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INTERVAL HISTOGRAM ANALYSIS OF EEG HEMISPHERIC ACTIVITY IN SCHIZOPHRENIA

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While research into the psychophysiological correlates of maladaptive behavior has expanded during recent years, the investigation of the hemispheric processes related to psychopathology has experienced unprecedented growth during the last few years (e.g., Flor-Henry, 1979). One particular branch of this type of hemisphericity research which has received considerable attention and yielded results of heuristic value has been the study of hemispheric activity in schizophrenics, see Flor-Henry, Koles & Reddon (this volume); Flor-Henry & Koles (1984); Newlin, Carpenter and Golden (1981) and Walker, Hoppes and Emory (1981) for comprehensive reviews on this subject.

Within this general area we have developed a special interest in the electrophysiological (versus behavioral) asymmetries often observed in schizophrenics. While the literature generally provides strong support for left hemisphere abnormality, theories such as those exposed by Flor-Henry (1979) and Gur (1979), numerous disparities between studies are apparent. Most often, these disparities have been accounted for by the revision of existing theories (e.g., Walker & McGuire, 1982). Possibly a sounder approach to accounting for these discrepancies would be to examine methodological issues, rather than theoretical ones. Indeed, if methodological problems would account for the varied results reported in the literature, then the validity of existing theories would, in turn, be highly questionable.

While one could raise numerous methodological questions, one which has largely been ignored has been the measurement of dependent variables. It is not unusual for investigators using electroencephalographic (EEG) measures to use different electrode placements, filtering systems, and methods of analyses. While spectral or frequency analysis has been the most widely accepted method of EEG analysis, it is possible numerous statistical assumptions are typically violated when using this approach. Central to the assumptions underlying frequency methods of analysis is that the EEG wave is a periodic, unchanging variable (Burch, 1959). This assumption becomes especially critical since most investigators (due to the large amount of data obtained in EEG studies) tend to sample EEG for several seconds and then generalize to the entire period from which the sample was taken (usually minutes). In this study, we were interested in examining the hemispheric activation of schizophrenics using standard experimental paradigms (e.g., Galin & Ornstein, 1972) but analyzing the EEG from a time

Table 1. Mean Demographic Variables by Group

Variable	Group: Brain-damaged Schizophrenic	Non-Brain-Damaged Schizophrenic	Affective Disorders
Age	46.2	30.2	34.6
Year of Onset	31.5	21.4	29.3
Number of Hospitalizations	1.7	5.0	2.3
Current Length of Hospitalization (in days)	1163.1	113.7	57.5

rather than a frequency domain. Thus, the assumption of periodicity of the EEG would not be violated, in this technique.

METHOD

Subjects

From the in-patient population of a 1,200 bed state-supported psychiatric hospital, 57 volunteers participated in this study. To be included in the study patients had to be 18 years of age, have good corrected or uncorrected vision, be right-handed by report and observation, and had to read, comprehend, and sign an informed consent form. Additional biographical information is contained in Table 1.

From the pool of 57 subjects, three groups of 19 participants were formed. The first group was composed of schizophrenics without brain damage while a second group was composed of schizophrenics with brain damage. Diagnosis of schizophrenics with brain damage was ascertained using a standard diagnostic manual (DSM III) (American Psychiatric Association, 1980). Diagnoses were made independently by psychiatrists and psychologists using the history as well as the results of a clinical interview, the Shearn and Whitaker (1969) schizophrenic symptom checklist and the Whitaker Index of Schizophrenic Thinking (1973). The results of the scores are shown in Table 2. Brain lesions were determined by history of diffuse brain pathology as documented by medical examination and laboratory tests (e.g., CAT Scan) as well as by the Luria-Nebraska Neuropsychological Battery (Golden, Hammeke & Purish, 1978). A third group of affective disorders was included as a reference-control for the first two groups. Diagnoses were determined in the same manner as schizophrenia but using the criteria outlined in the DSM-III for affective disorders.

Experimental Procedure

Each subject participated in psychological and electroencephalographic (EEG) testing. Odd numbered subjects (e.g., 1, 3, 5, . . .) participated in the EEG part of the test in the morning and the psychological testing in the afternoon. Even numbered subjects (e.g., 2, 4, 6, . . .) did the reverse. Morning testing began at 9:00 am and was completed by 11:00 am while afternoon testing began at 1:00 pm and ended by 3:00 pm.

Table 2. Mean WIST and LNNB Scores by Group

Test	Scale	Group: Brain-Damaged Schizophrenic	Non-Brain-Damaged Schizophrenic	Affective Disorder
WIST;	Similarities	5.9	8.5	2.4**
	Word Pairs	2.7	3.4	1.3
	New Inventions	3.1	3.1	3.4
	Time	15.0	19.8	15.10
	Index	26.7	34.8	22.2
LNNB;				
	Motor	40.3	14.2**	
	Rhythm	12.0	6.6*	
	Tactile	13.5	8.9*	
	Visual	15.1	10.0	
	Receptive Speech	18.0	10.4*	
	Expressive Speech	26.3	15.2*	
	Writing	12.2	7.2*	
	Reading	9.3	6.5	
	Mathematics	17.8	8.4*	
	Memory	18.4	13.3*	
	Intellectual	38.5	30.0	
	Pathognomic	26.0	15.7	
	Left Hemisphere	11.8	5.4	
	Right Hemisphere	14.8	6.3	

* $p < .05$

** $p < .01$

Variables Measured.

Neuroleptic dosages were converted to chlopromazine equivalents according to the method suggested by Davis (1976). Dosages were altered during the course of the study. These conversions are found in Table 3.

Table 3. Chlorpromazine Equivalents (CPZE) by Groups

	CPZEmg		
Group	Mean	SD	Range
Brain-Damaged Schizophrenic	378.95	306.10	0-1200
Non-Brain-Damaged Schizophrenic	1628.95	2091.00	0-7500
Affective Disorder	531.59	656.85	0-2250

The EEG was recorded from the O_1 and O_2 sites referenced to respective ear-lobes (10-20 system) using a Grass Model 16 EEG. Signals were recorded graphically (for visual inspection) and on magnetic tape via an Ampex FM Recorder (for statistical analysis). Data from the tape was digitized using a PDP 8 by an individual unaware of group composition using the period analysis technique of Sharp, Smith and Surwillo (1975). Data was then coded "blind" by another technician to disc via an Apple II Plus.

The half-wave period was obtained using two manipulations. First, noise was subtracted using averaging of a specific number of sample waves. In addition, the peaks and troughs of a particular wave were selected relative to its opposite using a combination of criterion amplitude (measured in μV) and criterion duration (in msec). Once a half-wave had been selected, it was dumped into one of 250 possible bins, each having a duration of 1 msec. For the purposes of this study, 20 five msec bins were constructed to cover the entire spectrum of duration extending from 0 to 100 msec. A total of 50 half-wave were analyzed half way through the testing period for each period of the EEG testing.

There were five separate Test periods (each three minutes long and with the subject sitting facing away from the polygraph operator and towards a wall approximately six feet in front of the individual). During the first Test period, the participant sat quietly with eyes open while a resting baseline was obtained. A simple eye exercise involving fixating on a black circle and on a black square as well as performing a series of sequential eye movements followed. The next two Test periods were counter-balanced. For odd-numbered subjects, a visuo-spatial task involving the solution of both "easy" and "hard" (as determined by a pilot study with clinical subjects) problems from the Minnesota Paper Form Board Test followed the eye exercise. For even-numbered subjects, a task involving solving one and two digit (i.e., "easy" and "hard" as determined in a pilot study) multiplication problems followed the eye exercise. During presentation of the stimuli, the subjects were instructed to solve the respective problems in their head and that, after presentation of all the stimuli the subject would have the opportunity to provide the Experimenter with the solutions. (Indeed after completion of all problems, the polygraph was turned off and each stimulus was presented for five seconds once more and the verbal responses were then recorded). After the verbal reports, subjects were then presented with the alternate set of tasks; that is, for odd numbered subjects, the multiplication problems and the even numbered subjects, the geometric problems.

RESULTS

Two main sets of analyses were performed on the half-wave EEG data, using the statistical package developed by Steinmetz, Romano and Patterson (1981) on an Apple IIe.

The first set of analyses entailed examining within subject variables. Histograms were constructed for each subject, across Test periods and hemispheres, and were grouped according to clinical diagnosis. The grouped histograms were analyzed by means of correlated t-tests from Test period to Test period as well as within Test periods with respect to laterality. Thus, three sets of t-tests were performed, one for each group, in order to determine whether changes occurred in the last two Test periods relative to the baseline Test period and whether hemispheric measures differed (within Test periods). Regardless of the fact that a total of 30 t-tests were performed, no significant differences were observed. The lack of significance appears to be due to the wide dispersion of data within the histograms.

The second set of analyses employed the dominant interval recorded. Thus, instead of concentrating on the entire frequency distribution this set of analyses focused only on the EEG period during which time most waves were observed. An 3 x 2 analysis of variance, split-plot design was used. The design consisted of three between groups variables (clinical diagnosis) and two within group variables (hemispheres). In total, three 3 x 2 ANOVAs were performed, one from each major Test period of the experiment.

In Test period I, or "baseline", no significant interaction or main effects for group was noted. However, a main effect for hemisphere was observed ($F = 14.59$; $p < .01$). The means indicate that there is preponderance of right hemisphere activity for slower EEG periods (mean = 24. 31 msec) while faster intervals were observed in the left hemisphere (mean = 18.16 msec). For the geometric design Test period, a main effect of hemispheres was noted ($F = 22.76$; $p < .01$). A highly similar pattern to "baseline" was noted with regards to slow and fast activity across Hemispheres. The interaction indicated that this main effect appears to be due to the relatively slow right hemisphere (especially in brain-damaged schizophrenics) activity with the relatively fast duration-periods for the left noted for the two schizophrenic groups (especially the brain-damaged sample). During the last Test period, or the multiplication problem task, only a main effect for Hemisphere was noted ($F = 30.42$; $p < .01$). In general, the same pattern of right versus left hemisphere activity seen in the geometric Test period was observed with the largest left-right difference being noted for the brain-damaged schizophrenic group. The means for each group across Test periods and Hemispheres are found in Table 4.

DISCUSSION

The results indicate the hemispheric dysfunction in schizophrenia is a complicated phenomenon tempered by numerous variables. As Flor-Henry (1983) has suggested, hemispheric dysfunction is not a static but a dynamic situation.

Across the three Test periods, results indicate that faster EEG activity was observed for all three groups in the left hemisphere. Conversely, slower activity was noted in the non-dominant hemisphere. Baseline EEG indicated that largest hemispheric difference were found for the Affective group. Indeed, the non-brain damaged Schizophrenic group exhibited relatively similar activity for both hemispheres. Large left-right differences were observed in the geometric task Test period, this was especially true for the Brain-damaged sample. While slowing of right hemisphere activity was noted for the Brain-damaged Schizophrenic sample, slight increases in activity were noted for the two other groups. With regards to left hemisphere activation during this task, both Schizophrenic groups increased activity (especially the Non-damaged sample). Interestingly, the relatively large hemispheric differences noted for the affective disorders during the baseline Test period were eradicated during

Table 4. Group x Hemisphere x Group Interval (Half-wave) EEG Mean

Test Period	Hemisphere	Group: Brain-Damaged Schizophrenic	Non-Brain-Damaged Schizophrenic	Affective Disorder	Total
Baseline "resting"	Left	16.6	21.4	16.4	18.
	Right	22.1	25.3	25.6	24.
	Difference	5.5	3.9	9.2	6.
Geometric	Left	15.5	16.7	18.3	16.
	Right	28.0	21.4	21.3	23.
	Difference	12.5	9.7	3.0	6.
Multi-plication	Left	16.4	15.8	15.9	16.
	Right	30.5	24.9	24.6	26.7
	Difference	14.1	9.1	9.0	10.7

the geometric Test period. During the final Test period, similar hemispheric differences were noted between the non-brain-damaged schizophrenic and affective groups. Nevertheless, relative to the baseline Test period, the former group exhibited not only the fastest EEG activity but had a large increase in the activity generally. While slowing of the right hemisphere was not observed in the Non-brain-damaged Schizophrenic an Affective groups, significant decreases were noted for the Brain-damaged Schizophrenic sample.

Several conclusions can be reached. Foremost, period analyses of hemispheric EEG activity is a robust measure when considering group and tas comparison. While wide variability of the data complicated analysis of frequency means, "dominant-wave" analysis provided a fruitful measure of EE activity. Secondly, the use of brain-damaged schizophrenics as well as patients with affective disorders appear to be useful in defining the boundaries for the limits of laterality abnormalities in putatively CNS-intact schizophrenics. Indeed, the data derived from the subjects alone provide useful information into the role of brain dysfunction in schizophrenia as well as of affective pathology in hemisphericity issues. Finally, hemispheric differences in these groups appear to exist in respons to task demands and, to a lesser degree, at rest.

Superficially these findings support those of Gur (1979) as well as interpretations of Newlin, Carpenter and Golden (1981), and Walker and McGuire (1982). While dominant hemisphere overactivation was noted, the data obtained indicate that sweeping generalizations about overactivation must be tempered by numerous factors including baseline-task Test period differences. Additionally, while changes were noted for left hemisphere activation care should be taken in considering right hemisphere activation (seen in the non-damaged schizophrenic group in response to geometric

designs) and slowing (seen in the brain damaged-schizophrenic group in response to both tasks).

More definitive interpretations await replications and consideration of several limitations. Primarily, while dispersion of histogram data complicated the analysis of means, that in itself may be worthwhile to examine. As Surwillo (1978) indicated, variability (rather than central tendency) may be a more important factor in period analysis of the EEG. Secondly, "change score" analysis may have resulted in more accurate interpretation of the data. Differences were noted during the baseline Test period and while not significant, they do appear large enough potentially to mask group differences observed during task activity.

Period analysis provides a less restrictive approach to EEG interpretation of hemispheric activity. With further development, a more comprehensive interpretation of psychopathology and laterality should emerge as both frequency and time approaches to EEG analysis are considered.

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