebral differentiation and, thus, reduced information processing capacity. This interpretation does not preclude the appearance of specific neurological and neuropsychological deficits, e.g., those that arise from damaged frontal and/or temporal lobes. Rather, mild head trauma patients appear to exhibit 2 components of cerebral damage: (1) localized dysfunctions specific to areas of maximal injury, and (2) a global or generalized state of reduced information processing capacity.

Stability of EEG discriminant pattern

The percentages of mild head-injured patients that report persistent symptoms, such as headaches, dizziness, memory loss, short attention span and reduced ability to process complex information, have been estimated in a number of studies to range from 15% to 79% from 3 to 12 months post injury (Gronwall and Wrightson 1974; Rutherford et al. 1979; Rimel et al. 1981; Alves et al. 1986). In a recent study of the quality of survival after head injury, Uzell et al. (1987) found that 53% of the mild head-injured patients had not returned to work 16 months after injury and that they complained of memory loss as well as verbal, learning and visuomotor deficits. This study also showed that both mild and severe head injury adversely influenced the quality of life through increased unemployment and neuropsychological dysfunction with differences in the 2 groups being largely a matter of degree. Given the enhanced detection sensitivity of the power spectral EEG and differences in experimental design, the approximately 80–95% discriminant accuracy in the present study is not inconsistent with the magnitude of neuropsychological deficits reported in the literature. Although, 80–95% may seem high, it is important to note that patients tested in the outpatient clinics at the University of Maryland and by University Services were referred because they were exhibiting persistent symptoms. Thus at least

2 factors most likely contributed to the high 'hit rates': (1) a selection bias toward testing of patients whose mild head injuries had, in fact, resulted in neurological damage, and (2) the increased detection sensitivity afforded by power spectral analysis of the EEG.

Recently, Bernad (1988) divided mild head-injured patients into 2 groups: type I represented patients with a benign injury and fairly good prognosis for recovery, and type II represented patients that have persistent symptoms and many of whom never completely recover. Presumably, the false positive hit rate for mild head-injured patients in the present study represents the type I patients that have not suffered structural damage. In contrast, the majority of the patients in the present study may be members of Bernad's (1988) type II category in which there are persistent symptoms. Future studies explicitly comparing type I versus type II mild head patients may help clarify this issue.

Recovery of function issues

A noted feature of the EEG discriminant pattern was its appearance within hours or days following mild head injury and its steady but relatively minor decline over long post-injury intervals (see Figs. 2 and 3 and Table V). The strength and temporal stability of the EEG pattern are indicative of a new equilibrium state of the cerebral cortex with allow for an individual to cope and adapt to the environment even though the nervous system has suffered mechanical damage. The new equilibrium state appears to exhibit a globally reduced level of neurophysiological complexity and a corresponding reduction in information processing capacity which is combined with localized neurophysiological dysfunction. An important aspect of this hypothesized dynamical 'new equilibrium' is that it appears to arise shortly after injury and persists with only slight decline in magnitude over time.

The neuropsychological deficits observed in mild head-injured patients are not inconsistent with the results of this study. For example, a set of commonly related symptoms are a loss in the ability to process complex information or to simultaneous operate on different information or to rapidly shift attention (Alves et al. 1986; Silver et al. 1988). All of these symptoms would be expected in a neural system with a diminished level of functional complexity. The anatomical locations of maximal EEG deviation from normal such as observed in the discriminant function may relate to specific neuropsychological deficits. For example, short-term memory loss and reduced auditory language comprehension may reflect temporal damage while reduced motivation, erratic mood swings and reduced ability to plan and sequence may reflect frontal damage. However, the present results indicate that following mild injury the neocortex assumes, independent of the total magnitude and location of neurophysiological damage, a new state of functional organization which is essential in order to manipulate, operate on and cope with sensory inputs, abstractions and motor output demands. Although there may be a reduction in the quality and magnitude of function, the fact remains that most individuals with mild head injury continue to be adaptable and intelligent in their every day activities and often show improvement on neuropsychological tests. The functional significance of the relatively permanent and stable EEG discriminant pattern may be the degree to which it allows individuals to utilize available cerebral resources.

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