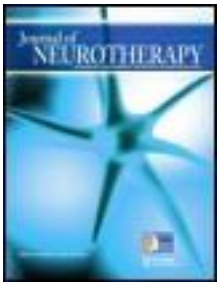

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Exploratory Analysis

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Exploratory Analysis: Mild Head Injury, Discriminant Analysis with High Frequency Bands (32-64 Hz) Under Attentional Activation Conditions & Does Time Heal?

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QEEG variables (5 activation, 2 relationship variables, 19 locations and 5 bands up to 64 Hertz) were collected under three activation conditions (auditory attention, visual attention and listening to paragraphs) on 84 subjects, consisting of 32 mild head-injured subjects (no loss of consciousness) and 52 normals over the age of 14. Additional variables collected included years of education, time since accident, sex, handedness and Shipley Institute of Living measures of IQ, verbal and abstraction scores.

The results were encouraging for future development of a discriminant employing activation conditions, as the results varied from 88% to 100% correct classification. Very few of the variables, which distinguished the groups under the three conditions or were used in the discriminant analysis, were shown to increase as the time since accident increased. This result, tentatively, indicates little effect of time on the improvement in the electrophysiological functioning of the brain. Time (spontaneous improvement) does not appear to heal the brain in any significant manner.

Key Words: QEEG, High Frequency Bands, Mild Head Trauma, Discriminant Function, Activation Conditions

LITERATURE REVIEW

There have been several previous attempts to analyze the electrophysiology of the mild head trauma victim. Thatcher, R.W., Walker, R.A., Gerson, I., & Geisler, F.H. (1989) is the most comprehensive in terms of its database of 608 subjects. Thatcher et al. (1989) were able to develop a discriminant function from 264 mild head injured patients and 83 age-matched controls which was able to achieve a successful discriminant classification accuracy rate of 94.8%. Two independent cross validations were conducted; the first of which obtained an overall discriminant accuracy of 87.3% and the third an overall accuracy of 95.2%. The discriminating variables included (a) an increased coherence and decreased phase in the frontal and frontal-temporal regions, (b) decreased power differences between anterior and posterior cortical regions and (c) reduced alpha power in posterior cortical regions.

The Thatcher et al. (1989) study evaluated subjects who experienced no loss of consciousness or loss of consciousness under 20 minutes, were over the age of 13 and had a Glasgow coma scale between 13 and 15.

Randolph, C., and Miller, M.H. (1988) (N=20) examined head injured and normal subjects during several cognitive tasks and employing T3, T4, O1, & O2 electrode placements. They found significantly worse performance in the head-injured subjects, and increased (in comparison to normals) EEG amplitudes and amplitude variances (task conditions), particularly in the beta band. The authors noted no significant differences in the relative power figure of the bands between the two groups. The subjects in this study were 2 to 4 years post injury.

Hooshmand, H., Beckner, E., and Radfar, E. (1989) discussed the issue of TBM (topographic brain mapping) in a sample of 135 head injuries and reported EEG abnormalities in 40 subjects, which consisted mostly of mild, nonspecific generalized slowing. Of the 135 patients, 75 (56%) had abnormal TBM's, with the temporo-frontal involved in 65% of the abnormal subjects. An additional 25% had abnormalities in the temporo-occipital regions. Hooshmand et. al. found that the most common type of abnormality was in the absolute voltage asymmetry. The subjects were 1 to 22 years post injury.

Thatcher, R.W., Biver, C., McAlaster, R., Camacho, M. & Salazar, A. (1998) were able to demonstrate a relationship between increased Theta amplitudes and increased white matter T2 MRI relaxation times (indicator of dysfunction) in a sample of head injured subjects. Decreased Alpha and Beta amplitudes were associated with lengthened gray matter T2 MRI relaxation times. Neuropsychological measures. These measures were correlated with decreased cognitive function. The subjects were 10 days to 11 years post injury.

EEG signals above 32 Hertz have traditionally been considered muscle activity and have been the focus of some controversy in the area. The two issues of concern are (a) whether gamma (above 20 Hertz, depending upon the author) activity exists in the brain, and (b) whether it can be measured at the scalp. Menon, V., Freeman, W.J., Cutillo, B.A., Desmond, J.E., Ward, M.F., Bressler, S.L., Laxer, K.D., Barbaro, N., and Gevins, A.S. (1996) concluded that if such gamma band (20-50 Hertz) spatial patterns exist in the brain, there is no technology which is capable of measuring them at the scalp.

In terms of internal manifestations of 40 Hz activity, Sheer, D.E. (1976, 1984) has focused his attention on the relationships between focused arousal and attentional resources as being reflected in 40 Hz activity. Llinas, R. et al. (1993) were able to demonstrate with MEG technology the presence of coherent 40 Hz magnetic oscillation during REM (rapid eye movement sleep) and awake states. Jefferys, J.G.R. et al. (1996) summarized the research to date on the 40 Hz activity. Jefferys notes that 50-60 Hz activity has been described in the olfactory bulb. olfactory cortex, visual cortex, auditory cortex, somatosensory cortex, and motor cortex and added that "neurons in many parts of the brain have the intrinsic capacity to oscillate at about 40 Hz...at least some cortical neurons with intrinsic oscillator mechanisms project to contralateral areas, and to the thalamus, providing routes for long range synchronization of these oscillations." (pg. 205) This line of research indicates that the gamma activity can exist in brain structures.

Basar-Eroglu, C. et al. (1996) in their short review of gamma activity (40 Hz) report the presence of this activity at the cellular level and in a number of brain structures of different species which can be evoked, induced or emitted with respect to sensory cognitive events.

In terms of the correlation of internal and external manifestations of 40 Hz activity, Steriade, M. et al. (1991) was able to demonstrate in intracellularly recorded thalamocortical cells of the cat the presence of 20-40 Hz activity. They also confirmed that this activity potentiates the 40 Hz waves of the "background of the cortical electroencephalogram". In addition, "the brainstem-induced facilitation of cortical 40 Hz oscillations was blocked by scopolamine, a muscarinic antagonist." Tiitinen, H. et al. (1993), however, warns against generalization to humans from animal research given some fundamental differences.

In relation to external manifestations of 40 Hz activity being related to cognitive events or abilities, DePascalis, V. et al. (1989) were able to demonstrate a differential response of high hypnotizable subjects during different emotional states. During positive emotional imagery under hypnosis conditions, the high hypnotizable subjects showed an increase in 40 Hz activity over both hemispheres and during negative emotional states an increase in gamma activity in the right hemisphere and reduction in the left hemisphere. It is difficult to believe that external muscle activity would differentially respond to internal emotional events.

Lutzenberger, W. et al. (1994) examined 30, 40 and 60 Hz activity in response to words and pseudowords and found that words and pseudowords responses, recorded at the scalp, evoked significantly different 30 Hz activity over the left hemisphere, but not the right. This pattern was independently validated in a study investigated "biomagnetic response to auditory presentation of words and pseudowords." Increased 40 Hz activity was observed over the right hemisphere. The authors interpreted this activity as due to the left-hand response, which was required in the experiment.

DePascalis, V. et al. (1989) separated out 40 Hz scalp recorded activity from EMG activity in the neck in the 40 Hz range as well as 70 Hz activity originating from either the neck or scalp. The 40 Hz activity was still present after this elimination and correlated with hypnotizability. The 40 Hz activity showed a decrease in left hemisphere activity and an increase in right hemisphere activity during a negative emotional task.

Pfurtscheller, G. et al. (1994) demonstrated event related synchronization in the 30-40 Hz band and its ability to add significantly (to 10 Hz activity) to successful discrimination in four motor tasks (fingers, toes, and tongue). The activations were related to the known anatomical locations for these body parts.

The presence of cortical 40 Hz activity has been shown to be differentially evident under selective auditory attention (Tiitinen, H., et al. (1993). Gamma activity has also been shown to be task dependent (verbal vs spatial) by Spydell, J.D. et al. (1979.1982), and separate from 40 Hz EMG activity. Sheer, D.E. (1976) had been able to demonstrate the lack of activation of the 40 Hz activity in learning disabled children. In conclusion, arguments can be rendered for both sides of the issue.

METHOD

Subjects

A total of 84 subjects underwent the experimental procedure. The following breakdown represents the demographics of the subjects involved. Subjects were paid $25 for their participation and signed an informed consent form as required in human research situations. The head injured group consisted of 32 subjects, while the normal group consisted of 52 subjects. The mean number of months since injury was 64.9 months or 5.34 years. Twelve subjects were within one year of the injury and additional seven subjects were within ten years of the accident. The longest period of time since the accident was for one subject who was 43 years post injury. All the subjects (in the no loss of consciousness group) reported that they were conscious and at least somewhat alert immediately following the accident. There were no Glasgow coma scale ratings available.

There were an additional 7 head injured subjects available for analysis who were not included because their reported duration of unconsciousness was greater than 20 minutes. T-test comparisons revealed a different pattern of significant differences between the groups. However, as the sample size was small, the results will not be presented. Twenty-eight of the thirty-two head injured subjects reported hitting their head. The one subject who was 43 years post accident was not included in any of the high frequency analysis. His pattern of results was that of a statistical outlier. All normal volunteer subjects signed an informed consent form and were paid $25 for their participation. Although there were 32 subjects available not all subjects underwent all procedures. The tables reflect the data, which was available. Of the 32 subjects, 24 had completed a neuropsychological evaluation. The remaining 8 subjects had volunteered for the research and subsequently reported a preexisting brain injury. Of the 24 subjects who had neuropsychological evaluations completed, 12 were within one year and 12 one year post accident. Three of the subjects under one year post accident showed minimal problems on the neuropsychological testing. All the subjects greater than one year post accident demonstrated significant enough problems (varying in degree) to be referred for cognitive rehabilitation.

As indicated in Table 1 there were no significant differences between the groups in terms of age, handedness, sex, and level of education or Abstraction IQ. Significant differences, however, were present in terms of Raw Verbal and Abstraction scores on the Shipley and Verbal IQ. Demographics cover only subjects with no significant loss of consciousness.

Table 1 - Subjects

	Head Injured	Normals	t-value	p-level
Age (yrs.)	41	37	1.21	0.23
Handedness				
Right	29	41		
Left	3	11	1.31	0.16
Sex				
Female	21	28		
Male	11	24	1.34	0.29
Education	13	14	0.99	0.34
Shipley*				
Raw Verbal	28.6	32.8	3.33	0.0013**
Raw Abstraction	24.2	31.4	3.94	0.00017**
Verbal IQ	105.6	114.7	4.15	0.00008**
Abstraction IQ	99.2	105.4	1.76	0.08

**-Significant differences

*-IQ obtained from Shipley Institute of Living Scores and employed the Paulson, M.J. & Lin, L. (1970) formula. The formula was averaged across all age groups.

Apparatus and Measurements

While the subjects underwent the experiment, they were videotaped and recorded using a combination of computer, video and audio recording equipment which allows an experimental recording session to be saved to a hi 8 mm tape with all pertinent information. The videotape, which is saved, is split screen videotape, with the left side reflecting the EEG recording with the appropriate epoch number and the right side of the screen showing the subject during the experiment.

Lexicor Medical Technology's NRS-24C recording equipment was employed. The sampling rate was set to 256 to allow for examination of up to the 64-Hertz range. The bandwidths were divided according to the following division: Delta: 0-4 Hertz, Theta: 4-8 Hertz, Alpha: 8-13 Hertz, Beta1: 13-32 Hertz, Beta2: 32-64 Hertz.

All measurements available through the Exporter software program provided by Lexicor Medical Technology were employed. These included the following for each bandwidth: Absolute Magnitude, Relative Magnitude, Peak Amplitude, Peak Frequency, Symmetry, Coherence, and Phase.

Roland, P.E. (1993) discusses the issues of connectivity of the brain in terms of the anatomical organization of the neocortex, which is approximately 3 mm thick and contains six layers (with layer I being closest to the scalp). The pyramidal cells (excitatory) in layer II and the upper part of layer III send their axons to the cortex in the same hemisphere while the pyramidal neurons in the lower part of layer III send their axons to the other hemisphere. Thus, apart from other subcortical considerations, these are the physiological foundations of the coherence and phase figures.

The total number of activation variables resulting from 19 locations, 5 bandwidths and 4 parameters (excluding symmetry) is 380. The symmetry measures produce 855 variables. The total number of connection measures resulting from 19 locations, 5 bandwidths and two parameters is 1710. The resulting total number of variables under consideration is 2945. For each of the 84 subjects the resulting epochs (1 second duration) were visually analyzed for artifacts and marked for deletion if they appeared to be significantly affected by artifact issues (eye movements, muscle activity).

Procedure

The auditory, visual attention and listening to paragraphs conditions were collected as part of a larger experiment during which subjects underwent approximately 1 to 1 ½ hours of testing with 28 cognitive tasks. The three tasks reported in this paper were conducted in the beginning of the procedures.

The auditory attention task consisted of the subject (with eyes closed) raising his index finger whenever they heard the sound of a pen tapping on the table. The visual attention task required the subject to look at a page of written material (Spanish text) upside down and to raise their index finger whenever they saw a laser beam on the paper in front of them. Both tasks required a response to ensure that the subject was paying attention. The listening to paragraphs task involved the subject listening to four short stories with the instruction to memorize the information for subsequent recall (eyes closed). The auditory and visual attention tasks were set to 100 epochs (100 seconds) for all subjects. The listening to paragraphs condition averaged about 30 epochs per story or 120 seconds in all.

Data Analysis

The raw data, once artifacted for eye movement and EMG activity by visual analysis, was analyzed with the Exporter program available from Lexicor Medical Technologies. The Exporter software program was commissioned by the experimenter to solve the cumbersome time problem of obtaining the required figures from the raw data file. The Exporter program was written by the programmer of Lexicor, under guidance by the experimenter. The program generates the values for the variables under consideration from the raw data file and generates ASCII, comma delimited files which can then be imported into Excel or CSS Statistica. The Exporter program was employed with all the subjects to generate the raw values for the variables.

RESULTS OF DISCRIMINANT ANALYSIS

A t-test analysis was conducted between the head-injured group and the normal group for all conditions. The variables, which were significant, were chosen for use in a discriminant analysis and converted to Log10 base numbers for the visual attention and listening to paragraph tasks. The following tables represent the result of the discriminant analysis for the three conditions. As there were only 84 subjects available for the analysis, the normal acceptable subject to variable ratio of 10 to 1 is not maintained. Thus these results must be considered preliminary and not definitive. The subject to variable ratio for each of the separate analysis is presented in the table title in the S/V= figure.

For the auditory attention task, variables were selected from a t-test comparison of all head injured versus normals. The following results were obtained with the raw data.

Table 2 – S/V=1.08/1
Auditory Attention Discriminate Analysis

	Percent Correct	Head Inj.	Normal
Head Inj.	86.67	13	2
Normal	98.08	1	51
Total	95.52	14	53

Rows: Observed classifications
Columns: Predicted classifications

Sixty variables were involved in the discriminant. Sixty-three percent of the variables employed in the discriminant involved coherence and phase Beta2 activity from the frontal lobes. The group was divided randomly into two groups and the same variables were employed in two separate discriminant analyses. Table 3 and Table 4 present these results. For group A, 16 variables were employed in the discriminant and for group B there were 28 variables. Thirty-three of these 44 variables (75%) involved the frontal lobes.

Table 3 – S/V=4/1
Auditory Attention
Discriminate Analysis-Group A

	Percent Correct	Head Inj.	Normals
Head Inj.	92.31	12	1
Normals	98.08	1	51
Total	96.92	13	52

Rows: Observed classifications
Columns: Predicted classifications

Table 4 – S/V=2.4/1
Auditory Attention
Discriminate Analysis-Group B

	Percent Correct	Head Inj.	Normals
Head Inj.	86.67	13	2
Normal	98.08	1	51
Total	95.52	14	53

Rows: Observed classifications
Columns: Predicted classifications

The visual attention comparison involved a similar approach, but in this case the values were transferred to Log10 values. Table 5, 6, & 7 present the results of this analysis. Of the 46 variables involved in the discriminant, 36 or 78% of these involved the frontal lobes and 28 (78%) of these frontal lobe measures involved the high frequency range. A similar pattern of frontal lobe participation was in the separate Group A and Group B breakdown. Each of these groups involved 46 variables in the discriminant.

Table 5 – S/V=1.7/1
Visual Attention
Discriminate Analysis – All subjects

	Percent Correct	Normals	Head Inj.
Normals	96.08	49	2
Head Inj.	82.14	5	23
Total	91.14	54	25

Rows: Observed classifications
Columns: Predicted classifications

Table 6 –S/V=1.3/1
Visual Attention
Discriminate Analysis – Group A

	Percent Correct	Normals	Head Inj.
Normals	100	51	0
Head Inj.	100	0	14
Total	100	51	14

Rows: Observed classifications
Columns: Predicted classifications

Table 7 – S/V=1.4/1
Visual Attention
Discriminate Analysis – Group B

	Percent Correct	Normals	Head Inj.
Normals	100	51	0
Head Inj.	100	0	14
Total	100	51	14

Rows: Observed classifications
Columns: Predicted classifications

The listening to paragraphs data was analyzed in a similar manner. Variables were selected for this condition on the basis of the highest F value obtained with Levene's test of homogeneity of variances. The variables were then converted to a Log10 format. Table 8 presents the results of the total group comparison. There were 17 variables involved in the discriminant, with 12 (70%) involving the frontal lobe. Tables 9 and 10 present the separate Group A and Group B analysis. For these analyses, there were respectively 18 and 11 variables required for the discriminant and a similar pattern of frontal lobe involvement (88% and 82% respectively). The results for groups A and B are presented in Figure 1.

Table 8 –S/V=5/1
Listening to Paragraphs
Discriminate Analysis

	Percent Correct	Normal	Head Inj.
Normal	92.59	50	4
Head Inj.	81.25	6	26
Total	88.37	56	30

Rows: Observed classifications
Columns: Predicted classifications

Table 9 –S/V=3.8/1
Listening to Paragraphs
Discriminate Analysis – Group A

	Percent Correct	Normal	Head Inj.
Normal	94.34	50	3
Head Inj.	93.75	1	15
Total	94.20	51	18

Rows: Observed classifications
Columns: Predicted classifications

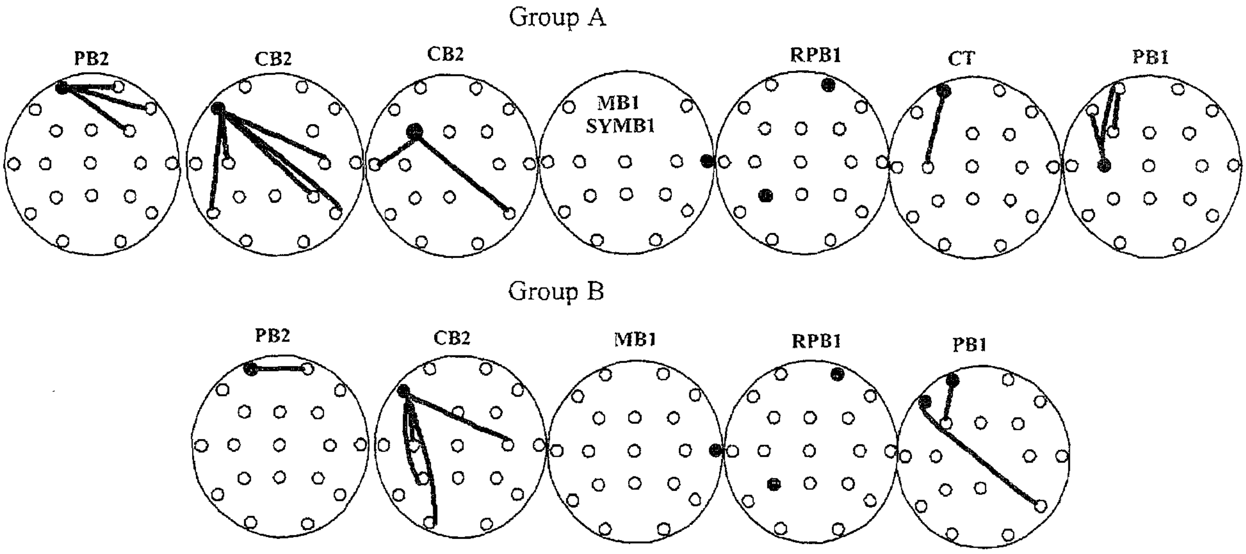
Table 10 –S/V=6/1
Listening to Paragraphs
Discriminate Analysis – Group B

	Percent Correct	Normal	Head Inj.
Normal	100.00	53	0
Head Inj.	78.57	3	11
Total	95.52	56	11

Rows: Observed classifications
Columns: Predicted classifications

Figure 1

Variables Involved in Discriminate for Listening to Paragraph Condition



Legend

PB2 refers to phase beta2, CB2 refers to coherence beta2, MB1 refers to magnitude beta1, SYMB1 refers to symmetry beta1, RPB1 refers to relative power of beta1, CT refers to coherence theta, PB1 refers to phase beta1. Symmetry is calculated by averaging symmetry measures from all locations to a single location.

To understand the effect of time of these variables, a correlational analysis was conducted between the variables, which were employed in the discriminant function tests or were significantly different between the two groups for the separate conditions and the time since accident. The Beta phase and coherence values were, in general, the variables which separated the groups most successfully in all three comparisons. A positive correlation would indicate that the greater the time since the accident the higher the number and thus improvement (since all of the high frequency variables were lower for the head injured group).

In terms of the auditory attention condition, all the variables, which were significantly different between the head injured and normal group, were analyzed in terms of time since accident. None of the variables correlated significantly with time (at the .05 alpha level), thus reflecting no healing effect of time. In terms of the visual attention task, of all the variables which were statistically significant in the original analysis only two variables correlated (.05 alpha) with time- Coherence Beta2: Fp1-Fp2, Fp2-F4. For the listening to paragraphs conditions, none of the discriminant variables (at either .05 or .10 alpha) correlated significantly with time. All the variables, which were found to be significantly different in the original analysis, were conducted to the same analysis. Of the variables, which were significantly different, there were two patterns of significant improvement. The first involved the F7 position in its relationship (phase Beta2) to the F2, F3, Fz, & F4 positions) and the second pattern involved the F4 position and its relationship (phase Beta2) to the T3, C3, and T5 positions. These relationships showed significant improvement as time increases.

Therefore, time appears to have a limited healing effect as very few of the total number of variables employed showed any significant improvement with time. However, this methodology is a cross sectional one and a longitudinal design offers a more definitive answer.

A different type of methodology was employed to increase the sample size. This involved the combination of the three conditions into one file. This increased the sample size to 252 (as the same subjects were in all 3 conditions). This approach to the discriminant function would rely upon a strong pattern of similar deficits across all conditions to be effective. The variables for a subgroup of half the head injured subjects were selected employing Levene's test (F values) to differentiate the highest discriminating variables. The variables were then converted to Log^{10} values. The discriminant values were obtained. The results were not as encouraging as the separate condition analysis and will not be reported.

DISCUSSION

This exploratory research was conducted to ascertain if the high frequency values might be of value in a discriminating between the mild head injured subject and normals. Due to the small sample size the results can only be considered encouraging to future research in this area. The overall classification accuracy varied from 88% to 100% for the three conditions. This represents an encouraging finding for the continuation of this approach. Of some interest to note is that as the task became more demanding (listening to paragraphs) there was a decrease in the number of variables required for a successful discrimination. The pattern of frontal lobe involvement in the variables employed in the discriminant function was strong in all the tasks and is consistent with previous research in the area of mild head trauma.

The separate analysis of the effect of time on the variables, which differentiated the groups, resulted in a discouraging finding. Time does not appear to spontaneously heal many of the phase and coherence figures. None of the head injured subjects, however, had been involved in any form of rehabilitation prior the evaluation. The cross sectional design of this research does not offer a definitive answer to this question as can be obtained with a longitudinal design. Thatcher et al. (1989) had found a similar effect of no improvement when employing the discriminant over different time periods since the subject's accident.

A related and important theoretical question with significant practical applications is how do these parameters affect cognitive functioning. This question and others will be the focus of the future analysis of the data obtained with 151 subjects involved in numerous cognitive challenges.

The effect of other variables (emotional status, intelligence level, previous brain injuries) into this analysis requires notation. Table 1 shows the differences between the groups in terms of Shipley IQ scores. It is certainly the case that head injury will generally affect problem solving ability (hence the Abstraction score). Verbal skills, however, are generally considered the least affected. The statistically significant difference between the brain-injured group and normals in terms of both the Verbal and Abstraction Raw scores belies a possible preexisting difference in the groups.

An additional factor is the effect of emotional differences between the groups. Twenty-three of the 32 brain injured subjects had received a diagnosis of Post Traumatic Stress disorder and 5 an overlapping or separate diagnosis of depression. Hughes, J.R. and John, E.R. (1999) note that depression (unipolar) is marked by increases in alpha and theta, asymmetry and hypocoherence in anterior regions. Bipolar depressed patients are marked by decreased alpha and increased beta activity. Hughes and John (1999) have noted that consistent patterns in other psychiatric disorders (anxiety, obsessive-compulsive and eating disorders) have not been discerned by the research at this point in time. This pattern of results for depression is not totally consistent with the results of this study, and thus cannot fully explain the results. Previous research has not addressed the effect of a previous brain trauma. Six of the subjects in this research had a history of a previous head trauma.

The limitations of discriminant function analysis in delineating between clinical groups has been discussed by Duffy, F. et al. (1994) and in the brain injured situation in specific by Nuwer, M. (1997). One of the primary problems with this approach is the requirement of uncontaminated group membership. To differentiate between clinical groups, the groups must not have overlapping membership in different clinical conditions. As this research included head injured with PostTraumatic Stress disorder, the results are potentially contaminated by this overlapping diagnosis. Nuwer's (1997) conclusion regarding the lack of usefulness of the QEEG in the brain injured situation has been challenged by Hughes, J.R. and John, E.R. (1999) conclusion that there is high consistency of findings in the mild to moderate brain injury subjects, in sports related head impact injuries and in patients with severe brain injury as they recover. These findings indicated increased focal or diffuse theta, decreased alpha, decreased coherences and increased asymmetry issues. The results of this study are in agreement with the general findings noted by Hughes, J.R. and John, E.R. (1999) which is the most recent and most extensive review of the literature to date in terms of decreased alpha activity and decreased coherences.

The problem of EMG artifact is somewhat attenuated by the lack of significant increase in terms of absolute or relative power of the Beta2 band in the head injured group. If the assumption is made that an increase in Beta2 activity (if due to muscle artifact) would result in lowered coherences and phase values to the posterior sections, then one would expect not just lowered coherence and phase figures but increased Beta2 activity as well. The results do not support this line of reasoning. In addition, what is deficient in the head injured group is not the presence or absence of 40 Hz activity, but the phase and coherence values of the upper frequency range which includes 40 Hz activity. This is a relationship issue, not a level or presence of activity issue.

The value of the results of this study resides not only in their potential discriminating power, but also in their ability to direct rehabilitation efforts. The field of Neurotherapy (EEG biofeedback) has been growing rapidly for the past several years and has been demonstrating its effectiveness in a number of clinical and cognitive conditions. The results of this research, hopefully, can direct the interventions in a very specific manner.

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