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THE UNIVERSITY OF ALBERTA

A STUDY OF EEG ASYMMETRIES RELATED TO HEMISPHERIC DOMINANCE IN NORMALS AND PSYCHOTICS

by

Peter Christian Bo-lassen

A THESIS

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, a thesis entitled A Study of EEG Asymmetries Related to Hemispheric Dominance in Normals and Psychotics submitted by Peter C. Bo-Lassen in partial fulfilment of the requirements for the degree of Master of Science.

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ABSTRACT

Intragroup and intergroup asymmetries in the electroencephalogram (EEG) recorded from normals, schizophrenics, and manic depressives during various experimental conditions were studied by applying methods of digital spectral estimation. In both normal and psychotic groups significant EEG differences were found between verbal and spatial tasks. Significant differences were found in (a) the R/L ratio of EEG energy recorded from homologous regions in the right and left hemisphere and (b) inter and intra hemispheric coherence values. Intergroup differences for (a) and (b) didn't reach significance.

Various other EEG parameters were analyzed during the eyes closed resting condition. Psychotics differed significantly from normals in the proportion of EEG energy present in the alpha, beta, and gamma frequency bands. Significant differences occurred more frequently in the left temporal region for schizophrenics and in the right temporal region for manic depressives. Manic depressives displayed EEG hypovariability with respect to normals and schizophrenics in certain comparisons.

Multivariate discriminant analysis was applied to each group separately to test for intragroup differentiation between verbal and spatial tasks and also to test for

intergroup differences during a given experimental condition.

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CHAPTER 1

INTRODUCTION

The primary application of human electroencephalography has been in clinical neurology. Electro-encephalographic manifestations of epileptic states and tumored brain regions have rendered the electroencephalogram (EEG) a useful tool in partial assessment of a subject's neurological state. Other routine medical uses include monitoring during surgery and providing a useful index for depth of anesthesia. Relatively less clinical success has been achieved in other disciplines. In psychology and psychiatry for example, attempts to relate EEG features to behavioral and psychopathological states have been of limited value in either aiding the diagnosis of mental disorders or providing assessment of clinical change during the treatment of a psychosis. Part of the lack of success may be attributed to the lack of suitable quantitative methods for an objective assessment of EEG features. In particular the application of modern techniques of digital spectral analysis to the human EEG is still in it's seminal stages. Particularly few are (a) applications directed toward the detection of behaviorally induced changes in the EEG and (b) attempts to ascertain EEG correlates of psychopathologic states. The study reported in this thesis concerned itself with (1)

verifying and expanding recent electrophysiologic evidence demonstrating task dependant EEG asymmetry in normals during the performance of verbal and spatial tasks and (2) attempting to find EEG abnormalities in psychotics related to their diagnostic classification in both the resting EEG and in the EEG recorded during various tasks.

Chapters 2 to 4 are literature reviews. Chapter 2 considers some of the evidence for lateralization of cortical functions. Chapter 3 is a review of EEG manifestations of psychopathology and Chapter 4 considers methods of spectral estimation relevant to the data analysis used in this study. The following chapters, 5 and 6, describe the experimental procedures used in obtaining the EEG recordings and the analytic methods used to analyze them. The results are presented in Chapter 7 and discussed in Chapter 8.

CHAPTER 2
EVIDENCE FOR LATERALIZATION OF CORTICAL FUNCTIONS

2.1 Evidence From Brain-Damaged Subjects

Based on observations from patients with unilateral brain lesions the concept of lateral localization of elementary cerebral functions (sensation and movement for example) was well established in the early 19th century (1). It was common knowledge that lesions of the motor cortex lead to paralysis of the opposite limbs, lesions of the post central region to loss of sensation on the opposite side of the body and lesions of the occipital region to loss of vision in the opposite visual field. Some of the earliest observations leading to the hypothesis that complex mental functions may be laterally localized were made by Broca and Wernicke in 1861 and 1873 respectively. Broca showed that lesions of a particular brain area, the posterior third of the left inferior frontal gyrus led to a loss of expressive speech. Wernike showed that lesions in the posterior third of the left superior temporal gyrus led to an inability to understand audible speech. Encouraged by these findings contempory neurologists and psychiatrists began amassing facts from patients with local brain lesions resulting from wounds or hemorrhage. Cortical centers for various other

higher mental functions were hypothesized as a result. Early conceptions of mental functions and their lateralization were over simplified. Investigators assumed that disturbances of a particular function resulting from destruction of a certain area of brain tissue were proof that the function was an intrinsic property of the intact tissue.

The more modern viewpoint , as outlined by Luria, 1973 (1), conceives of higher cortical functions as "functional systems" embracing many cortical zones (often in distant brain regions) working in conjunction with each other. Systematic investigations of the presence or absence of an effect on different mental faculties resulting from a lesion of a particular cortical area and also the different effects on a particular mental faculty resulting from lesions in different brain areas have contributed considerably in delineating the particular cortical zones constituting the functional system for a particular mental faculty. Delineation of the cortical zones necesary for a particular faculty has led to what Luria has called the law of progressive lateralization of cortical functions (1). Brain areas responsible for lower cortical functions (body sensation, vision, hearing) are, to a large extent, projection areas for contralateral receptor pathways and neither hemisphere can be regarded as dominant for them.

With functions involving handedness and with the cerebral organization of speech and associated faculties, lateralization of functions takes place. In right-handers the left hemisphere becomes dominant for speech and related faculties with the right hemisphere playing a subordinate role or no role at all. Since many higher psychological processes are speech related, lesion based deliniation of cortical zones responsible for those processes has been based more on the symptomatology of dominant hemisphere lesions. Information regarding non-dominant processes has come more from other areas.

Evidence from split brain expetiments and studies on patients who have undergone lobectomy have provided much evidence to support the hypothesis of lateralization of higher cortical functions. Right temporal lobectomy produces impairment on visual and tactile mazes while left temporal lobectomy leaves verbal memory severely impaired but has little effect on spatial processing. Ingeniously designed experiments carried out by Sperry and Gazzaniga and their associates on patients with a severed corpus callosum and anterior commisure have shown each hemisphere separately carries out cognitive processes for which it is specialized (2). Using dichotic and dioptic stimulation techniques, problems were posed to each hemisphere separately without the other hemisphere's knowledge. The evidence obtained

suggested that each hemisphere is characterized by s's own particular mode of processing sensory information; the left hemisphere best at dealing with tasks requiring speech related logical and analytic faculties, for example writing and arithmetic calculations; the right for cognitive processing best dealt with in a gestalt, holistic mode of thinking, for example spatial relationships and musical patterns.

2.2 Evidence From Normal Subjects

In drawing inferences on cognitive lateralization from lesion studies and split brain experiments, the possibility exists that the lateralization exhibited is wholly or partly an aftereffect of the neurological damage surgery performed. Recent evidence from neuropsychology and electrophysiology, however, has demonstrated lateralized effects in intact normal subjects and provides strong support for conclusions drawn from studies on brain damaged subjects. Galin and Ornstein (3) have summarized much of this recent evidence, part of which is outlined below.

Electropysiological evidence from evoked response and electroencephalographic studies has demonstrated that left and right hemispheres are asymmetrically implicated in tasks requiring a particular mode of cognitive processing.

Buchsbaum and Fedio (4) recorded evoked responses to visually presented words and geometric stimuli from left and right occipital areas. Responses for both classes of stimuli were identical in the right hemisphere but differed in the left. Wood et al (5) recorded evoked responses to aurally presented stimuli while processing the stimuli under two different conditions. Differing responses were found in the left but not the right hemisphere. Morell and Salamy (6) reported that evoked responses to speech sounds were larger in the left hemisphere than in the right. Vella et al discovered that evoked responses to complex visual forms were larger in the right hemisphere (7). Mc Adam and Whittaker (8) recorded D.C. potentials over right and left temporal areas. A negative shift in the potentials occurred just before speech took place. The negative shift was more pronounced on the left hemisphere than on the right.

Evidence for lateral specialization derived from electroencephalographic studies on subjects engaged in tasks designed to engage one hemisphere relatively more than the other has, to this writer's knowledge, been published only since 1970, with the exception of Cornil and Gastaut's 1947 account (9). Cornil and Gastaut, based on visual inspection of the raw EEG trace reported relatively greater suppression over the dominant hemisphere during arithmetic calculation. Morgan et al (10), (11) recorded occipital EEG alpha from

the left and right hemisphere. They found the percentage difference in alpha amplitude between left hemisphere and right hemisphere alpha measures was significantly different between analytic and spatial tasks. Galin and Ornstein (12,13) report task dependant EEG asymmetry during the performance of verbal and visual spatial tasks. They found a significantly higher right to left ratio of total EEG power in verbal than in spatial tasks. They recorded EEG's from parietal and temporal leads referenced to the vertex. Mc Kee et al (14) utilized the technique of Galin and Ornstein to demonsrate scaled lateralization of alpha activity during linguistic and musicogenic tasks. The assymetry reported by Galin and Ornstein was verified and in addition right to left ratios were found to increase progressively with increasingly "difficult" liguistic tasks. Butler and Glass (15) demonstrate significant left hemisphere EEG suppression during the performance of mental arithmetic. Recording was bipolar from homotopic areas in left and right hemispheres. Significant assymetry of the filtered alpha component, as opposed to the total EEG energy, was found in parito-central derivations.

Luria feels the dominance of the left hemisphere for verbal-analytic processing is only a relative rather than an absolute lateralization. He cites recent investigations estimating 1/4 of all normals as completly left hemisphere

dominant, 1/3 markedly left hemisphere dominant, with 1/10 showing a complete absence of left hemisphere dominance and the remainder a relatively slight dominance (Zangwill, 1960 (16), Surbirana, 1969 (17)). Other investigators, Eccles for example (18), feel the incidence of marked left hemisphere dominance is much higher.

CHAPTER 3
EEG MANIFESTATIONS OF PSYCOPATHOLOGY

3.1 Introduction

Since the discovery of the EEG by Hans Berger in 1928 psychiatrists and electoencephalographers have attempted to correlate specific EEG abnormalities with specific mental disorders. Early work was based on qualitative visual inspection and/or hand-scoring of an EEG trace. Later research efforts applied machine quantification of the EEG using first analog then digital techniques. This review of EEG findings in relation to psychopathology will arbitrarily be divided into three sections. Section one will consider early findings (pre 1950) based on qualitative inspection and/or hand-scoring of the EEG, section two will consider findings based on the technique of "quantitative amplitude analysis", and section three will deal with findings based on frequency analysis utilyzing both analog and digital techniques.

3.2 Early Findings

Most early attempts at relating EEG patterns to psychopathology relied on qualitative visual analysis. A few studies, however, attempted to quantify specific EEG

parameters in an effort to discriminate between normal and patient populations. Studies based on qualitative analysis will be surveyed first followed by mention of a few early quantitative studies.

MacMahon and Grey Walter in 1938 authored one of the earliest published reports on EEG studies in psychotic patients (19). They found certain schizophrenics characterized by increased delta discharges in the frontal lobes. The problem of blinking and eye movement artifacts was also discussed. Davis, in a series of reports (20), (21) and (22), studied the EEG's of schizophrenics and manic-depressives both separately and on a comparative basis. The most prominent abnormality in schizophrenic EEG's was the presence of "choppy" activity. "Choppy" was the term applied to EEG's where continuous high frequency activity dominated the record. In (21) manic-depressives in a depressed state were reported to have patterns consisting of alpha activity mixed with slow waves. Manic-depressives in a manic phase tended to have patterns consisting of alpha plus fast activity. In comparison to manic-depressives schizophrenics were found to have a higher proportion of "choppy" records and more EEG's with fast alpha activity (22). Lemere (23) considered only alpha rhythm in a study of EEG patterns in psychotics. He reported lowered alpha activity in schizophrenic disorders and toxic psychoses and higher

activity in the affective disorders. The findings were explained by postulating lower "cortical energy" in schizophrenia and higher energy in the affective disorders. This explanation ~~is at~~ variance with recent variability studies hypothesizing hyperarousal of the cortex in the schizophrenic syndrome. Clardy et al (24) studied seven children with schizophrenic symptoms. He reported that all seven displayed abnormal EEG activity and four showed non equivalence of the two hemispheres. Finley et al (25) noted a great variety of patterns in the EEG's of schizophrenic patients. The only abnormality approaching consistency in the records was the presence of fast activity. The greatest proportion of abnormalities was found in the catatonic - hebephrenic group. In a later study in collaboration with Semrad (26) he attempted to relate pneumoencephalographic (PEG) and electro-encephalographic findings in chronic mental patients. Out of seventy-seven chronic mental patients 69% had a borderline or abnormal EEG and 58% an abnormal pneumoencephalogram. Fifty of seventy-seven subjects were of the catatonic-hebephrenic type. In this sub-group 58% possessed abnormal PEG's and 64% abnormal EEG's. No correlation between EEG and PEG abnormalities was discovered. Rubin (27) reported on the effect of hyperventilation on the EEG's of schizophrenic and normal subjects. Hyperventilation affected the alpha rhythm of both

groups similarily but slow waves appearing in the majority of normals in hyperventilation were noticed in only one schizophrenic. Mc Neel et al (28) in a study of the EEG's of schizophrenics under insulin shock treatment suggested catatonics "showing marked psychomotor inertia" are characterized by an "abnormal fast frequency in the electro encephalogram".

One of the earliest attempts at "quantification" of the EEG and a study which predated more modern work on quantitative amplitude analysis was reported by Rubin in 1938 (29). Rubin quantified a conventional voltage versus time EEG trace by determining the "percent time alpha" of successive one meter epochs of an EEG trace recorded at 30mm/sec . Percent time alpha referred to the percentage length of a one meter of EEG record occupied by sequences of alpha waves of a certain duration and amplitude. For purposes of analysis he considered 5 meter tracings recorded on different days. Mean percent time alpha averaged over the five meter records was lower for schizophrenic but not significantly. Analysis of variance showed inter epoch differences not significantly different for either group but schizophrenics showed significantly more day to day and less interindividual variation in percent time alpha than normals. Rubin and Cohen (30) studied percent time alpha in two classes of schizophrenic patients versus normals . The

two patient groups were differentiated with respect to the predominant imagery in their hallucinations. The percent time alpha for patients of kinesthetic imagery type was the same as for normals but their day to day variability was twice as great. The percent time alpha for patients with tactual type imagery was significantly lower than normals but day to day variability was the same. In (31) Rubin showed individuals displaying cerebral atrophy in the PEG were characterized by differences in the distribution of percent time alpha at homologous locations in the two hemispheres. The position of the atrophied area in relation to the front and back of the head could be determined but laterality of the atrophied tissue could not be assessed. Gibbs (32) performed a Fourier analysis of 30 second records of EEG's recorded from the left occipital area of normals and schizophrenics. Frequencies between 2 and 50 Hz were analyzed. The average spectrum for the schizophrenic group had peaks in the 15-30 Hz range not found in normals and a less pronounced alpha band peak. In a discussion following the paper the similarity of frequency patterns of certain schizophrenics, especially catatonics, to those of epileptics was noted.

3.3 Quantitative Amplitude Analysis

Quanitative amplitude analysis is the term applied to

the technique of EFG analysis suggested by Drohocki (33) and pioneered by Goldstein et al. The technique consists of dividing an EEG record into N epochs and electronically obtaining a measure of of the energy content of the signal for each epoch. By performing simple statistics on the set of energy values for the N epochs measures for the "mean energy content" (MEC) and coefficient of variation (CV) of the EEG signal may be obtained. While the importance of the coefficient of variation as an EEG parameter was developed mainly by Goldstein and Sugerman et al, it is worth noting that Rubin (29) compared EEG's of normals and schizophrenics by a similar statistical technique as early as 1938.

Sugerman et al (34) found significant differences in the variability of mean integrated energy, as measured by the coefficient of variation, between chronic schizophrenics and normals. Chronic schizophrenics had a lower coefficient of variation and a significantly higher mean integrated energy than normals in EEG's recorded from a left occipital electrode referenced to both ears. Analysis was based on an epoch length of 20 seconds. Significant correlation was found between behavioural variables of a psychiatric rating scale indicating schizophrenic disorientation and these two EEG variables. Patients under drug therapy who showed clinical improvement as indicated by the same behavioural variables of the psychiatric scale also showed changes

toward more normal values of variability and mean integrated energy. Goldstein et al (35) extended the research to a larger population of patients and controls and performed a more detailed analysis of the data than had been reported by Sugerman et al (34). The hypovariability of chronic schizophrenics, especially catatonics, with respect to normals was replicated. The hypovariability was found to be essentially independent of the basic time unit of analysis and held for epoch lengths of 1,5,10,20 and 60 seconds. Schizophrenics showed less interindividual variability of EEG measure and , in the absence of medication , showed less week to week variation than normals. Mean energy content was found to be uncorrelated with the coefficient of variation in both groups. Trends in MEC and CV were unrelated to either age or length of institutionalization. Changes in recording conditions produced statistically significant changes in the CV for normals but not patients. For normals opening the eyes produced a significant increase in CV but not MEC and sitting up led to a significant decrease in both MEC and CV.

The findings of Goldstein et al were replicated by Marjerrison et al (36) using the left occipital to left ear EEG recorded in awake subjects in a supine eyes closed resting situation. Chronic schizophrenics had significantly lower coefficients of variation than either acute

schizophrenics or normals. Ten acute schizophrenics who actually hallucinated during the recording also had significantly lower coefficients of variation than normals. The majority of patients were receiving phenothiazine medication. The authors found no significant difference in either "mean integrated amplitude" (MIA) or variability between chronics on or off drug therapy. The measure of mean integrated amplitude is equivalent to Sugerman's measure of mean energy content. This finding should be contrasted with Sugerman's finding of a tendency toward increased variability of the EEG in chronic schizophrenics receiving medication. Of related interest is the observation of Marjerrison that five acute schizophrenics without medication had significantly higher CV's than the 55 acutes receiving medication. " Sugerman et al (37), in a summary of research on EEG amplitude analysis, stated that, in their experience, chronically hospitilized patients characteristically show low EEG variability while recently admitted schizophrenics may show a wide range of variability.

D'Elia and Perris (38) applied quantitative amplitude analysis to EEG's recorded from right and left occipital electrodes in a group of patients suffering from psychotic depression. EEG measurres were calculated in and out of depressive episodes. During depressive episodes the within

patient variance of mean integrated amplitude was significantly lower in the left hemisphere. After therapy within patient variance of MIA became equal in both hemispheres. An additional significant finding was the negative correlation between the L/R ratio of MIA and the depression score both before and after treatment.

Saletu et al (39) studied the EEG's of chronic schizophrenics with and without thought process disorder in comparison with a normal control group. Average amplitude and amplitude variability were highest for normals and lowest for patients with thought process disorder. Differences, however, were not statistically significant.

Additional evidence for lower inter individual and intra individual variability in certain groups of schizophrenics has also been found using frequency analysis and will be mentioned in the next section.

3.4 Frequency Analysis

Although instrumental frequency analysis of the EEG had been reported as early as 1939 (32), the research of Kennard et al was among the earliest studies to apply frequency analysis to the EEG's of mental patients. In (40) the authors performed frequency analysis using a bank of bandpass filters on the EEG's recorded from three groups;

normals, criminal psycopaths, and mental patients - the majority of whom were schizophrenics. Schizophrenics were found to be characterized by records with marked activity above 20 Hz. They observed more marked variability among the EEG's of schizophrenics than in the other groups except for the alpha band. This finding should be contrasted with (29), (34) and (35) who found less interindividual variation in schizophrenics than in normals. "Synchrony" of the EEG record between different cortical areas was poor. The most distinguishing EEG features of the group of psycopaths were the presence of a high peak of alpha activity and the presence of relatively large amounts of theta activity. The authors noted, however, that theta was present only in records also containing slow alpha activity; possible leakage from one bandpass filter to another was not considered. In (41) similar techniques were applied in studying the EEG records of normals and mental patients over time. Clinical improvement in patients between recordings was correlated with more normal EEG's on successive recordings. The EEG patterns of the most acutely disturbed patients were more abnormal in their variation from area to area on the scalp than in the variation of the pattern from a particular area over time.

Lester and Edwards (42) found significant differences in precentral fast (18-26 Hz) activity between

schizophrenics and normals. Differences were significant during waking, periods of drowsiness, and REM sleep but not during slow wave sleep. The same normal controls under stress also displayed increased amounts of fast. Apparently normal relatives of schizophrenics also displayed abnormal amounts of fast in relation to a normal group with no overt signs of stress or a history of mental illness.

Volavka et al (43) studied the parieto-temporal EEG's (P3-T3) of periodically depressed patients by frequency analysis. The experimental design allowed separation of the effects of both drug influences and clinical state. Depressive states were found to be accompanied by significantly higher levels of alpha and beta than were measured during remissive phases. Significantly increased quantities of delta and theta activity were found to result from treatment with anti-depressive medication. The same technique was applied to 42 member groups of schizophrenics and normals matched for age and sex (44). The schizophrenics were all off medication for a period of at least two weeks, and usually longer. The two groups were compared on the basis of EEG's recorded from the right parieto-temporal region (P4-T6). The experimental design allowed evaluation of the possible effects of age in the two groups. The overall analysis between schizophrenics and normals showed significantly higher theta and alpha mean quantities in

schizophrenics. For schizophrenics interindividual variance was significantly higher in the delta, alpha 1 and alpha 2 bands and the coefficient of variability was higher in all bands but alpha 1. No age related differences were found within the schizophrenic group in any frequency band but younger controls displayed significantly greater amounts of mean delta and theta activity. Interindividual variance was also lower for younger controls in the theta band. Differences in beta activity, the predominant discriminator in most studies, were not significant.

Itil et al (45), (46), (47) and (48) have studied electroencephalograms in (a) chronic schizophrenics versus normals matched for age and sex and (b) in children with a high risk for schizophrenia versus a control group matched as in (a). Digital period analysis was used in all studies. It was supplemented by qualiatative visual analysis in (45) and (46) and analog frequency analysis in (47). The studies on chronic patients versus normals analyzed the right occipital to right ear lead in (45) and (47) and the right occipital to anterior vertex in (48). The study on high risk children analyzed eight leads; right and left monopolar central and occipital leads and right and left bipolar temporo-parietal and parieto-occipital leads. In (47) period analysis of the primary wave revealed schizophrenics have more slow delta waves (1.3-3.5)Hz and significantly less

(13-20) Hz activity. In first derivative measurements schizophrenics had significantly more (40-50) Hz activity and significantly less (10-16) Hz and (16-20) Hz activity. Frequency analysis data based on analog filters was in agreement with these findings. In (48) a similar digital period analysis of all night and REM sleep records demonstrated schizophrenics had significantly fewer slow delta (0-3) Hz waves than normals and significantly more fast delta (3-5) Hz , theta (5-8) Hz and fast activity (>20Hz) than normals. Amplitude variability and average amplitude were significantly lower in the psychotic group. Differences were more significant for the all night records than for the REM records alone. A stability study of the EEG's of age and sex matched chronic schizophrenics and normals appeared in (45). The EEG's of both groups remained stable in both week to week and month to month recordings. Statistically significant differences between the two groups supported the previous findings and remained stable over a three month recording period. Itil et al point out that the studies reported in (45), (46) and (48) suffer from the methodological shortcoming of being "retrospective studies". EEG examinations took place after the disease had developed and as a result could possibly have been influenced by epiphenomena. This methdological shortcoming was overcome in the study reported in (47), a study carried out in a group

of children of schizophrenic parents. Although the children selected were free of any overt schizophrenic symptoms statistical studies have shown similar children to have a high risk for schizophrenic illness. EEG abnormalities were similar to those found in chronic adult schizophrenics and definitely psychotic children. Discriminant analysis showed the most significant differences in the following leads; left central to left ear, right temporal to right parietal, and right parietal to occipital.

Lifshitz and Gradijan studied various EEG parameters in chronic schizophrenic and control subjects using frequency analysis in conjunction with quantitative amplitude analysis in a series of reports. In (49) both the coefficient of variability of the raw EEG potential and spectral intensities calculated via the FFT were examined in normal and patient groups. Two EEG leads and a para orbital lead were used for EEG quantification. The location of the EEG leads depended on the hemispheric dominance of a subject as determined by handedness. One lead was located 2 cm lateral to the vertex in the dominant hemisphere, the other at O1 or O2, whichever lay in the dominant hemisphere. Both leads were referenced to a lead tied to both ears through summing resistors. The CV of the integrated EEG potential recorded from the occipital area was lower for chronic schizophrenics than control subjects. For both groups the coefficient of

variation was positively correlated with delta band intensity. The significance of the correlation was higher for controls than patients, especially in vertex lead. The authors noted a significant tendency for the coefficient of variation to decrease the longer the patients had been off medication. In terms of spectral intensities significant differences were found in the occipital lead between patients and controls. Patients had significantly more power in the beta 1 (17.8-32.1) Hz and beta 2 (33.8-54.0) Hz bands. A second study reported in (50) used the lead configuration described in (49) plus two additional leads. The coefficient of variation of both the raw EEG and selected spectral bands were calculated in conjunction with power spectra for 30 chronic schizophrenics and 30 matched controls. The finding of a lower coefficient of variation for the integrated EEG potential for the occipital area was verified. Power spectral differences between the two patient groups were found primarily in the beta 1 and beta 2 bands as defined above. The authors found higher significances for the beta 2 band, especially for the ear referenced channels, and considered the possibility of muscle artifact. Time off medication was found to be significantly related to the delta band spectral intensity. Patients in the transitional stage of medication withdrawal were characterized by greater occipital lead delta power than either those receiving

medication or those completely off. Variability was also studied in the frequency domain. Coefficients of variation were calculated for the delta, theta, alpha, beta 1 and beta 2 bands and also for the total power band (.54-54) Hz. Significant differences were found in various bands for different leads, all in the hypothesized direction of lower CV's in patients. The coefficient of variation of beta 1 power in a bipolar anterior-posterior lead 2 cm from the vertex in the dominant hemisphere was found to be the most efficient discriminator between the two groups. A significant positive correlation was found between the coefficient of variation and age especially for the patients. As in their earlier study the authors found evidence of a lower CV in patients with the greatest medication exposure. A tendency for sicker patients to have a lower CV was also noted.

Giannitrapani and Kayton (51) studied the EEG's of a group of young schizophrenics (mean age 19.6 years) with a group of age and sex matched normals by spectral analysis. Monopolar recordings were from 16 brain areas referenced to a lead tied to both ears through summing resistors. The activity was analyzed into 17 frequency bands. In the lowest frequency range schizophrenics relative to normals showed greater amounts of activity in the frontal poles and less in the occipital poles. Normals had greater amounts of activity

than schizophrenics in the (10-18) Hz band in most areas and schizophrenics more activity than normals in most areas in frequencies above 18 Hz. In all frequency bands schizophrenics were a more heterogeneous group in terms of EEG amplitudes. The mean dominant alpha frequency of the schizophrenic group was also significantly lower than the mean dominant alpha frequency of the normal group and the variance of the dominant alpha frequencies higher. The authors considered the possibility of prominent peaks in the activity of schizophrenics being harmonically related to alpha frequency.

CHAPTER 4

SPECTRAL ESTIMATION

4.1 Introduction

Spectral analysis is concerned with the estimation of frequency domain measures, auto and cross-spectra, from time series of finite duration.

Auto-spectra provide a breakdown of the variance or mean square power of a single time series as a function of frequency. For a continuous zero mean random process $\{x(t)\}$ a one sided auto-spectral density $S_{xx}(f)$ may be defined such that:

$$\sigma_x^2 = \int_0^\infty S_{xx}(f)\,df \qquad 0 < f < \infty \tag{4.1}$$

It may readily be shown that a suitable definition for $S_{xx}(f)$ is given by

$$S_{xx}(f) = \lim_{T\to\infty} \left\{ \frac{1}{T} \left| \int_0^T x(t) e^{-j2\pi ft}\,dt \right|^2 \right\} \qquad 0 < f < \infty \tag{4.2}$$

or equivalently by the well known Wiener-Khinchin theorem as

$$S_{xx}(f) = 2 \int_{-\infty}^{\infty} R_{xx}(\tau) e^{-jw\tau}\,d\tau \tag{4.3}$$

where $R_x(\tau)$ is the auto-correlation function of the process.

Cross-spectra, through the derived squared coherency and phase spectrum to be defined in section 4.5, provide respectively a measure of the linearity of common frequency components in a pair of time series and an indication of whether these components lead or lag one another in time. For a pair of continuous random processes x(t),y(t) a definition of a one sided cross spectral density may be logically be derived as

$$S_{xy}(f) = \int_{-\infty}^{\infty} R_{xy}(\tau) e^{-j2\pi f\tau}\, d\tau \qquad (4.4)$$

where $R_{xy}(\tau)$ is the cross-correlation function of x(t),y(t).

Digital spectral analysis is concerned with the problem of estimating $S_{xx}(f)$ and $S_{xy}(f)$ from sampled time series of finite duration. At the basis of digital auto and cross - spectral estimation is the discrete Fourier transformation. The discrete Fourier transform (DFT), by decomposing a sampled non-periodic function into a finite linear sum of sines and cosines defined at discrete frequencies and sample times provides a mapping from the time to frequency domain. This chapter begins with a brief consideration of the sampling process via the sampling theorem and the phenomenon of aliasing and next deals with a few general considerations

in computing power spectral density. The remainder reviews the so-called direct method of auto and cross-spectral estimation via the Fast Fourier Transform (FFT), a highly efficient computational algorithm for evaluation of the DFT.

4.2 Time Sampling and Aliasing

The representation of a continuous signal s(t) by series of equally spaced samples is based on the well-known sampling theorem of Shannon (1949), (52). This theorem states that a band limited signal containing power from 0 to B cycles per second (Hz) may be reconstructed uniquely in the time domain by discrete signals spaced $\Delta = 1/2B$ apart. To be explicit:

Let s(t) be band limited to frequencies $f < B = 1/2\Delta$ Hz.

Then $$s(t) = \sum_{n=-\infty}^{\infty} \frac{\sin \pi\left(\frac{t}{\Delta} - n\right)}{\pi\left(\frac{t}{\Delta} - n\right)} s(n\Delta) \qquad (4.5)$$

where $s(n\Delta)$ is the n^{th} sample of s(t).

If s(t) contains frequencies greater than B Hz and the sampling interval remains unchanged a phenomenon termed aliasing occurs. Aliasing refers to the process whereby frequencies greater than B Hz are confounded with

frequencies in the range 0 to B Hz. This is an unavoidable problem, particularly with uniform sampling, whereby time samples of a cosine wave could have been obtained from many other cosine waves. This will be illustrated following Enochson and Otnes (53).

Let $S(t)=\cos 2\pi ft$ where $f=B(m+q)$, m integer and $0<q<1$.

Then

$$\begin{aligned} S(n\Delta) &= \cos 2\pi fn\Delta \\ &= \cos 2\pi B(m+q)\, n\Delta \\ &= \cos 2n\pi (m+q) \\ &= (-1)^{m.n} \cos 2\pi q\, Bn\Delta \end{aligned} \qquad (4.6)$$

For m even $S(n\Delta)=\cos 2\pi q\, Bn\Delta$ and f is aliased with qB.

For m odd

$$\begin{aligned} S(n\Delta) &= -\cos n\pi \cos 2\pi q\, Bn\Delta \\ &= \cos (n\pi - 2\pi q\, Bn\Delta) \\ &= \cos (2\pi B(1-q)\, n\Delta) \end{aligned} \qquad (4.7)$$

and f is aliased with (1-q)B. S(t) can therefore be uniquely reconstructed only if it is a band limited signal. Its Fourier components and hence spectra will be unique subject to the same constraint. While this requirement may never be satisfied completely in practice choice of a sufficiently high sampling rate and/or the use of suitable low pass filters before sampling will yield satisfactory results.

4.3 Leakage and Statistical Variability

Two main problems common to either the classic Blackman-Tukey method of spectral estimation or the more modern "direct" approach are: (1) the phenomenon of leakage and (2) the problem of obtaining a statistically efficient estimate.

Problem (1) is a direct consequence of an estimate based on a time series of finite duration. Consider the continuous time definition of the PSD given by equation 4.3,

$$S_{xx}(f) = \int_{-\infty}^{\infty} R_x(\tau) e^{-j2\pi f\tau} d\tau$$

For a finite duration time series of length 2T an estimate of $S_{xx}(f)$ may be obtained from

$$S_{xx}(f) = \int_{-T}^{T} R_{xx}(\tau) e^{-j2\pi f\tau} d\tau \qquad (4.8)$$

$R_{xx}(\tau)$ may be regarded as the product of $R_{xx}(\tau)$ and the so called rectangular lag window $w(\tau)$ defined by

$$w(\tau) = \begin{cases} 1 & |\tau| \leq T \\ 0 & |\tau| > T \end{cases} \qquad (4.9)$$

In virtue of the well known convolution theorem of Fourier Transform theory

$$S_{xx} = \int_{-\infty}^{\infty} w(f') \, S_{xx}(f - f') \, df' \qquad (4.10)$$

where $W(f) = \int_{-\infty}^{\infty} w(t) \, e^{-j2\pi ft} \, dt$

$$= 2T \frac{\sin 2\pi fT}{2\pi fT} \qquad (4.11)$$

$S_{xx}(f)$ may be regarded as $S_{xx}(f)$ viewed through the spectral window $W(f)$.

If $S_{xx}(f)$ were, for example, the Fourier transform of a pure sinusoid of frequency f_o, (considering only positive f):

$$S_{xx}(f) = \frac{A^2}{2} \delta(f - f_o) \qquad (4.12)$$

$S_{xx}(f)$ would be given by:

$$S_{xx}(f) = \frac{A^2 T \sin 2\pi(f - f_o) T}{2\pi(f - f_o)} \qquad (4.13)$$

function centered at $f=f_o$ has become of form $\sin x/x$ due to truncation in the record length. Power is no longer localized at f_o but has leaked into a number of spurious side lobes. Methods of reducing this leakage through either specially designed data windows or their equivalent convolution operation in the frequency domain will be dealt with when direct spectral estimation is considered.

The efficiency of statistical estimators is evaluated on the basis of two criteria: (a) bias and (b) mean square error. Bias, by definition, is the deviation of the first moment or mean of an estimator from the true value of the parameter being estimated:

$$\text{Bias} = E[\hat{\phi} - \phi] = E[\hat{\phi}] - \phi \tag{4.14}$$

Mean square error is the second moment or mean square deviation of an estimator from the true parameter:

$$\text{MSE} = E[(\hat{\phi} - \phi)^2] \tag{4.15}$$

A statistical estimate is said to be consistent if

$$\lim_{T \to \infty} E[(\hat{\phi} - \phi)^2] = 0 \tag{4.16}$$

Statistical uncertainties in an estimate, while mainly

due to the finite length of the time series being estimated and the stochastic nature of the data recorded are also a function of the estimator as will be shown in the next section. In the literature statistical uncertainties are quantified in either of two ways: (a) in terms of normalized standard error or (b) through the confidence interval approach based on the distribution properties of the spectral estimator. In the next section the sample spectrum estimator based on the direct approach will be shown to be an inconsistent estimator and methods for reducing the statistical uncertainty discussed in terms of (a) and (b).

4.4 Direct Auto-Spectral Estimation

Direct digital auto spectral estimation begins with calculation of the discrete Fourier transformation:

$$A_r = \frac{1}{N} \sum_{k=0}^{N-1} x_k \exp\left(\frac{-2\pi jrk}{N}\right) \qquad r = 0,1,\ldots,[N-1] \tag{4.17}$$

x_k is the k^{th} value of the sampled time series of N samples, A_r is the r^{th} complex Fourier coefficient. Based on the discrete Fourier transform a one sided sample auto spectrum may be defined as

$$\hat{S}_{xx}(f_r) = 2N\Delta t \left|A_r\right|^2 \qquad r = 0,1,\ldots,[N/2]$$

$$= 2N\Delta t \; A_r^* A_r$$

$$= 2N\Delta t \left(\frac{1}{N} \sum_{k=0}^{N-1} x_k \exp\left(\frac{2\pi jrk}{N}\right)\right)\left(\frac{1}{N} \sum_{i=0}^{N-1} x_i \exp\left(\frac{-2\pi jri}{N}\right)\right) \quad (4.18)$$

Using a result stated by Bingham et al (54) for x_k real this may be re-expressed in the form.

$$S_{xx}(f_r) = 2\Delta t \sum_{\ell=-N+1}^{N-1} \hat{c}_\ell \cos \frac{2\pi r \ell}{N} \quad (4.19)$$

where

$$\hat{c}_\ell = \left(\frac{1}{N}\right) \sum_{s=0}^{N-\ell-1} x_s x_{s+\ell} \qquad \ell \geq 0 \quad (4.20)$$

c_ℓ is an estimator for the true auto-correlation c_ℓ and

$$\hat{c}_\ell = \hat{c}_{-\ell} \quad \text{for} \quad \ell \leq 0 \quad (4.21)$$

By assuming the N term sequence $\{x_k\}$ a realization of discrete time white noise with variance σ^2 Otnes and Enochson (53) show that $\hat{S}_{xx}(f_r)$ is an unbiased though inconsistent estimator. Consider the first moment or expected value of $\hat{S}_{xx}(f_r)$:

$$E[(\hat{S}_{xx}(f_r))] = 2\Delta t \sum_{\ell=-N+1}^{N-1} \left(1 - \frac{\ell}{N}\right) \hat{c}_\ell \cos \frac{2\pi r \ell}{N} \quad (4.22)$$

Since for uncorrelated white noise $c_\ell = \sigma^2$ for $\ell = 0$ and zero otherwise we have

$$E[\hat{S}_{xx}(f_r)] = 2\Delta t\, \sigma^2 \qquad (4.23)$$

The estimate at f_r corresponds to a bandwidth of $1/N\Delta t$ Hz. Integrating over N/2 independent bands yields a total variance of σ^2. We can conclude that, for white noise at least, $S_{xx}(f_r)$ is an unbiased estimator.

The inconsistency of $\hat{S}_{xx}(f_r)$ has been shown by many authors.

Otnes and Enochson (53) show that the normalized standard error of $\hat{S}_{xx}(f_r)$ for $\{x_k\}$ as defined above is given by

$$\epsilon = \left(\frac{E\left[\hat{S}_{xx}(f_r) - S_{xx}(f_r)\right]^2}{\left|S_{xx}(f_r)\right|^2} \right)^{\frac{1}{2}} = 1 \text{ for } f_r = \frac{r}{N\Delta t} \qquad (4.24)$$

Thus, for Gaussian white noise at least, the standard deviation of an estimate is of the same order of magnitude as the estimate itself. Although the above results are exact only for white noise they can be shown to be approximately true for any normal stochastic process (55). That is

$$E[\hat{S}_{xx}(f_r)] \approx S_{xx}(f_r)$$

$$\text{Var}\left[\hat{S}_{xx}(f_r)\right] \simeq S_{xx}^{\,2}(f_r) \tag{4.25}$$

Another important approach to the problem of statistical error is based on the distribution properties of the sample spectrum estimator. Knowledge of an estimators distribution allows confidence intervals to be constructed for the true parameter.

Consider the discrete sequence A_r r=0,....N/2. The complex sequence $\{A_r\}$ may be decomposed into real and imaginary parts:

$$A_r = \text{Re}(A_r) + j\,\text{Im}(A_r)$$

$$= \frac{1}{N}\sum_{k=0}^{N-1} x_k \cos\frac{2\pi rk}{N} + \frac{j}{N}\sum_{k=0}^{N-1} x_k \sin\frac{2\pi rk}{N} \tag{4.26}$$

If x_k k=1,2.....N is a zero mean uncorrelated Gaussian sequence with variance σ^2 it may be shown that

$$\text{Var}\left[\text{Re}(A_r)\right] = \text{Var}\left[\text{Im}(A_r)\right] = \frac{\sigma^2}{2N} \quad r = 1,2\ldots\frac{N}{2}-1 \tag{4.27}$$

$$= \frac{\sigma^2}{N} \quad r = 0, \frac{N}{2}$$

Also, for any r:

$$E\left[\text{Re}(A_r)\,\text{Im}(A_r)\right] = 0 \tag{4.28}$$

From properties of the chi-squared distribution, (55) p87, it follows that for all r except end points the expression

$$\frac{A_r^* A_r}{\sigma^2_{2N}} = \frac{\hat{S}_{xx}(f_r)}{\Delta t \sigma^2}$$

is distibuted as χ^2_2 ...

While the above result holds exactly only for white noise it may be shown to be approximately true for most non-white non-normal processes (55). The sampling distibution approach will be elaborated further when smoothing is considered.

The problem of leakage in direct spectral estimation is approached through a process termed tapering or equivalently linear modification. Tapering consists of multiplying the time series by a specially designed data window and may be contrasted with quadratic modification or multiplying the correlation function by a lag window in the Blackman-Tukey method. It may also be implemented by an equivalent convolution operation on the DFT but there is usually little to choose between the two approaches computationally. The particular data window employed must be a compromise based

on considerations of allowable leakage, loss of degrees of freedom, and resolution. (Otnes and Enochson (53), Jenkins and Watts (55)). For calculations in this thesis the so called Hanning window was chosen:

$$x'_k = \tfrac{1}{2}(1 - \cos 2\pi\tfrac{k}{N})\, x_k \qquad k = 0,\ldots N-1 \tag{4.29}$$

where x'_k is the k^{th} Hanned sample point. Equivalently the DFT may be convolved according to

$$A_r = -\tfrac{1}{4} A_{r-1} + \tfrac{1}{2} A_r - \tfrac{1}{4} A_{r+1} \tag{4.30}$$

$$B_r = -\tfrac{1}{4} B_{r-1} + \tfrac{1}{2} B_r - \tfrac{1}{4} B_{r+1} \tag{4.31}$$

Use of this window results in a highest side lobe with a peak amplitude considerably less than 1% of the main lobe and secondary lobes falling rapidly to zero.

In direct spectral estimation the variability of the sample spectrum estimator is reduced through either of two basic approaches: (1) averaging over spectra of segmented overlapped records or (2) averaging over a band of spectral components. Method (1), developed by Welch (56), has definite computational advantages when implementing an analysis on a machine with limited core storage and was adopted for the calculations in this thesis. Welch shows that if $\hat{S}_{xx}(f_r)$ is an average of K periodograms calculated

from K segmented records overlapped L-D points then

$$\mathrm{Var}(\hat{S}_{xx}(f_r)) = \frac{S_{xx}^2(f_r)}{K}\left[1 + 2\sum_{j=1}^{K-1}\frac{K-j}{K}\rho(j)\right] \qquad (4.32)$$

L denotes the number of data points per segment; D denotes the number of data points separating the initial points of adjacent segments. $\hat{S}_{xx}(f_r)$ refers to the smoothed or averaged spectral estimator; $\rho(j)$ is a function of D and the particular tapering function employed. It is shown in Welch that: (a) for non overlapping segments the variance of $S_{xx}(f_r)$ is reduced by a factor of K and (b) for a fixed number of data points a near maximum reduction in variance is obtained by overlapping the segments one half their length. For a particular K,D and tapering function it follows from properties of the chi-square distribution that the degrees of freedom of the approximating chi-square distribution may be calculated from

$$\nu = \frac{2\left[E\left[\hat{S}_{xx}(f_r)\right]\right]^2}{\mathrm{Var}\left[\hat{S}_{xx}(f_r)\right]} \qquad (4.33)$$

and a $100(1-\alpha)\%$ confidence interval for the true spectrum $S_{xx}(f_r)$ given by

$$\frac{\nu S_{xx}(f_r)}{Z_\nu(1-\alpha/2)} < S_{xx}(f_r) < \frac{\nu S_{xx}(f_r)}{Z_\nu(\alpha/2)} \qquad (4.34)$$

$z_{\upsilon}(1-\alpha/2)$ and $z_{\upsilon}(\alpha/2)$ are respectively the $1-\alpha/2$ and $\alpha/2$ points on the cumulative chi-squared distribution with υ degrees of freedom (55). It may be shown that as υ increases the confidence band for $S_{xx}(f_r)$ becomes narrower, or in other words $S_{xx}(f_r)$ is less variable. For case (a) above it may be shown that $\upsilon=2K$ an increase of a factor of K over the degrees of freedom of the sample spectrum estimator $S_{xx}(f_r)$.

The decrease in variability achieved may also be considered in terms of the standard error ε of $S_{xx}(f_r)$. The standard error of $S_{xx}(f_r)$ will be given by:

$$\varepsilon = \left[\frac{\mathrm{Var}\left\{S_{xx}(f_r)\right\}}{S_{xx}(f_r)}\right]^{1/2} = \frac{1}{\sqrt{K}} \qquad (4.35)$$

, a decrease in ε by a factor of $1/\sqrt{K}$ over ε for $S_{xx}(f_r)$.

4.5 Direct Cross-Spectral Estimation

For a pair of sampled time series x(t), y(t) consisting of N samples x_k, y_k for k=0, N-1 discrete Fourier transforms A_r, B_r may be calculated in accordance with equation (4.7). A sample cross spectrum $S_{xy}(f_r)$ may be defined by

$$S_{xy}(f_r) = 2\Delta t/N\left|A_r^{*} B_r\right| \quad r = 0,1,\ldots(N/2) \qquad (4.36)$$

The sample cross-spectrum estimator, like the sample auto-spectrum estimator, is a statistically inconsistent estimator. Statistical uncertainties may be reduced by smoothing techniques similar to those discussed in section 4.4. The pair of time series are segmented into K possibly overlapped segments of L points each and K cross spectra calculated from temporally corresponding pairs of segments. The K segments are then averaged to obtain a smoothed cross-spectral estimate $S_{xy}(f_r)$. The smoothed cross-spectral estimate is generally a complex quantity:

$$\hat{S}_{xy}(f_r) = C_{xy}(f_r) + j\,Q_{xy}(f_r) \tag{4.37}$$

or in polar form

$$\hat{S}_{xy}(f_r) = M_{xy}(f_r)\, e^{j\,\hat{\theta}_{xy}(f_r)} \tag{4.38}$$

where

$$M_{xy}(f_r) = \sqrt{C_{xy}(f_r) + Q_{xy}(f_r)} \tag{4.39}$$

and

$$\hat{\theta}_{xy}(f_r) = \tan^{-1}\frac{Q_{xy}(f_r)}{C_{xy}(f_r)} \tag{4.40}$$

The magnitude of the cross spectrum estimate is a quantity of little direct practical use. In practical problems estimates of either the transfer function or squared coherence and phase spectrum, equation 4.40, are more meaningful.

The magnitude squared coherence function γ^2_{xy} is defined in terms of auto and cross spectral densities as

$$\gamma^2_{xy}(f) = \frac{|S_{xy}(f)|^2}{S_{xx}(f)S_{yy}(f)} \tag{4.41}$$

$S_{xy}(f)$ may be shown to satisfy the inequality $|S_{xy}(f)|^2 \leq S_{xx}(f)S_{yy}(f)$ implying

$$0 \leq \gamma^2_{xy}(f) \leq 1$$

The magnitude squared coherence function is analogous to the correlation coefficient in applied statistics and may be interpreted as providing a measure of the linearity between $x(t), y(t)$ as a function of frequency. Methods for estimating $\gamma^2_{xy}(f)$ from finite sampled time series will be dealt with in the next section.

Transfer function estimation for a single input-single output system given by

$$Y(f) = H(f)\,X(f) \tag{4.42}$$

is concerned with estimating H(f) from finite duration sampled time series y(t),x(t). The relevant theoretical spectral relationships are (57):

$$S_{yy}(f) = |H(f)|^2 S_{xx}(f) \tag{4.43}$$

$$S_{xy}(f) = H(f) S_{xx}(f) \tag{4.44}$$

where $S_{xx}(f)$, $S_{yy}(f)$, $S_{xx}(f)$ are cross and auto -spectral densities for y(t),x(t). Obtaining estimates for H(f) from $S_{xy}(f_r)$, $\hat{S}_{xx}(f_r)$, $\hat{S}_{yy}(f_r)$ is of more interest in control and modelling problems than in the data analysis employed in this thesis and will not be developed further.

4.6 Direct Coherence Spectrum Estimation

An estimate for sample coherence $\gamma^2(f)$ based on the sample auto spectrum and cross spectrum estimators is given by

$$\hat{\gamma}^2(f_r) = \frac{|\hat{S}_{xy}(f_r)|^2}{\hat{S}_{xx}(f_r)\hat{S}_{yy}(f_r)} = \frac{|A_r^* B_r|^2}{|A_r|^2 |B_r|^2} \tag{4.45}$$

where A_r and B_r are defined as above. The sample coherence estimator based on the sample auto and cross spectral estimates is identically unity. To obtain consistent coherence estimates properly smoothed auto and cross spectral estimates must therefore be employed in equation 4.45. A consistent coherence spectrum estimator is then given by

$$\hat{\gamma}^2(f_r) = \frac{|S_{xy}(f_r)|^2}{S_{xx}(f_r)S_{yy}(f_r)} \qquad (4.46)$$

Carter et al (58), based on Fishers work on the statistics of the estimate of the squared correlation coefficient, have derived exact expressions for the probability density of the magnitude squared coherence estimator calculated by the method of Welch. Exact expressions for bias and variability of the estimator as a function of true coherence γ^2 and K, the number of disjoint data segments, were calculated and approximations valid for sufficiently large K derived as

$$B(\hat{\gamma}^2) = \frac{1}{K}[1 - |\gamma|^2]^2$$

$$\frac{1}{K}[1 - |\gamma|^2] \qquad (4.47)$$

$$V.(\hat{\gamma}^2) = \frac{1}{K^2} \quad , \quad |\gamma^2| = 0$$

$$= \frac{2\gamma^2}{K} (1 - \gamma^2)^2 \quad , \quad 0 < \gamma^2 \leq 1 \qquad (4.48)$$

These expressions give bias and variability in terms of K and true coherence γ^2. Practical correction factors in terms of the smoothed coherence estimator $\hat{\gamma}^2$ have been developed by Benignus (59).

An improved coherence estimate $\hat{\gamma}_I^2$ is given by :

$$\hat{\gamma}_I^2 = \hat{\hat{\gamma}}^2 - B(\hat{\gamma}^2) \qquad (4.49)$$

where $B(\gamma^2)$, the bias correction factor is calculated from:

$$B(\hat{\gamma}^2) = \frac{1}{K} (1 - \hat{\hat{\gamma}}^2) \qquad (4.50)$$

Enochson and Goodman (60) show the distribution of sample coherences transformed by Fishers z transformation :

$$Z(\gamma) = \tanh^{-1} \hat{\hat{\gamma}} \qquad (4.51)$$

is accurately approximated by a normal distribution. Confidence intervals may therefore be calculated in terms of the mean and standard deviation of the z transformed

smoothed coherence estimates. The mean and variance of z for a single input-single output system are given by (53)

$$\mu_z = \tanh^{-1} \gamma + \frac{1}{K-2} \tag{4.52}$$

$$\tilde{\sigma}_z = \left(\sqrt{\frac{1}{2(K-V)}}\right) [E(\sigma_z)] \tag{4.53}$$

$E(\sigma_z) = 1 - 0.004^{(1.6\hat{\gamma}^2+0.22)}$ is a correction factor derived by Benignus to make $\tilde{\sigma}_z$ valid for $\gamma^2<.3$. Enochson and Goodmans results showed the transformation valid subject to the constraints $K>20$, $.3<\gamma^2<1$. The correction factors developed by Benignus extend the interval downward to essentially zero. Using equations (4.49), (4.51), (4.52) and (4.53), for a measured smoothed coherence $\hat{\gamma}^2$ and given K (1-α) confidence limits for γ will be given by

$$\tanh\left(Z(\hat{\gamma}_I) - \frac{1}{K-2} - \tilde{\sigma}_z z_{\frac{\alpha}{2}}\right) \leq \gamma \leq \tanh\left(Z(\hat{\gamma}_I) - \frac{1}{K-2} + \tilde{\sigma}_z z_{\frac{\alpha}{2}}\right) \tag{4.54}$$

where z_α is the 100α percentage point of the normal distribution.

CHAPTER 5

METHODS

5.1 Subjects

Electroencephalograms were recorded from three groups of dextral subjects whose laterality was assessed by a handedness questionnaire. Subjects were classified as dextral in that, with the occasional exception, they used their right hand for all of the following: writing, throwing a ball, holding a racquet in tennis, squash or badmington, holding a match, cutting with scissors, threading a needle, dealing cards, hammering a nail, unscrewing a jar lid and holding a toothbrush while cleaning their teeth (61). Recordings were also obtained from three sinistrals and one subject classified as right-hemisphere dominant by the neuropsychological test battery in use at the Alberta Hospital. These were not included in the final analyses since, unlike dextrals, the cerebral dominance of sinistrals bears no consistent relationship to their handedness. Staff members and students of the University of Alberta and Alberta Hospital staff members made up the group of normals. Psychotic subjects were drawn from patients diagnosed as schizophrenic or manic-depressive by Alberta Hospital psychiatrists. Subjects were diagnosed as schizophrenic or manic depressive according to formalized diagnostic criteria

advocated by Feighner et al (62). According to these criteria primary affective disorders (mania and depression) and schizophrenia are mutually exclusive disorders. The specific diagnostic criteria of each are documented in (62) but generally speaking mania and depression are disorders characterized primarily by marked disturbances in mood or affect. While the ability of affectives to think and/or concentrate may be altered the changes are usually in degree only. In schizophrenia, on the other hand, there is a characteristic distortion of perception and thinking typically manifested by delusions, hallucinations and verbal production without apparent logical or understandable organization. Changes in affect are secondary to the changes in perception and thinking. Recordings were obtained on a total of 31 normals, 28 schizophrenics, and 20 manic-depressives although all subjects could not be utilized due to missing or contaminated data. The initial recordings made on 9 normal subjects utilized fewer tasks than were employed in subsequent recording sessions and, in addition, lacked data from the temporal areas. Some psychotic subjects were able to complete only a few of the experimental tasks. In other psychotic subjects recordings from a particular task were deemed excessively contaminated by movement artifacts and deleted from the analyses. Mean ages of the subjects were: schizophrenics, 36.7±12.9; manic-depressives,

37.9±11.9; normals, 31.8±11.1.

5.2 Recording Techniques

Monpolar EEG recordings were obtained with platinum needle electrodes inserted subcutaneously at locations T4, P4, T3, P3 and C_z according to the International 10-20 system of electrode placement (63). All electrode potentials were amplified differentially with respect to C_z using Textronix RM122 preamplifiers. The preamplifiers, connected differentially, have an input impedance of 10 megohms. The cable connecting the electode junction box to the preamplifiers was electrically shielded. Preamplifier gains were set at approximately 1,000. Additional gain and bandwidth adjustment was obtained using locally constructed band-pass amplifiers. Total gain required witin the passband of the cascaded system to obtain adequate resolution within the ±2.5 volt input range of the analog to digital converter was normally 80,000. Low amplitude recordings in some subjects, however, necessitated increasing the overall gain of the cascaded system to as much as 50,000. The bandpass amplifier was second order and adjusted for a Butterworth or "maximally flat" response within the passband. The passband of the cascaded system, determined by the upper and lower cutoffs of the bandpass amplifiers was 3-50Hz. Since the preamplifiers also had an adjustable bandpass, with uppper

and lower cutoffs set at .2Hz and 50Hz respectively, overall gain beyond the upper cutoff of the cascaded system fell off at approximately 60 db per decade.

The Hewlett Packard (HP) computer system in operation in the Neurophsiology Laboratory of the Department of Surgery at the University of Alberta was used for data acquisition. Software control of data recording and display was effected by DATAC, a general data acquisition program developed by a member of the laboratory. Data flow into the HP 2100 system began with analog signals from the outputs of the bandpass amplifiers entering an HP 5610 analog to digital converter for digitization. Initially data was digitized at 60 samples per second. Trial recordings on 9 normals employing parietal leads only revealed negligible energy above 20Hz suggesting (in virtue of the Nyquist theorem) 60Hz as a sufficiently high sampling rate for adequately sampled data. Later recordings from psychotics containing considerable high frequency activity necessitated choice of higher sampling frequency. Later recordings were sampled at 120Hz. Following A/D conversion data entered the 2100A where the digitized values were arranged into records of 256 words and recorded on IBM compatible 9 track digital magnetic tape. The digitized analog data channels were also displayed on a Textronix 604 monitor after conversion to analog voltages by an HP 1255B digital to analog converter.

Display of data was effectively simultaneous with it's acquisition and recording. The monitor allowed convenient recognition of gross artifacts and conditions such as open or shorted leads and loose electrodes.

5.3 Procedure

Normals were told that the purpose of the experiment was to study changes in brain activity occurring during tasks designed to engage either their right or left hemisphere predominantly. Patients were informed the procedure was merely another medical test. Subjects answered a handedness questionnaire while electrode locations were measured and electrodes affixed. The subjects were next seated in a straight back chair behind a small table. Electrode leads were then connected to a junction box affixed to the wall directly behind the subject. Signal integrity was verified on the monitor and recording started. The battery of experiments initially consisted of six tasks and finally evolved to a maximum of ten tasks. Patients, however were sometimes too disturbed or uncooperative to complete all ten tasks and only the tasks the individual was willing or able to perform were recorded.

Ten three minute tasks , outlined below, constituted a complete recording session:

1. Eyes Open (EO) Eyes open and the following task, eyes closed, were intended to provide baseline values for the remaining tasks. For the eyes open condition subjects were instucted to sit relaxed, as still as possible, with their gaze fixed on a particular spot on the facing wall trying to "think of nothing in particular".

2. Eyes Closed (EC) This task was essentially a repetition of the initial task with the additional requirement that subjects keep their eyes closed for the three minutes of recording.

3. Verbal Motor (VM) For the verbal motor condition subjects were instucted to write a letter for three minutes. This task and the next were intended to engage the dominant left hemisphere.

4. Verbal Non-motor (VNM) For the verbal non-motor condition normal subjects were instructed to mentally write a letter or mentally recite a favourite poem or speech for three minutes. This proved to be an unsuitable task for psychotics and was replaced by mental arithmetic.

5. Spatial Motor (SM) This task and the following were visual spatial in nature and designed to engage the non-dominant right hemisphere. For the spatial motor condition subjects were first given one minute to memorize a geometric

pattern consisting of a three by three checkerboard arrangement of blank and lined squares with lines of varying orientation. EEG activity was monitored but not recorded during this minute. Immediately following the minute of memorization subjects were given three minutes to reconstuct the pattern from nine separate squares. They were instructed to scramble the squares and repeat reconstruction if they completed the pattern before three minutes had elapsed. Completion of the pattern before three minutes elapsed was a common situation in normals.

6. Spatial Non-motor (SNM) for the spatial non-motor condition subjects were presented with two sheets of paper: one contained a group of arbitrary geometric shapes, the other the same shapes sectioned into a number of subshapes in a jigsaw puzzle fashion. The subjects were instructed to mentally attempt to assemble the subshapes into their composite forms. The subshapes were deliberately designed not to fit together perfectly into thir composite forms to ensure concentration of a subject for three minutes of recording.

Three spatial-tactile tasks constituted the next portion of the experimental session:

7. Formboard Left-Hand (FBL)

8. Formboard Right Hand (FBR)

9. Formboard Both Hands (FBB)

All three tasks were recorded with eyes closed. Before recording commenced the subjects preference for either holding their own eyes closed for nine minutes or blindfolding was ascertained and the nature of the tasks briefly explained. The tasks involved matching ten solid geometric shapes randomly arranged on the table directly in front of the subject to corresponding recessed locations on a formboard. The matching was attempted first individually with the right then left hands and then with both. Tactile perception of the geometric shapes and corresponding recessed locations on the formboard were the sole sensory cues. During FBR the subjects tendency for either predominantly left or right handed exploration of the formboard was noted.

10. Location and Memory For the final task subjects were handed a pencil and blank sheet of paper and given up to three minites to sketch the formboard as they had recollected it. They were instructed to pay attention both to the geometry of the particular shapes and also to the shapes relative location on the formboard.

CHAPTER 6
DATA ANALYSIS

This chapter first describes the manner in which the methods of spectral estimation outlined in chapter 4 were applied to the data recorded by the procedure outlined in chapter 5. Techniques of spectral estimation were applied to the data in two basic ways: (1) to obtain estimates of auto and cross spectra and (2) to obtain a measure of the variability of EEG power as function of time. EEG spectral parameters based on the results obtained from (1) and (2) were employed to investigate significant task dependent and intergroup EEG asymmetries. The remaining portion of the chapter outlines the statistical techniques employed to test the significance of task dependent and intergroup [illegible] differences. The spectral and statistical calculations employed were all performed by HP FTN4 programs executing in a DOS environment.

6.1 Auto and Cross Spectral Estimates

The first program to be described calculated auto spectra for EEG's recorded from the electrode locations P3, P4, T3, and T4 and cross spectra for the lead pairs P4-T4, P3-T3, P4-P3, and T4-T3. A floating point algorithm of the

FFT, adapted from Monro (64), was utilized. For both auto and cross spectral estimates 256 point sub-records were employed in the FFT. This resulted in segmentation of a 3 minute data record into 42 subrecords when sampling at 60 Hz and segmentation into 84 sub-records when sampling at 120 Hz. Subrecords were linearly modified by the cosine bell or Hanning window before transformation. Spectral resolution, (the spacing between successive spectral estimates) was approximately .25 Hz for 60 Hz sampling and approximately .5 Hz for 120 Hz sampling.

The program calculated an average auto-spectrum and cross-spectrum for each three minute data file for the leads and lead pairs described above. During program execution the average auto and cross spectra for each file were stored on an HP 2870 magnetic disk. When a specified number of data files had been analyzed (usually a complete reel of magnetic tape) the average auto and cross spectra were written onto a separate magnetic tape from the disc. Other programs used the average auto and cross spectra for plotting purposes and also to derive spectral parameters for detecting intertask and intergroup EEG differences. The spectral parameters used will be described in later paragraphs.

6.2 Variability Calculations

Three minute data files were segmented and the subrecords transformed as described in the preceding section. Estimates for the variability of the power spectral density in 5 bands [redacted] successive epochs of approximately 12 second length were obtained in the following fashion:

(a) for records sampled at 60 Hz the spectra from 3 successive Hanned 256 point subrecords were summed to obtain an estimate for the spectra of an approximately 12 second epoch. For records sampled at 120 Hz 6 successive subrecords were similarly employed.

(b) For a given 12 second epoch, for each of 5 bands, adjacent spectral estimates were added together to obtain an estimate for the total power witin each band the bands employed were Theta (4-7) Hz, Alpha (7-13) Hz, Beta (13-20) Hz, Gamma (20-30) Hz and "Total Power" (4-30) Hz.

(c) For each approximately 3 minute data file the coefficient of variability of successive 12 seconds epochs from each of the four leads was calculated for each of the bands. The coefficient of variability is defined by:

$$\hat{C.V.} = \frac{S.D.(B_K)}{B_K}$$

B_K and $S.D.(B_K)$ are respectively the mean and standard deviation of estimates of power in the k^{th} band.

6.3 Derived Spectral Parameters

(a) Right to Left EEG Power Ratios Following Galin and Ornstein (13) task dependent EEG asymmetry was intially investigated by calculating right to left (R/L) EEG power ratios. R/L power ratios were calculated for homologous parietal and temporal leads in the left and right hemisphere. Parietal and temporal ratios were denoted P4/P3 and T4/T3 respectively. In virtue of the findings of previous investigators (10), (11), (12), (13), and (15) as well as qualitative inspection of trial recordings and spectral plots, R/L ratios were calculated for the bands described in section 6.2(b) with the exception of the "total power" band. Frequencies less than or equal to 4 Hz were omitted to eliminate the effect of slow movement artifacts, eye roll and eye blink artifacts . Using the average auto-spectra, R/L average power ratios for the lead pairs and bands described above were calculated by summing adjacent spectral coefficients within a band for two leads then determining the R/L ratio of the band powers obtained. The ratios were calculated by the computer during a portion of the same program that plotted the average spectrum for the four regions on a Textronix 4010 graphics display terminal. Hard copy reproduction of the plots was available from a Textronix 4610 hard copy unit.

(b) Coherence Estimates The average cross spectra and auto spectra stored on magnetic tape for each data file were used to estimate the alpha band coherences between the lead pairs P4-P3, T4-T3, P4-T4, and P3-T3 . Estimates were calculated by formula 4.46 of section 4.6. Before substitution in the formula the cross-spectral and auto-spectral estimates were further smoothed by digitally filtering the estimates using the triangular weighting function $a(l) = .1a(l-1) + .8a(l) + .1a(l+1)$. Auto-spectra and cross-spectra were smoothed by 20 passes of the filter. The coherence differences were used to investigate further the task dependent asymmetry revealed by differences in R/L alpha ratios. For each group of subjects, coherence asymmetries between verbal and spatial tasks were investigated by (a) testing for significant intertask coherence differences for each lead pair separately and (b) for each task, by testing for coherence differences between the four lead pairs used. The non-motor tasks were used for this investigation.

(c) Normalized Auto Spectral Power Intergroup comparisons were also made on the basis of the relative amounts of energy in selected EEG bands. Qualitative inspection of both the raw EEG traces and spectral plots indicated that the greatest difference between normals and psychotic groups was in the amount of high frequency

activity present, especially in the temporal regions. Following Sklar and Hanley (65) relative amounts of power in selected EEG bands were calculated by normalizing the power in a given spectral band by the power in the signal in the frequency range (4-30) Hz. Utilization of a relative rather than an absolute measure of EEG power was chosen to allow comparisons based on differences in the shape of a subjects EEG spectrum rather than the absolute amount of energy in a given band. The effect of possible amplifier gain variations among the channels, for example, is eliminated by this approach. Other advantages of relative over absolute measures have been given by Matousek, 1967 (66).

6.4 Statistical Techniques

The statistical tests employed to detect both intragroup and task dependent intergroup EEG asymmetries utilized techniques from both classical parametric statistics and non-parametric or distribution free statistics. The following paragraphs will (a) compare briefly parametric and non-parametric methods and, (b) & (c), outline the statistical tests utilized in the analysis.

(a) Parametric Versus Non-parametric Statistics

Parametric and non-parametric statistical tests differ with respect to both (1) the strength of the measurement scale

applied to the data to obtain scores for statistical analysis and (2) the assumptions regarding parameters of the population from which the samples were drawn. The idea of a measurement scale, will be explained first followed by consideration of the assumptions underlying the parametric and non-parametric tests.

Siegel (68) defines measurement as the process of mapping or assigning numbers or symbols to objects or observations, and discusses four scales of measurement and the statistical analysis possible with each scale of measurement. The four scales discussed are (a) nominal, (b) ordinal, (c) interval and (d) ratio. A nominal scale of measurement occurs when symbols have been assigned to objects or observations simply to classify them. Siegel mentions the psychiatric system of diagnostic groups where a person is classified as schizophrenic or manic depressive, for example, as constituting a nominal scale. An ordinal scale exists where numbers or symbols have been assigned in such a way that scaled objects or observations are not just different in a nominal sense but also stand in some kind of releationship to each other. An employee classification scale with, say, technicians or technologists I to IV exemplifies an ordinal scale. The members of each classification are not only different from each other but stand in some sort of relationship to each other; e.g.

Technician II >Technician I . Measurement on an interval scale occurs when a scale has all the characteristics of an ordinal scale and additionally the distance between any two points on the scale is known although the zero point and unit of measurement are arbitrary. The Fahrenheit and centigrade temperature scales are examples of interval scales. A ratio scale is one with all the characteristics of an interval scale plus a true zero point. Many measurement scales in the physical sciences are ratio scales; mass, velocity, resistance, for example. More abstract definitions of the various measurement scales and a discussion of the statistics possible with each one of them are to be found in (68) and will not be pursued further here except to mention that measurement on at least and interval scale is necessary before parametric tests can be used. The quantification of the EEG discussed in sections 6.1 to 6.3 satisfied the requirements of at lest an interval scale and consequently other considerations are the deciding factor in choosing between a parametric and non-parametric test.

Parametric tests, for example the analysis of variance and the various t-tests, assume (a) normally distributed populations, (b) homogeneity of variances, and (c) independence of observations in addition to the measurement scale requirement mentioned above. In addition most models of analysis of variance assume: (d) additivity of effects

due to factors. Expressed equivalently means of populations must be linear combinations of effects due to factors hypothesized as significant in the design analyzed. For example in a two way analysis of variance where, say, independent samples of N individuals were each subjected to one of t different treatments under c different conditions variables representing measurements on each individual are assumed expressible in the form:

$$x_{ijk} = \mu + T_i + C_j + \gamma_{ij} + \varepsilon_{ijk} \qquad \begin{matrix} i=1,2....t \text{ (Treatments)} \\ j=1,2....c \text{ (Conditions)} \\ k=1,2....N \text{ (Samples)} \end{matrix}$$

μ is the hypothesized common population mean. T_i is the added effect of the i^{th} treatment. C_j is the added effect of the j^{th} condition. γ_{ij} represents a possible interaction term between the i^{th} treatment and j^{th} condition. ε_{ijk} is an error term. Although parametric tests are strictly valid only when the above assumptions are met studies have shown that departures from some of the assumptions do not affect the conclusions of a test markedly. According to Sokal and Rolf (67) the consequences of non-normality of a distribution are not too serious and only a very skewed distribution would have a marked effect on the significance level of a parametric test. Homogeneity of variances is a

more critical assumption but can be readily checked by the F-Test for a two sample analysis or Bartletts Test for Homogeneity of Variances for more than two groups. In situations where the assumptions of a parametric test are not met, as in some of the comparisons made in this thesis, two alternatives are possible. Alternative one consists of transformation of the data. Data not satisfying the requirements of a parametric test will often do so after a common mathematical transformation is performed; taking logarithms or square roots for example. The analysis of variance performed on R/L ratio data was performed on the logarithms of the ratios. As a second alternative a distribution free statistical test may be employed. Distribution free tests compare populations without the use of population parameters such as the mean and the variance. Hence, these tests are also called non-parametric tests. Most require only independence of observations and underlying continuity of the variable under study. Unlike parametric tests the accuracy of probability statements obtained from most non-parametric tests does not depend on the shape of the underlying distribution of the sampled population. They may assume, for example, identity of shape of two or more population distributions or a symmetrical distribution but the exact shape of the distribution need not be known. For non-normal populations with distributions

whose optimum location parameters are not means, distribution free tests will detect differences in location more readily than parametric tests (68). The term location parameter is used here in the sense of a measure of central tendency. The arithmetic mean, geometric mean, harmonic mean, median and mode are examples of statistics of location. For a normal population the arithmetic mean is also the median and mode and is the "optimum" measure of location. For non-normal asymmetric populations other statistics of location may give a more intuitively meaningful index of a populations center. Distribution free tests have the additional advantage of being applicable to data in ordinal form. Since many distribution free tests are based on the nuberical ranks of measurements and not on their absolute values, measurement on an interval scale is not a prerequisite to their use.

Non-parametric tests are not without some disadvantages. They have the disadvantage of being more wasteful of data than parametric tests when the underlying assumptions required for the latter are satisfied. Relative to a parametric test a non-parametric test requires more samples to achieve the same power (ability to reject a false null hypothesis) when the underlying assumptions of the parametric test are satisfied. However only about 5 to 10 percent more samples are required. An additional disadvantage arises in testing for interaction. Interaction

occurs when the joint effect of two variables differs from the sum of their separate effects. The joint effect of two drugs for example may be considerably different from the sum of their separate effects. In a parametric analysis of variance tests for such interactions are straightforward to make. This is not the situation with regard to non-parametric tests. Bradley (69) remarks that tests for interaction by non-parametric methods tend to be "complicated, awkward, and limited in application."

(b) Non-parametric Tests The non-parametric alternatives to the most widely used classical parametric tests are based on a principle initially conceived by R.A. Fisher. The principle, denoted the Method of Randomization is explained in detail in (69) and will not be elaborated further here. The tests are based on statistics derived by application of the principle to the size ranks of a set of experimental observations. The size ranks of a set of n observations are obtained by ranking the observations in order of size and assigning the integers 1 to n to the observations from either largest to smallest or vice versa. Both two sample and multi sample tests of "location" for either matched or independent samples have been derived. The two sample Wilcoxon Matched Pairs Signed Ranks Test and the Mann-Whitney U Test were applied to the results presented in this thesis. Their rationale will be breifly explained

below.

As applied in this thesis the Wilcoxon Matched Pairs Signed Ranks Test was used to test the null hypothesis that treatments X and Y applied to n individuals have identical effects against the alternative hypothesis that treatments X and Y produce (1) symmetric populations differing in location or (2) asymmetric populations differing in any way. Let X_i and Y_i be measurements on the i^{th} individual subsquent to treatments X and Y. If the null hypothesis is true then the population of difference score variates $X_i - Y_i$ should be symmetrically distributed about zero. For each $X_i - Y_i$ obtained there was an equally probable $X_i - Y_i$ value having the same value but opposite sign. Let S_i denote the algebraic sign of the difference score and R_i the rank of $|X_i - Y_i|$ in increasing order of size. Under the null hypothesis each of the 2^n possible assignments of the S_i to the n ranks R_i was as probable a priori as the actually obtained set of signed ranks $S_i R_i$. A test statistic given by

$$W_+ = \sum_{S_i = +} S_i R_i$$

or its complementary statistic

$$W_- = \sum_{S_i = -} S_i R_i$$

may be calculated for each of the 2^n possible sets of n ranks and a null distribution for W_+ obtained. The null distribution of W_+ has been tabulated extensively. The value

of W_i actually obtained from n $X_i - Y_i$ differences due to treatments X and Y may be compared to the null distribution of W_i to test for differences in treatment effects X and Y. W_i would be expected to lie in an extreme portion of its null distribution if treatments produced effects causing differences $X_i - Y_i$ to lie consistently in one direction.

The next test to be described, Wilcoxon's Two Sample Test For Independent Populations, is a non-parametric test for identical populations which is sensitive to unequal locations. It's parametric counterparts are found in the t sample t test for independent samples or a one-way classification analysis of variance for two samples. Assume the two populations to be tested for identity consist of n samples from a population X and m samples from a population Y where m>n. Under the null hypothesis, H_0, of identical populations the n obtained samples of population X and the m obtained samples of population Y are one of $\binom{n+m}{n}$ a priori equally probable selections of subsets of m and n observations from the combined sample of n+m observations. Wilcoxon's two sample test employs the test statistic $W_n = \sum_{i=1}^{n} R_i$ where R_i is the size rank of X_i in the combined sample of m+n observations. Under the null hypothesis for each of the equally likely $\binom{n+m}{n}$ selections of n and m observations there exists a value of W_n. Their frequency distribution under the null hypothesis defines the null

distribution of W_n. The value of W_n obtained for the actual experimental data may be compared with the null distribution of W_n, if the W_n obtained falls in an extreme portion of the null distribution of area α H_0 may be rejected at a significance level of α. The test is especially sensitive to differences in location between the two populations. Consistently larger values of population X would tend to yield a correspondingly large W_n while consistently smaller values tend to a correspondingly small W_n. The statistical test actually programmed for use was an equivalent test called the Mann-Whitney U-Test. The Mann-Whitney U statistic is related to W_n by

$$U=n(n+1)/2+nm-W_n$$

(c) Parameteric Techniques Parametric statistical techniques utilized were: (a) analysis of variance and (b) discriminant analysis. Univariate analysis of variance was implemented on the HP 2100S computer system in the neurophysiology laboratory of the Department of Surgery. The routine used was adapted from a program written by Rohlf (67) and was designed to perform either a single classification or nested analysis of variance for multiple groups with differing sample sizes. Included in the program was the facility to perform various common mathematical transformations to the data before the analysis of variance

was performed. A second routine, a factorial analysis of variance, was adapted from the IBM Scientific Subroutines Package. The program was designed primarily to analyze the experimental design known as a factorial design, but, by pooling various terms in the analysis variance table produced as output by the program, analysis of other experimental designs is possible. The analyses possible are restricted to groups with identical sample sizes.

Discriminant analysis is a multivariate statistical procedure used to classify an individual into one of two or more groups on the basis of a set of m measured attributes. Geometrically the m measured attributes may be visualized as defining a point in m dimensional space. If two or more groups are disparate with respect to these measured attributes the groups of points in m space corresponding to groups of individuals in distinct categories will tend to cluster into distinct regions. The Discriminant Analysis program in the IBM Scientific Subroutines Package, MDISC, was adapted for the calculations. The program was applied to the three groups of subjects to test for both intra group differences between verbal and spatial modes of thinking and intergroup differences during a given experimental condition. Program calculations follow Andersen 1958 (70). The analysis implicitly assumes the m parameters characterizing individuals in the ith group constitute an m

dimensional multivariate normal distribution with probability density function given by

$$p_i(x) = (2\pi)^{-m/2} |\Sigma_i|^{-1/2} \exp\left[-\tfrac{1}{2}(x-\mu_i)' \Sigma_i^{-1} (x-\mu_i)\right] \qquad (6.1)$$

Σ_i the covariance matrix for the i^{th} population. μ_i is the vector of means for the i^{th} population. For a two group discriminant analysis, assuming the [illegible] misclassification are equal, it can be shown that optimum classification in the sense of minimizing the probable [illegible] classification is achieved by the following rule. Let P_1, P_2 denote the two populations and $p_1(x), p_2(x)$ their respective probability density functions. Let the unknown individual to characterizedby a vector x of m observed attributes. The decision rule is:

$$\frac{p_1(x)}{p_2(x)} \qquad (6.2)$$

The unknown individual is assigned to P_1 if $p_1(x) > p_2(x)$ and to P_2 otherwise. For classification into one of more than two groups a similar decision rule is applied. Probability density functions are compared on a pair by pair basis and

the individual assigned to the population P_i for which $p_i(x)$ is largest. For a multivariate distribution, which the program assumes, (6.) is replaced by a decision rule derived by taking natural logarithms of the probability density function. The equivalent rule can readily be shown to be given by

In most practical situations discriminant analysis is used to test for differences between groups hypothesized as different. This is the analysis dealt with by MDISC. In this situation the true probability density functions are unknown and are replaced by probability density estimates. (6.) or it's extension to more than two groups is applied to the groups employed in the analysis. If the groups are widely separated most observations from population P_n will be classified as members of P_n. If the groups are strongly overlapping individuals from a given population will be classified randomly into other populations.

CHAPTER 7

RESULTS

7.1 Task Related R/L Power Ratio Asymmetries

R/L EEG power ratios were compared between verbal and spatial tasks for the theta, alpha, beta, and gamma bands as previously defined. The statistical significance of task related differences was determined separately for motor and non-motor tasks by the Wilcoxon Matched Pairs Signed Ranks Test and also two way analysis of variance (ANOVA) for "paired comparisons". Figures 7.1(a) and 7.1(b) are the spectral plots of a normal individual who displayed marked EEG asymmetries during performance of verbal and spatial tasks. In this subject alpha band asymmetries are particularily obvious, especially in the temporal regions. In the spatial tasks the alpha energy in the right hemisphere is suppressed relative to the alpha energy in the left hemisphere; in the verbal tasks the converse is true. Figures 7.2(a)-7.2(d), 7.3(a)-7.3(d), 7.4(a)-7.4(d) show the average R/L power ratios in the theta, alpha, beta, and gamma bands for normals, schizophrenics, and manic depressives. Tasks were coded as follows; VM-Verbal Motor, SM-Spatial Motor, VNM-Verbal Non Motor, SNM-Spatial Non Motor, and MA-Mental Arithmetic. Tables 7.1(a) to 7.1(c) give the means, standard deviations and two tailed values

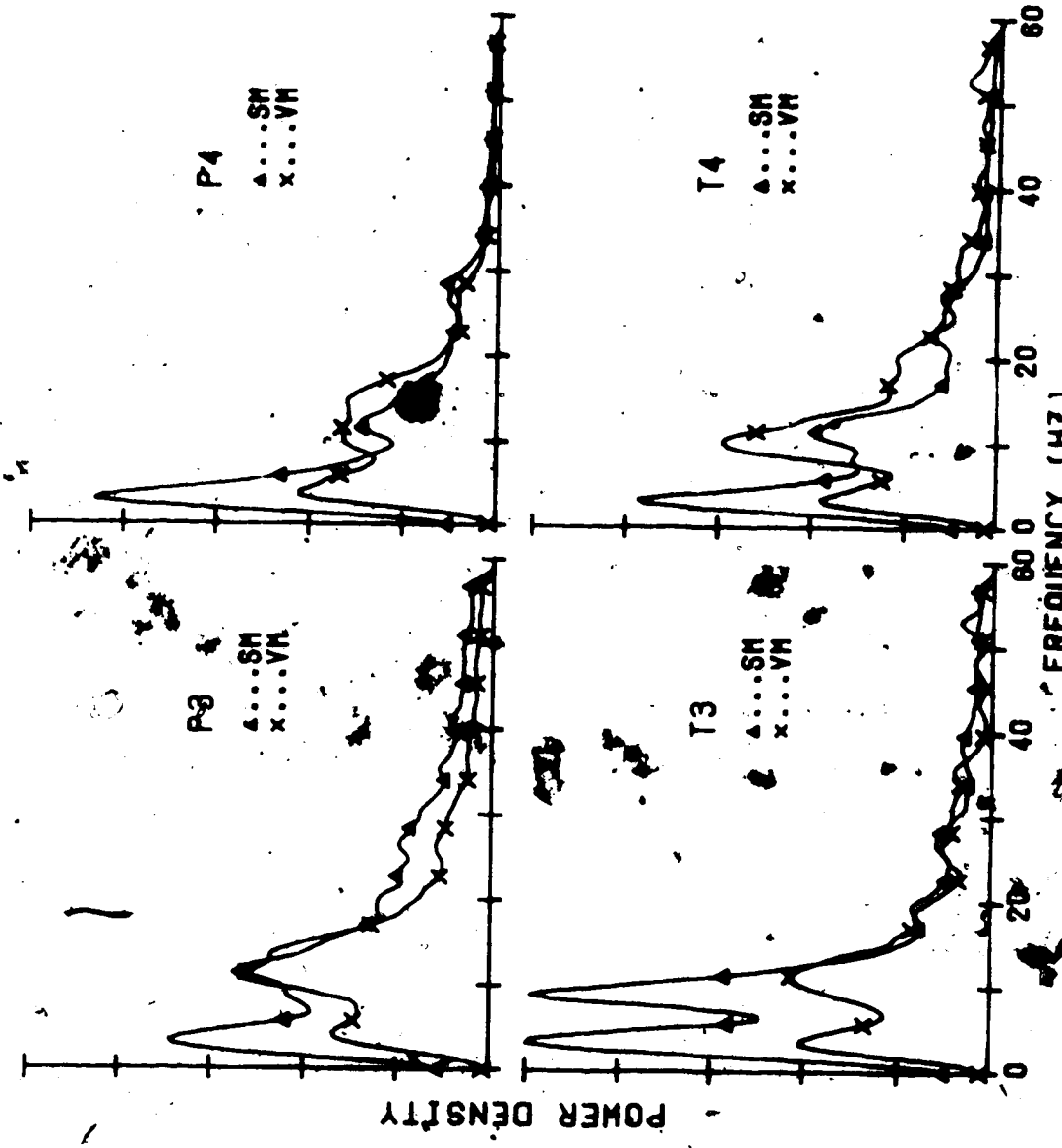


Figure 7.1(a) Power Spectra of the EEG from a Normal Human Subject During the VM and SM Tasks

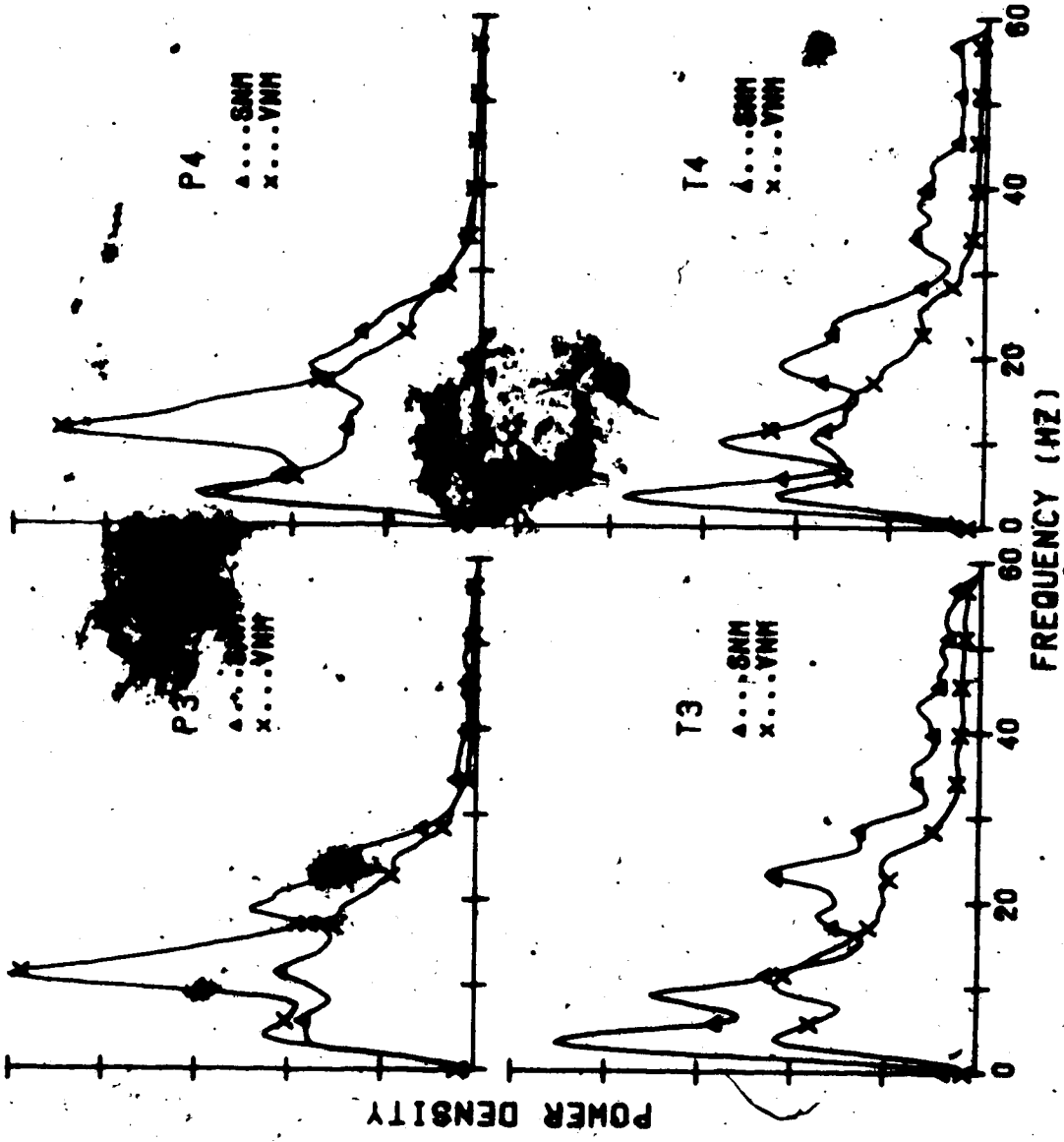


Figure 7.4(b): Power spectra of the EEG from a Normal Human Subject During the VNM and SNM Tasks

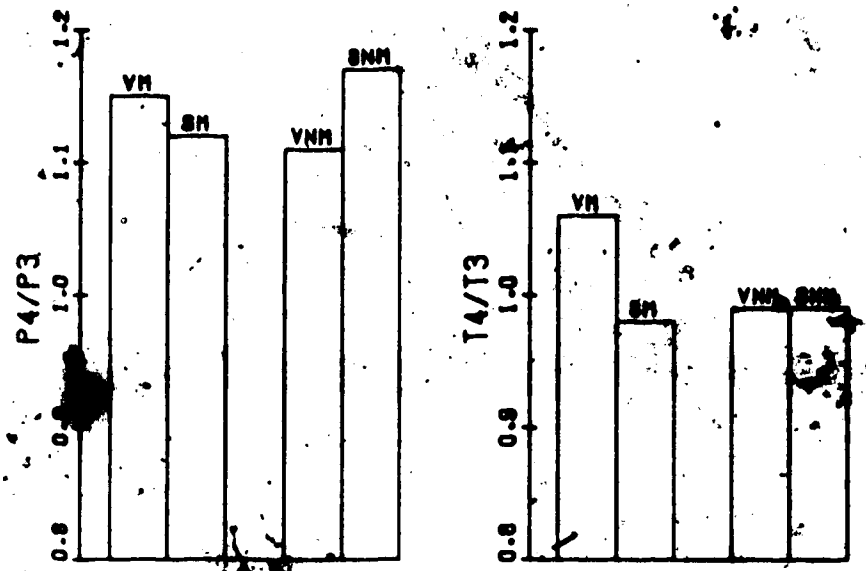


Figure 7.2(a) Average Theta Band R/L EEG Power Ratios For Normals (Bar codes in Sec. 5.3)

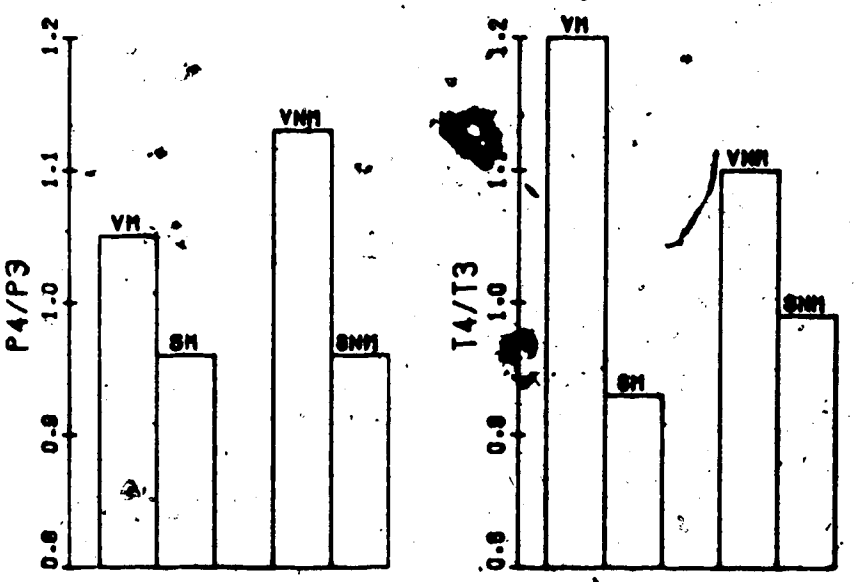


Figure 7.2(b) Average Alpha Band R/L EEG Power Ratios for Normals (Bar codes in Sec. 5.3)

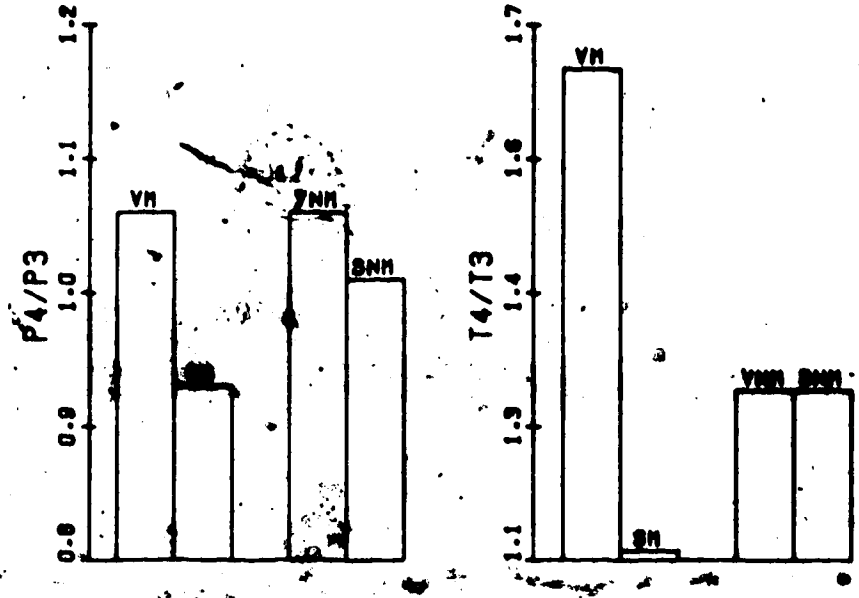


Figure 7.2(c) Average Beta Band R/L EEG Power Ratios For Normals (Bar codes in Sec. 5.3)

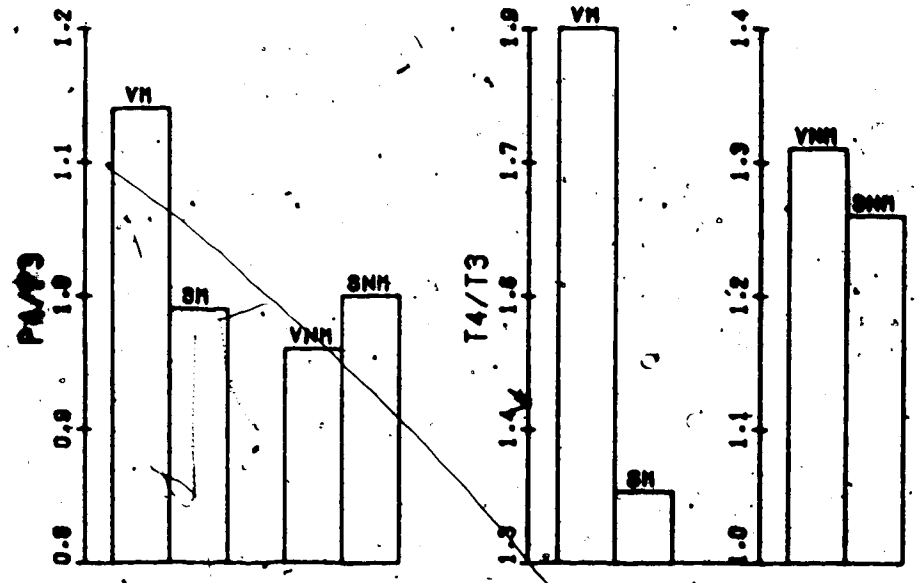


Figure 7.2(d) Average Gamma Band R/L EEG Power Ratios for Normals (Bar codes in Sec. 5.3)

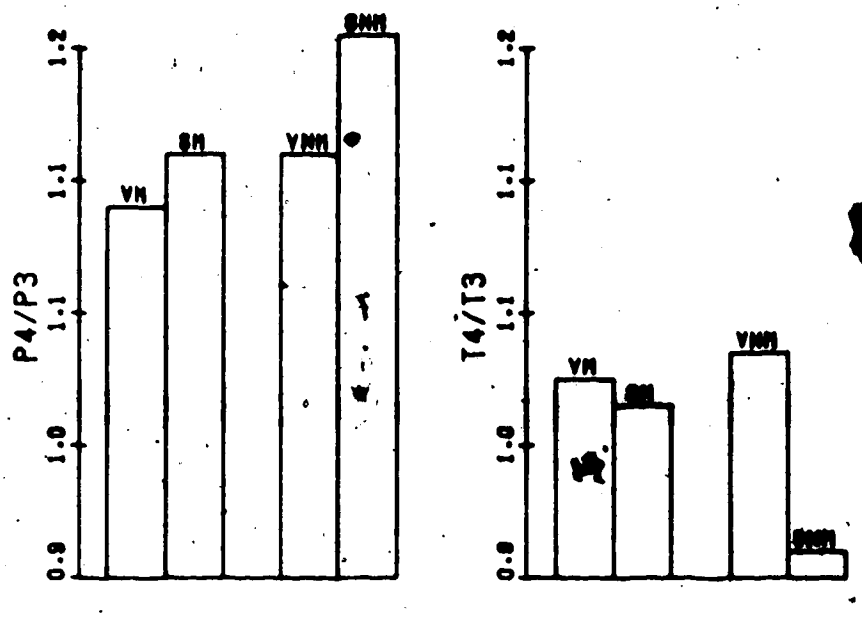


Figure 7.3(a) Average Theta Band R/L EEG Power Ratios for Schizophrenics (Bar codes in Sec. 5.3)

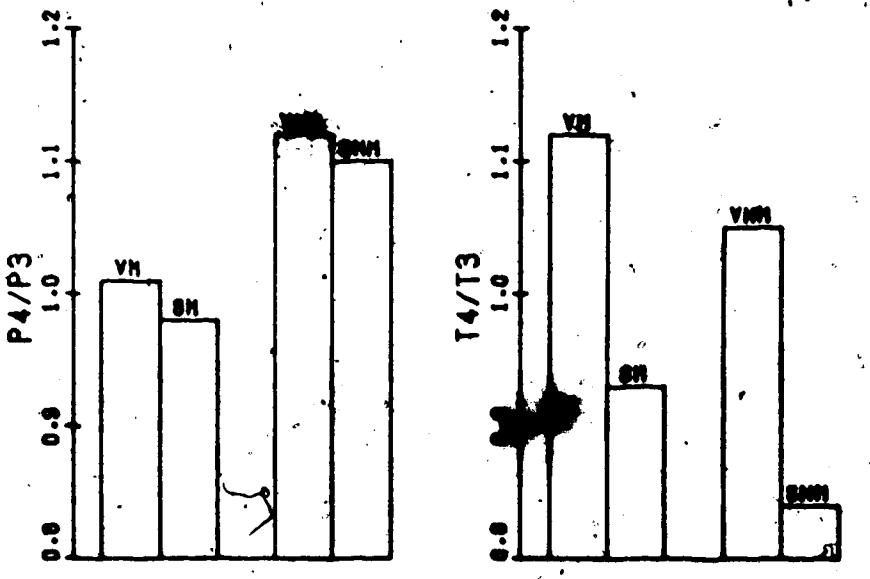


Figure 7.3(b) Average Alpha Band R/L EEG Power Ratios for Schizophrenics (Bar codes in Sec. 5.3)

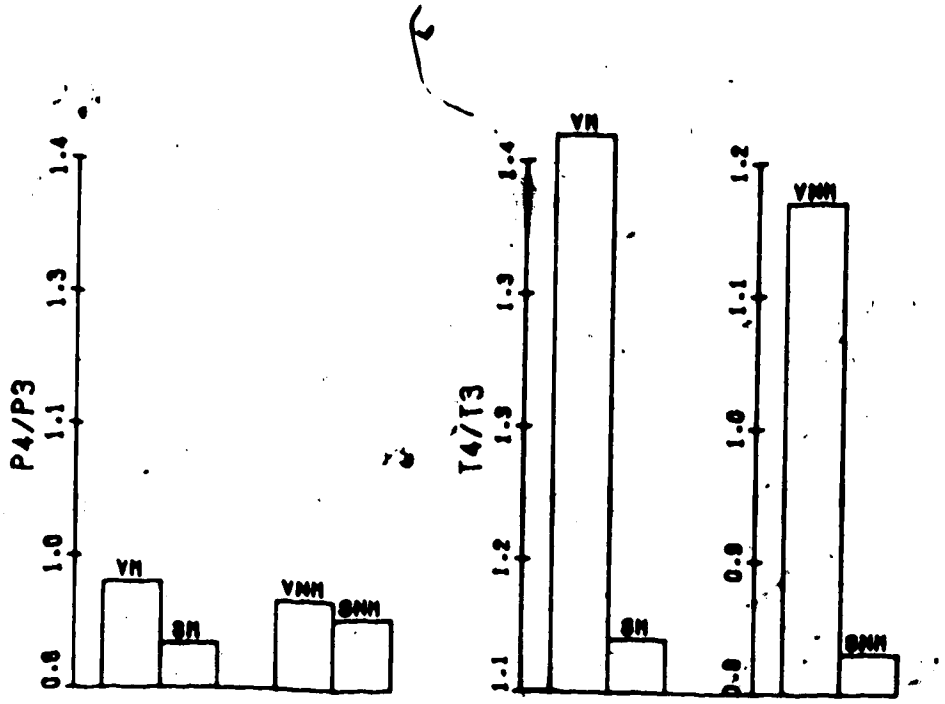


Figure 7.3(c) Average Beta Band R/L EEG Power Ratios for Schisophrenics (Bar codes in Sec. 5.3)

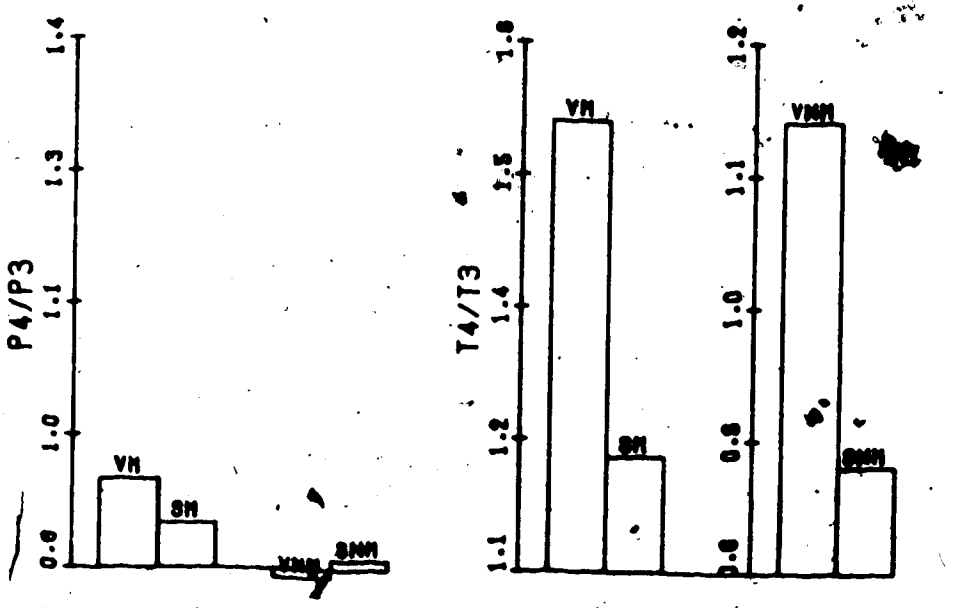


Figure 7.3(d) Average Gamma Band R/L EEG Power Ratios for Schisophrenics (Bar codes in Sec. 5.3).

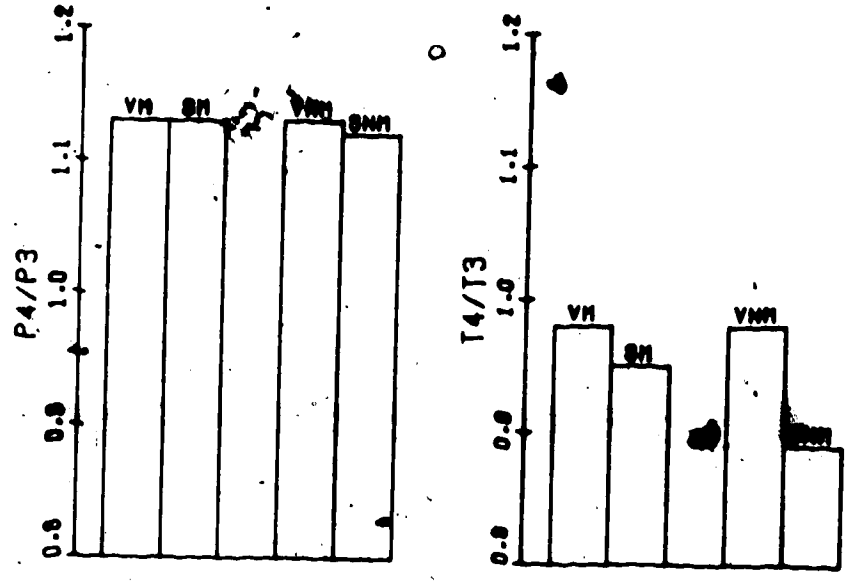


Figure 7.4(a). Average Theta Band R/L EEG Power ratios for Manic Depressives (Bar codes in Sec. 5.3)

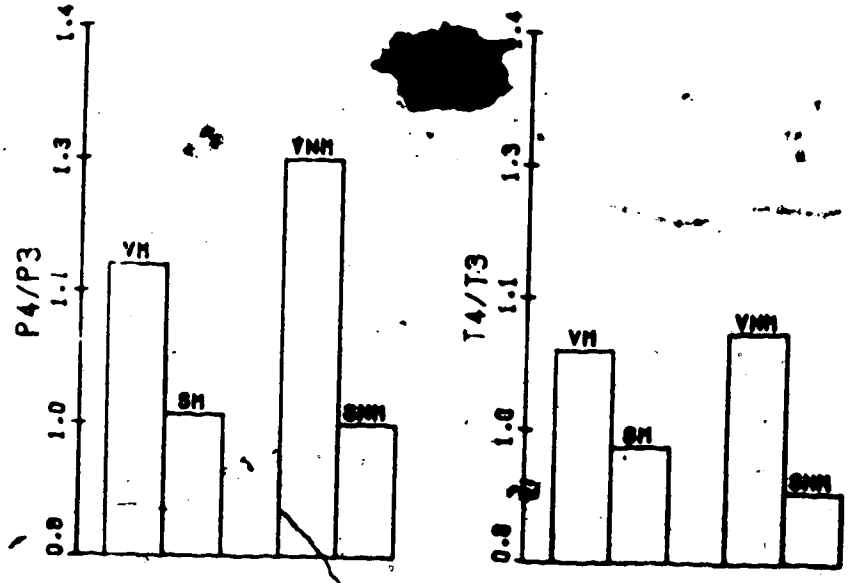


Figure 7.4(b) Average Alpha Band R/L EEG Power ratios for Manic Depressives (Bar codes in Sec. 5.3)

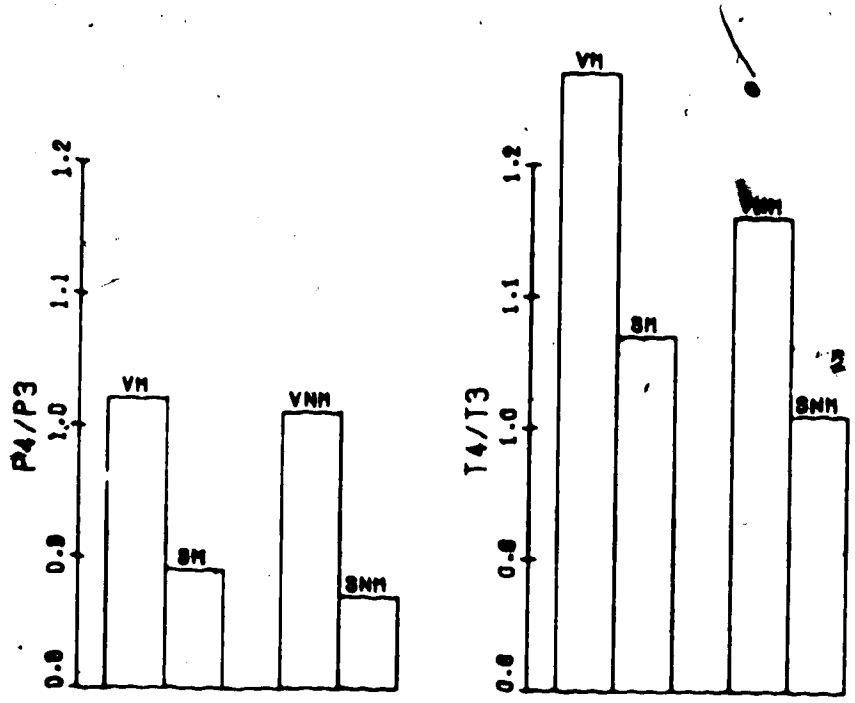


Figure 7.4(c) Average Beta Band R/L EEG Power Ratios for Manic Depressives (Bar codes in Sec. 5.3)

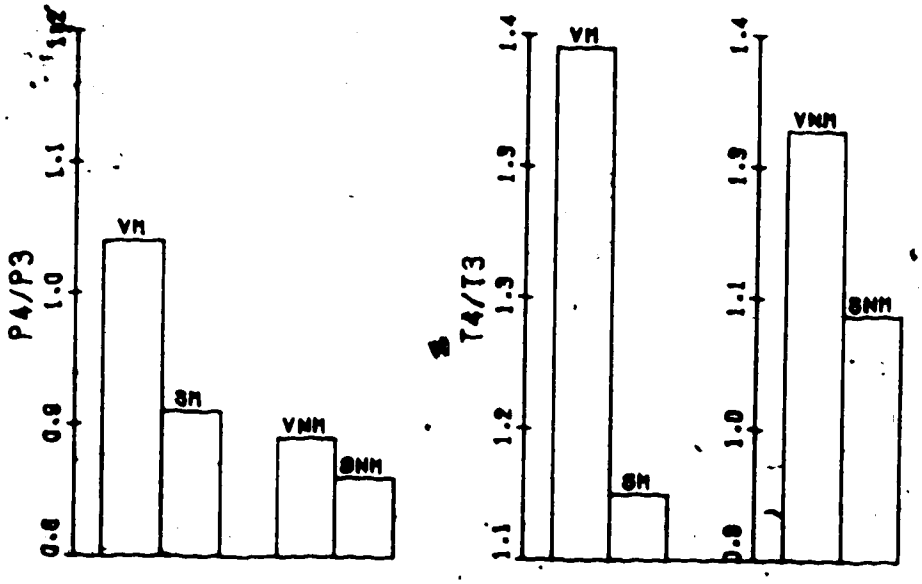


Figure 7.4(d) Average Gamma Band R/L EEG Power Ratios for Manic Depressives (Bar codes in Sec. 5.3)

PARIETAL RATIOS P4/P3								
TASK	THETA		ALPHA		BETA		GAMMA	
VM	1.15±.12		1.05±.33		1.06±.27		1.[illegible]±.5	
SM	1.12±.09		0.96±.19		0.93±.31		0.[illegible]±.5	
VNM	1.11±.09		1.13±.2[illegible]		1.06±.2[illegible]		0.9[illegible]±.26	
SNM	1.17±.11		0.96±.19		1.01±.2[illegible]		1.00±.29	
	+	*	+	*	+	*	+	*
M	ns	ns	.05	.05	.001		.025	.018
NM	.10	.056	.01	.016	ns		ns	ns

TEMPORAL RATIOS T4/T3								
TASK	THETA		ALPHA		BETA		GAMMA	
VM	1.06±.16		1.2±.30		1.65±.76		1.90±1.13	
SM	0.98±.16		0.93±.25		1.22±.67		1.38±1.05	
VNM	0.99±.11		1.10±.22		1.29±.53		1.31±.80	
SNM	0.99±.13		0.99±.20		1.29±.65		1.26±.81	
	+	*	+	*	+	*	+	*
M	ns	ns	.005	.004	.005	.008	.01	.019
NM	ns	ns	.10	.09	ns	ns	ns	ns

Table 7.1(a) Mean R/L EEG Power Ratios±Standard Deviations and Significance Values For Intertask Differences in Normals. The rows labelled M and NM contain the significance values of verbal versus spatial comparisons for pairs of tasks of the indicated modality, either motor or non-motor.

+ Significance Value for "paired comparisons" ANOVA

* Significance Value for Wilcoxon Matched Pairs Signed Ranks Test

PARIETAL RATIOS P4/P3

TASK	THETA	ALPHA	BETA	GAMMA
VM	1.13±.1	1.01±.17	0.92±.3	0.90±.42
SM	1.17±.14	0.98±.51	0.85±.23	0.85±.30
VNM	1.17±.12	1.12±.31	0.90±.2	0.79±.23
SNM	1.26±.25	1.10±.26	0.88±.29	0.81±.31

	†	*	†	*	†	*	†	*
M	ns	ns	ns	ns	ns	ns	ns	ns
NM	ns	ns	ns	ns	ns	ns	ns	ns

TEMPORAL RATIOS T4/T3

TASK	THETA	ALPHA	BETA	GAMMA
VM	1.00±.16	1.12±.26	1.47±.62	1.56±.90
SM	0.98±.16	0.93±.23	1.09±.58	1.18±.96
VNM	1.02±.18	1.05±.21	1.17±.36	1.14±.41
SNM	0.87±.12	0.84±.19	0.83±.31	0.88±.57

	†	*	†	*	†	*	†	*
M	ns	ns	.005	.006	.001	.008	.005	.022
NM	.01	.011	.025	.03	.025	.05	.1	.18

Table 7.1(b) Mean R/L EEG Power Ratios±Standard Deviations and Significance Values For Intertask Differences in Schizophrenics. The rows labelled M and NM contain the significance values of verbal versus spatial comparisons for pairs of tasks of the indicated modality, either motor or non-motor.

† Significance Value for "paired comparisons" ANOVA

* Significance Value for Wilcoxon Matched Pairs Signed Ranks Test

	PARIETAL RATIOS P4/P3							
TASK	THETA		ALPHA		BETA		GAMMA	
VM	1.13±.08		1.13±.20		1.02±.26		1.04±.33	
SM	1.13±.13		0.96±.19		0.89±.16		0.91±.19	
VNM	1.13±.18		1.25±.42		1.01±.31		0.99±.26	
SNM	1.12±.13		0.95±.20		0.87±.18		0.86±.24	
	+	*	+	*	+	*	+	*
M	ns	ns	.05	.064	ns	ns	ns	ns
NM	ns	ns	.05	.017	ns	ns	ns	ns

	TEMPORAL RATIOS T4/T3							
TASK	THETA		ALPHA		BETA		GAMMA	
VM	0.98±.11		1.04±.19		1.27±.6		1.44±1.13	
SM	0.95±.18		0.93±.21		1.07±.36		1.10±.5	
VNM	0.98±.16		1.06±.23		1.16±.41		1.29±1.02	
SNM	0.89±.12		0.88±.19		1.01±.30		1.08±.46	
	+	*	+	*	+	*	+	*
M	ns	ns	.1	.22	ns	ns	ns	ns
NM	.05	.016	.005	.018	ns	ns	ns	ns

Table 7.1(c) Mean R/L EEG Power Ratios±Standard Deviations and Significance Values for Intertask Differences in Manic Depressives. The rows labelled M and NM contain the significance values of verbal versus spatial comparisons for pairs of tasks of the indicated modality, either motor or non-motor.

+ Significance Value for "paired comparisons" ANOVA

* Significance Value for Wilcoxon Matched Pairs Signed Ranks Test

for the significance of verbal versus spatial differences as determined by the Wilcoxon Matched Pairs Signed Ranks Test and analysis of variance (ANOVA). Only results significant at $p<.1$ are included in the tables. The entry ns in a table means the comparison failed to reach significance at $p<.1$. R/L ratios were transformed to a log scale before analysis of variance since this transformation generally resulted in samples more homogeneous in variance.

The most consistent asymmetries between verbal and spatial tasks were found in the alpha band. Manic depressives and normals displayed significant alpha band asymmetries in both temporal and parietal regions for both motor and non-motor tasks. Schizophrenics displayed significant alpha band asymmetries for the temporal region only. Asymmetries in the beta and gamma bands were less consistent. Normals showed significant beta and gamma band differences only for motor tasks in both the parietal region and the temporal region. Manic depressives showed no significant beta or gamma band differences. Shizophrenics displayed significant beta and gamma band R/L ratio asymmetries for motor and non-motor tasks in the temporal region only. The significance of intergroup R/L ratio differences for the verbal motor, spatial motor, verbal non-motor, and spatial non-motor tasks was tested by single classification analysis of variance but none of the

differences reached significance for either the parietal region or the temporal region. Average values for the groups sometimes differed appreciably but large interindividual variability within a group prevented group differences from reaching significance.

7.2 Alpha Band Coherence Asymmetries

Task related differences in the magnitude squared coherence function were examined for the lead pairs P3P4, T3T4, P4T4 and P3T3. The other two possible lead pairs, P3T4 and P4T3, were not considered. For normals the VNM and SNM tasks were employed, for psychotics the MA and SNM tasks. Differences were examined only in the alpha band for the following reasons: (1) R/L ratio asymmetries indicated the alpha band showed the most consistent task dependent differences, (2) the significant R/L ratio diferences found in the beta and gamma bands were almost all for motor tasks suggesting the changes might be a concomitant of the associated motor activity rather than due to the verbal or spatial nature of the activity and (3) the alpha band normally contains the greatest proportion of EEG power and additionally is the band most likely to be free from the influence of slow body movement, eye movement, and muscle artifacts which influence, respectively, the delta, theta, and beta-gamma bands most strongly. Figure 7.5 is an example

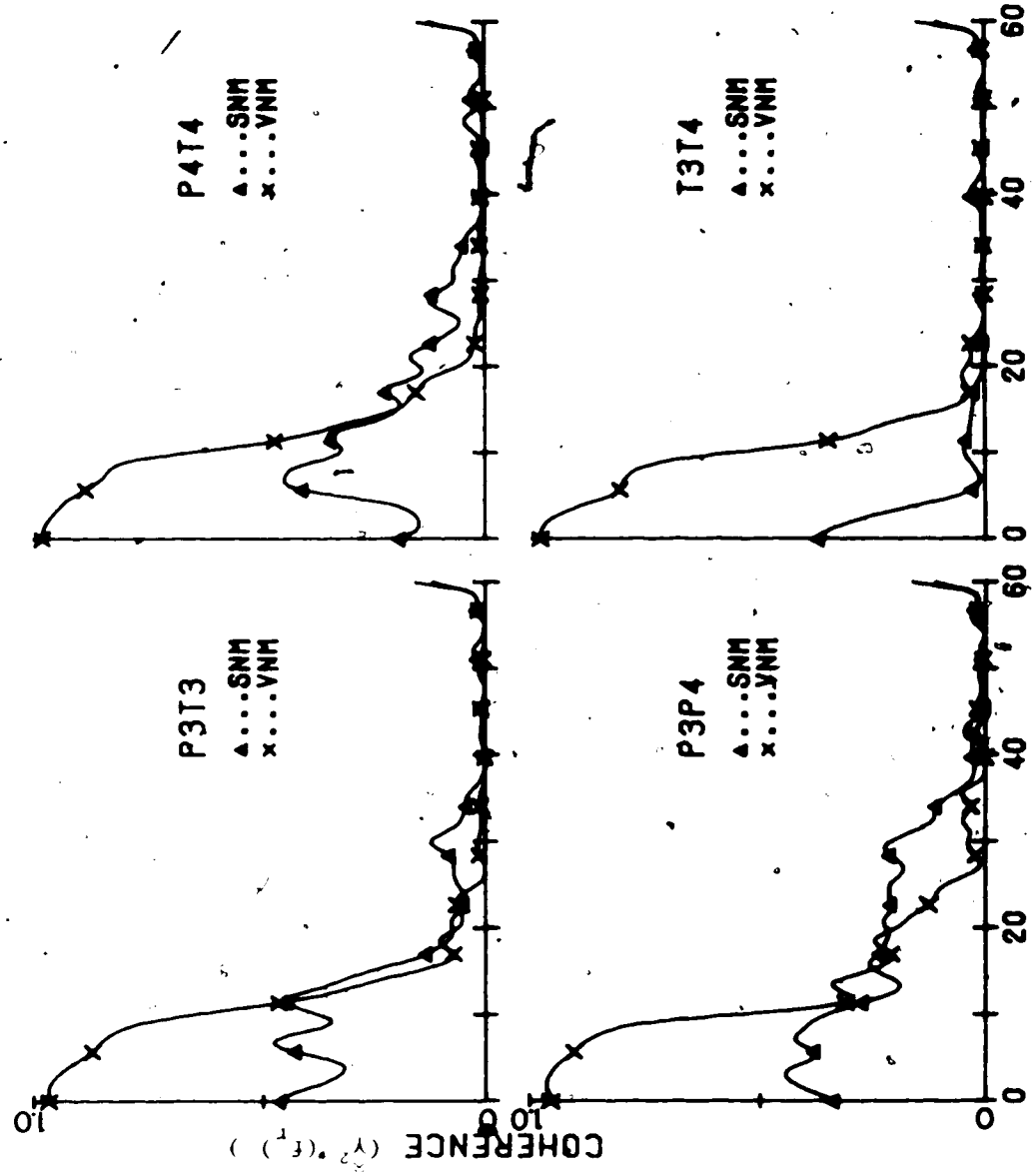


Figure 7.5 VNM and SNM Coherences for a Normal

of coherence differences between verbal and spatial tasks exhibited by a normal individual. In this subject coherence between all lead pairs considered was greater in verbal than in spatial tasks for most frequency bands. Figure 7.6 illustrates the average magnitude squared alpha band coherence for normals, schizophrenics and manic depressives for the described lead pairs. For normals the verbal non-motor task was compared to the spatial non-motor task. For psychotics mental arithmetic was compared to spatial non-motor. Table 7.2 gives the means, standard deviations, and two tailed significance values as determined by two way analysis of variance interpreted as a randomized blocks design. Both between task differences for each lead pair and interlead differences for a given task were analyzed for the coherences graphed in figure 7.6. For all three groups significant intertask differences were found for the lead pairs T4T3 and P3T3. No significant intertask differences were found for the P4P3 lead pair in any group; differences between verbal and spatial tasks for P4T4 reached significance only for normals. Interlead differences were highly significant for both verbal and spatial tasks for all three groups. As in section 7.1 single classification analysis of variance was employed to test for intergroup differences between normals, shizophrenics, and manic depressives in the spatial non-motor task and also between

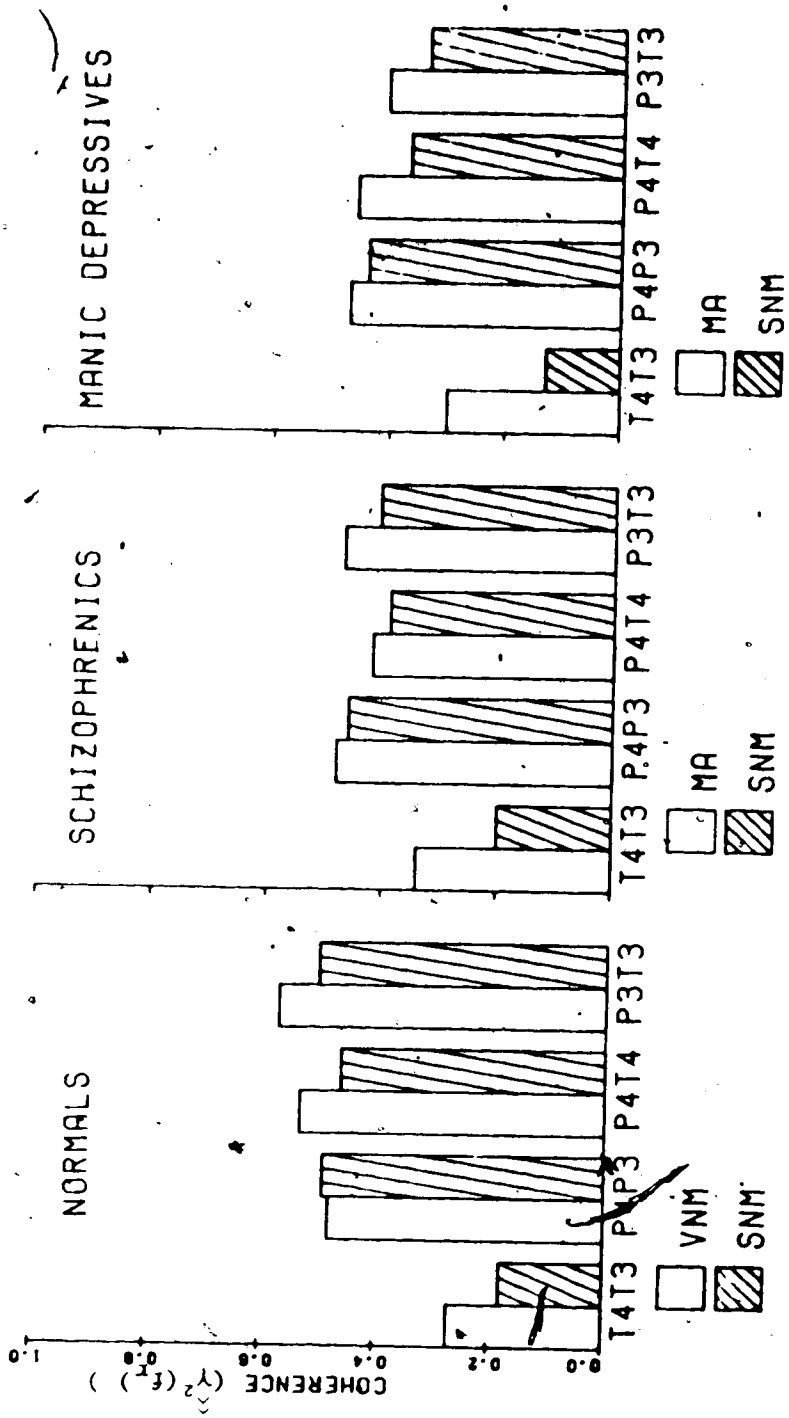


Figure 7.6 Mean VNM and SNM Alpha Band Coherences for Normals, Schizophrenics and Manic Depressives

	TASK	T4T3	P4P3	P4T4	P3T3	P_r
N	VNM	.27±.12	.48±.15	.53±.15	.57±.11	.001
	SNM	.18±.12	.49±.16	.46±.16	.50±.13	.001
	P_t	.025	NS	.1	.01	
MD	MA	.30±.16	.47±.13	.46±.15	.41±.14	.001
	SNM	.13±.11	.44±.11	.37±.14	.34±.16	.001
	P_t	.005	NS	NS	.1	
S	MA	.34±.21	.48±.17	.42±.2	.47±.15	.01
	SNM	.20±.13	.46±.15	.39±.19	.41±.19	.001
	P_t	.01	NS	NS	.05	

Table 7.2 Descriptive Statistics for Interregion and Intertask α-Band Coherence Asymmetries. P_r denotes the significance value for interregion differences. P_t denotes the significance value for intertask differences.

schizophrenics and manic depressives in the mental arithmetic task. No significant differences were found for any lead pair.

7.3 Normalized Auto-Spectral Differences

Qualitative inspection of EEG spectra of normals and psychotics suggested significant differences in the relative amounts of energy in the alpha, beta, and gamma frequency bands. To compare normals and psychotics on this basis intragroup and intergroup differences in normalized auto-spectral power as described in section and also R/L power ratios were examined for the eyes closed recording condition. Although intra and intergroup differences for tasks in which the subject was active would likely also reach significance, the eyes closed condition was chosen as subjects generally were the most relaxed in this situation and yielded the most artifact free recordings. Differences in normalized auto-spectral power, to be referred to hereafter as proportional power, were studied for the alpha, beta, and gamma bands for both temporal and parietal leads. Figures 7.7(a) to 7.7(f) portray the proportional power in the alpha, beta, and gamma bands for the regions P4, P3, T4, and T3 and mean proportional power differences for the parietal and temporal regions, P4-P3 and T4-T3 respectively. For each figure the graphs for the three diagnostic

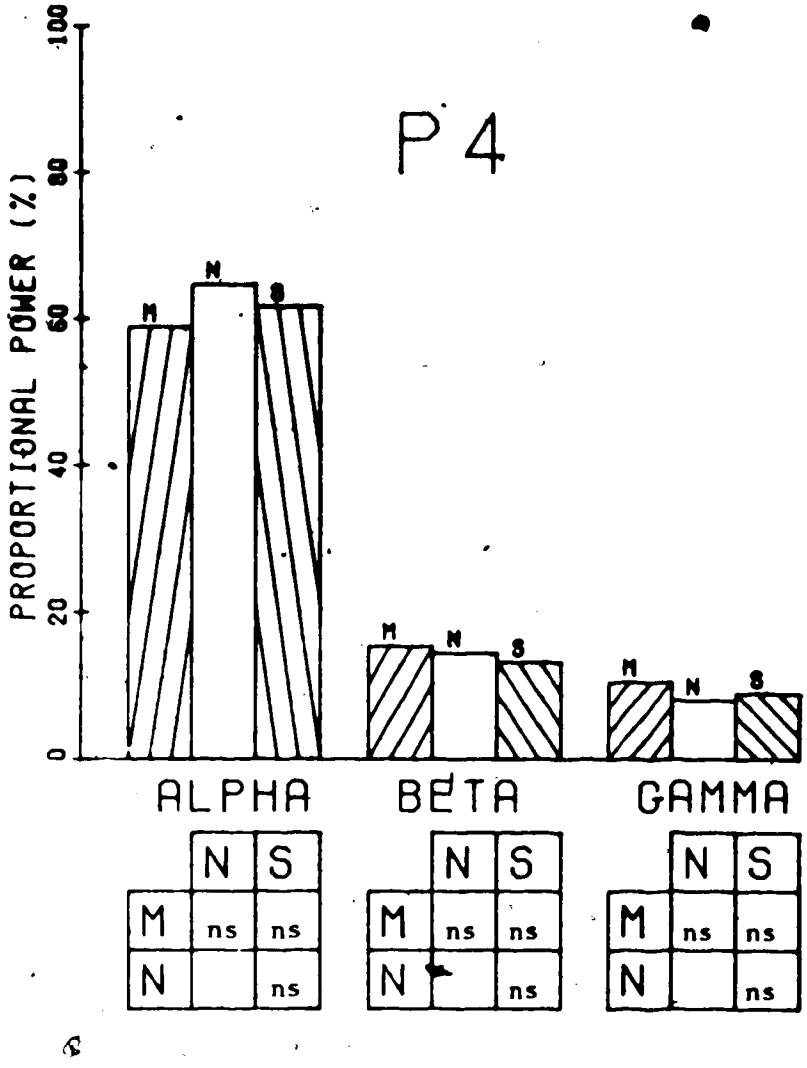


Figure 7.7(a) Average Proportional Power Values for the Right Parietal Region

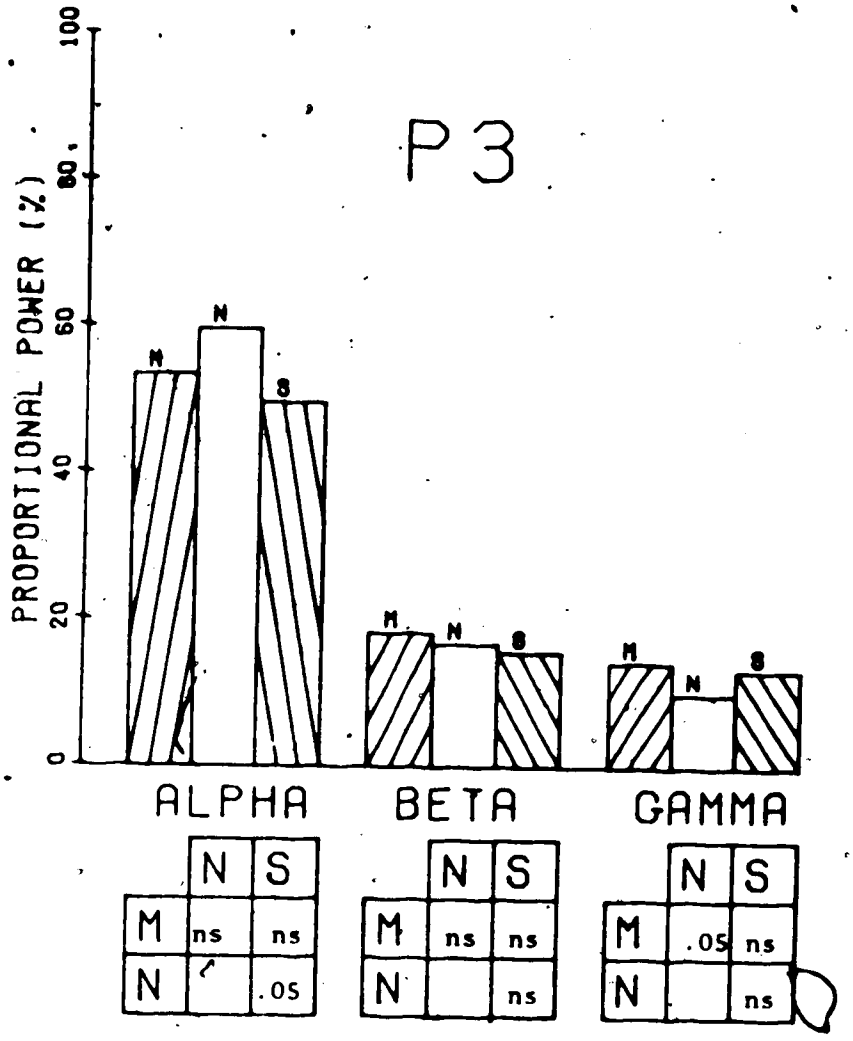


Figure 7.7(b) Average Proportional Values for the Left Parietal Region

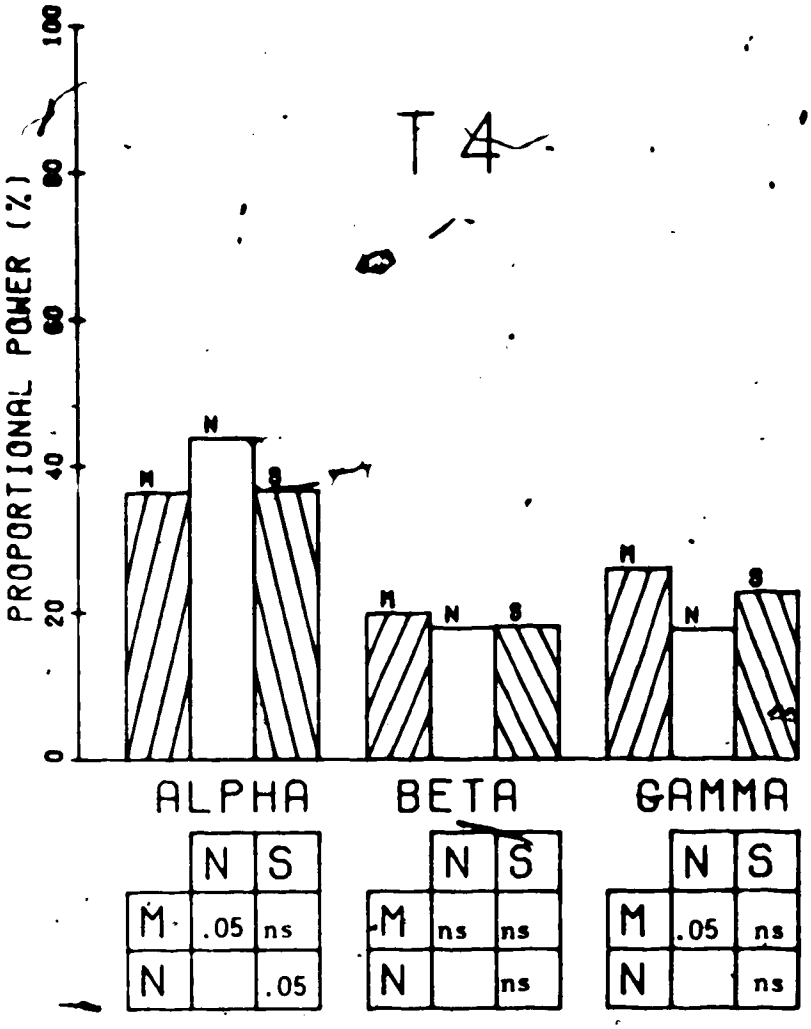


Figure 7.7(c) Average Proportional Power Values for the Right Temporal Region

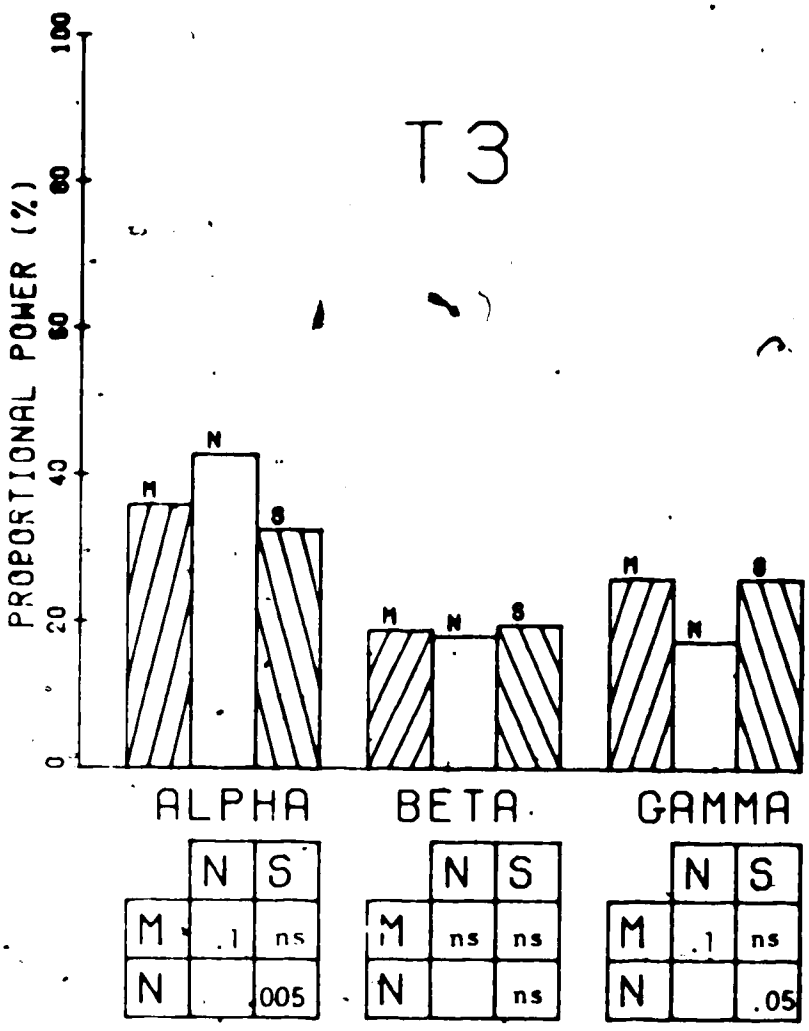
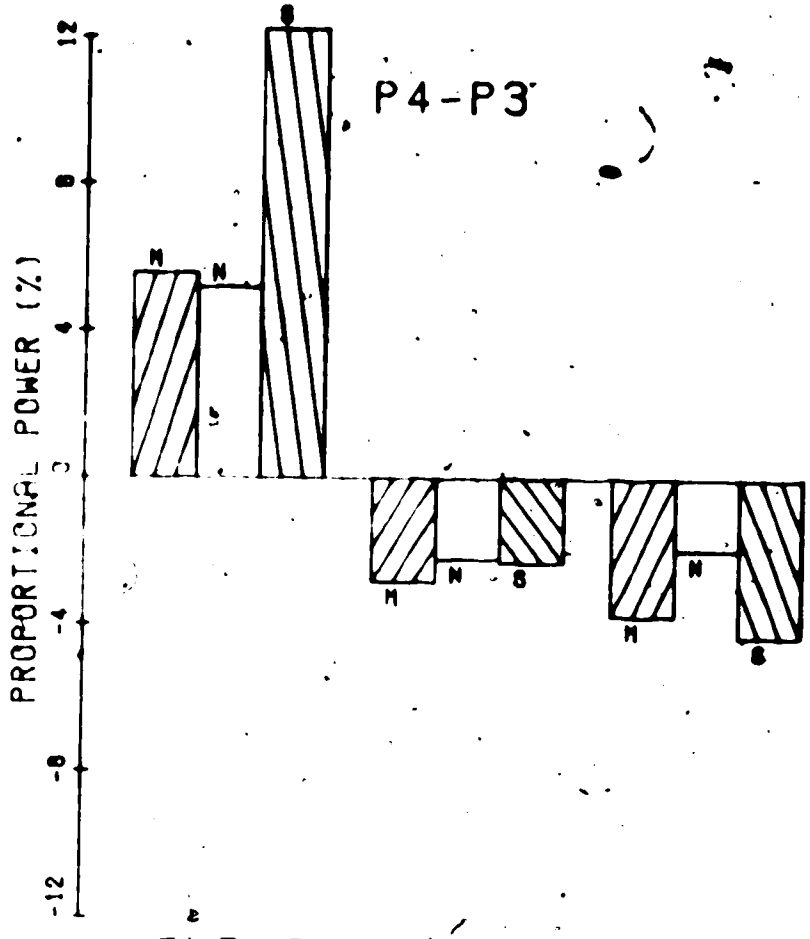


Figure 7.7(d) Average Proportional Power Values for the Left Temporal Region



ALPHA

	N	S
M	ns	.1
N		.1

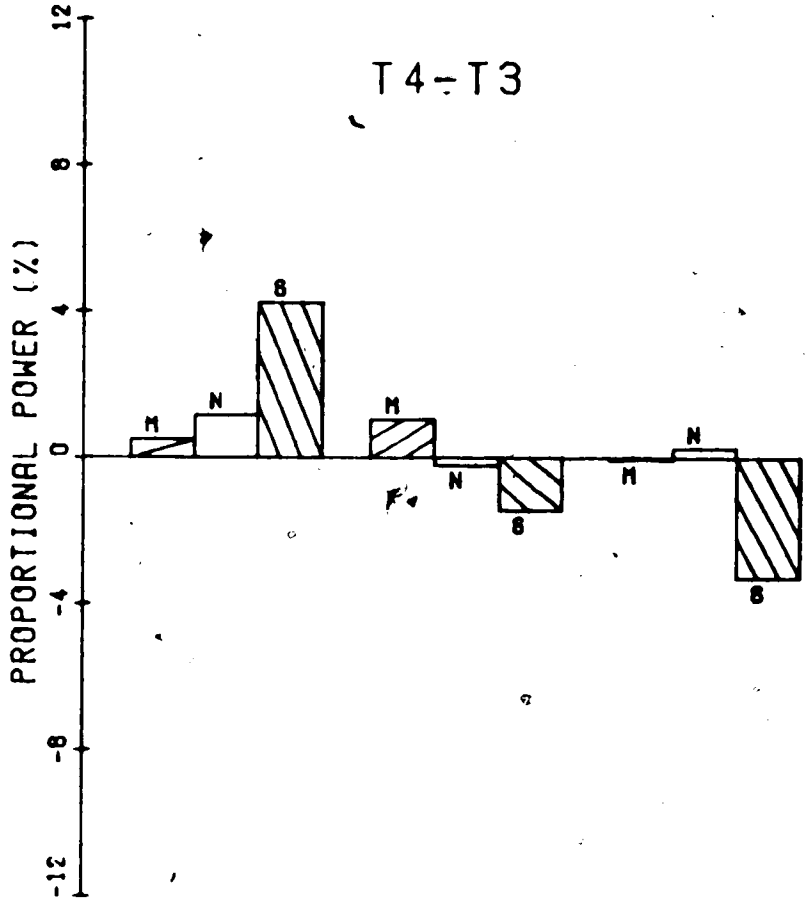
BETA

	N	S
M	ns	ns
N		ns

GAMMA

	N	S
M	.01	.1
N		ns

Parietal Proportional Power Differences



ALPHA

	N	S
M	ns	.025
N		.05

BETA

	N	S
M	ns	.025
N		ns

GAMMA

	N	S
M	ns	ns
N		.1

Figure 7.7(f) Average Temporal Proportional Power Differences

categories are juxtaposed.

The significance of intragroup comparisons between: (1) homologous temporal and parietal regions and (2) parietal proportional power differences versus temporal proportional power differences was tested by the Wilcoxan Matched Pairs Signed Ranks Test for each diagnostic category. The results appear in Table 7.3. For each diagnostic group proportionately more alpha band energy was present in the right parietal region than in the left parietal region. The converse was true for beta and gamma band energy. Significant differences in proportional power in homologous temporal regions were found only in the psychotics. Manic depressives had a small but significant proportional power excess in the right temporal region for the beta band. Schizophrenics had a significantly smaller proportion of alpha band power and a significantly greater proportion of beta and gamma band power in the left temporal region. Significant differences were also found in comparisons between homologous parietal and temporal mean proportional power differences, P4-P3 vs T4-T3. For the alpha band both P4-P3 and T4-T3 were positive for all three groups. The mean parietal difference was significantly greater than the mean temporal difference in each group. For the beta band both P4-P3 and T4-T3 were negative with the exception of temporal differences for manic depressives. For each group the mean

GROUP	BAND	P4vsP3	T4vsT3	ΔPvsΔT
MD		.004	NS	.03
		.002	.02	.002
		.002	NS	.002
N		.0008	NS	.007
		.005	NS	.03
		.0002	NS	.03
S		.0001	.006	.008
		.009	.08	.08
		.0001	.05	NS

Table 7.3 Significance of Intragroup Proportional EEG Power and Proportional EEG Power Difference Comparisons. In P4vsP3 and T4vsT3 proportional power values in the indicated bands were compared for homologous parietal and temporal regions by the Wilcoxon Matched Pairs Signed Ranks Test. In ΔPvsΔT proportional power differences between homologous parietal regions were compared with proportional power differences between homologous temporal regions.

parietal difference was significantly more negative than the mean temporal difference.. For the gamma band both mean parietal and mean temporal differences were negative with the exception of temporal differences for normals. Mean parietal differences were significantly more negative than mean temporal differences except for the schizophrenics.

Intergroup comparisons analyzed were MD vs N, MD vs S, and S vs N. Comparisons were made on the basis of proportional power values from the four recording areas and proportional power differences between homologous areas. Intergroup comparisons significant at $p<.1$ as determined by the Mann Whitney U-Test (one tailed) are included at the bottom of figures 7.7(a) to 7.7(f). Significant single region comparisons were confined to the alpha and gamma frequency bands. For the right parietal region non of the intergroup comparisons reached significance. For the left parietal region normals had a significantly greater proportion of alpha power than schizophrenics, manic depressives a significantly greater proportion of gamma power than normals. In the right temporal region normals had a significantly greater proportion of alpha band power than either manic depressives or schizophrenics; for the gamma band manic depressives had a significantly higher proportion of power than normals. In the left temporal region normals again had a significantly higher proportion of alpha band

power than either manic depressives or schizophrenics; both manic depressives and schizophrenics had a significantly higher proportion of gamma band power than normals in this region.

Significant comparisons involving differences between homologous temporal and parietal areas were found in all three frequency bands. For the parietal region the mean alpha band proportional power difference was significantly more positive for schizophrenics than for normals or manic depressives. Gamma band mean proportional power differences in the parietal region were negative with the mean difference for manic depressives being significantly more negative than the mean difference for normals and significantly less negative than the mean difference for schizophrenics. For the temporal region mean alpha band proportional power differences were in the same direction as in the parietal region with the mean proportional power difference for schizophrenics being significantly more positive than the mean proportional power difference for normals or manic depressives. The beta band mean proportional power difference was positive for manic depressives and negative for normals and schizophrenics. The schizophrenic versus manic depressive comparison reached significance here. The gamma band mean proportional power difference was negative for manic depressives and

schizophrenics and positive for normals with the normal versus schizophrenic comparison reaching significance.

Figure 7.8 shows the average R/L EEG power ratios in the alpha, beta, and gamma bands for the eyes closed recording condition. A number of intergroup comparisons reached significance at the p=.1 level or lower (one tailed Mann Whitney U-Test). Schizophrenics differed significantly from normals in the temporal region for the beta band ($p<.1$) and in both the temporal region ($p<.05$) and the parietal region ($p<.1$) for the gamma band. Manic depressives differed significantly from schizophrenics in both the parietal and temporal regions for the beta and gamma bands and in the parietal region for the alpha band. The differences were significant at $p<.1$ for the beta and alpha band comparisons and at $p<.05$ for the gamma band comparison. Comparisons between normals and manic depressives reached significance only in the parietal region for the gamma band ($p<.005$).

7.4 Variability

EEG variability, as defined in Chapter 6, was investigated by comparing psychotics to normals both on a region to region basis and also on the basis of differences in the coefficient of variation between homologous temporal or parietal regions. The significance of differences between

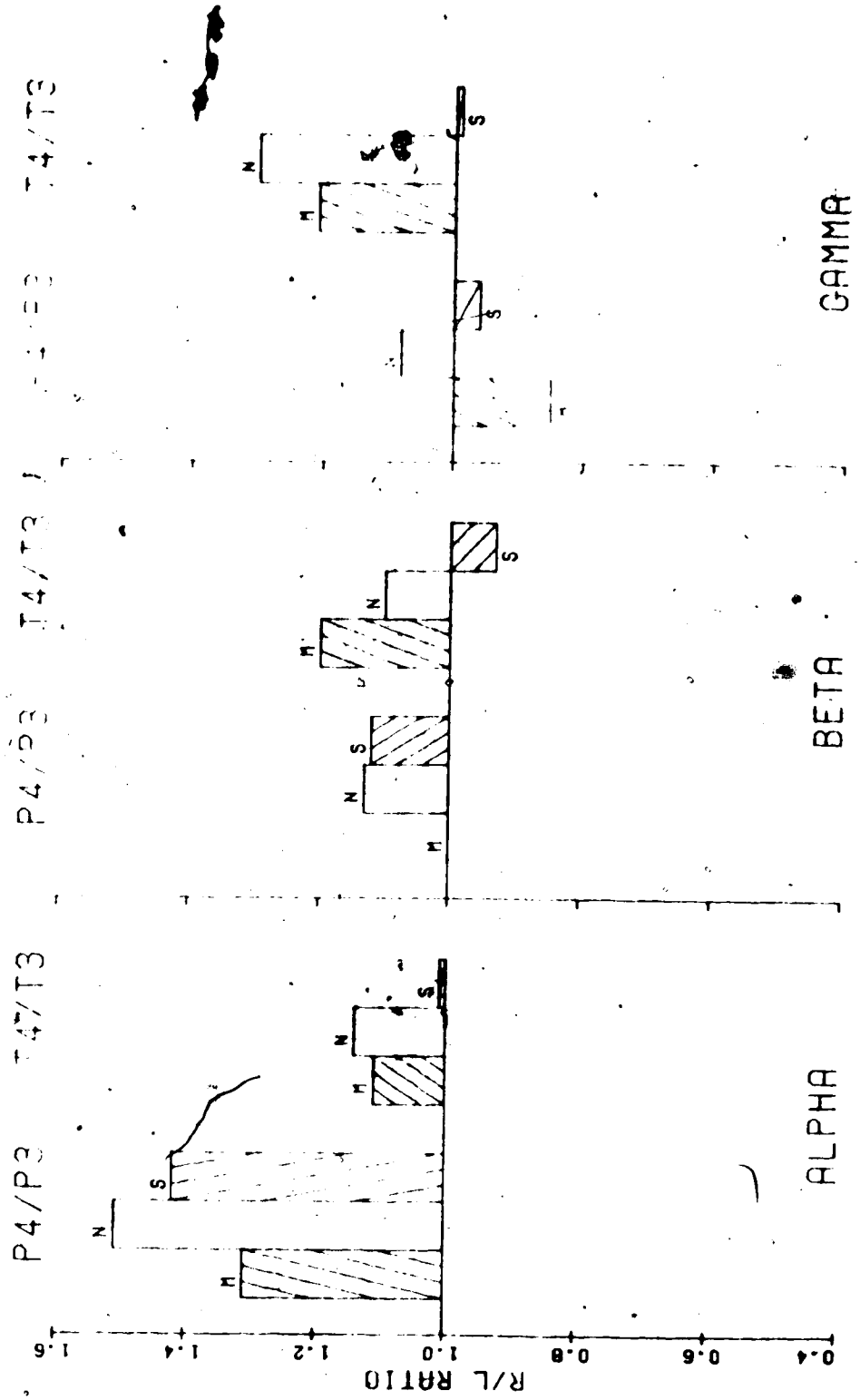


Figure [illegible] Average R/L Ratios During the Eyes Closed [illegible]

psychotics and normals was determined by the Mann Whitney U test. For each recording lead and homologous lead pair the following comparisons were made; normals versus schizophrenics, normals versus manic depressives and schizophrenics versus manic depressives. The comparisons were calculated for the alpha, beta, gamma and "total power" bands as defined previously. Figures 7.9(a) to 7.9(f) graph the mean CV for the right and left parietal and temporal regions and also CV differences for homologous parietal and temporal areas. The significant intergroup comparisons are included below the figures. Tables 7.4(a) to 7.4(c) give the corresponding means±standard deviations.

Significant intergroup differences were found in the manic depressive versus normal and manic depressive versus schizophrenic comparisons. None of the schizophrenic versus normal comparisons reached significance. Significant differences between manic depressives and normals were found in the alpha and "total power" bands. For the alpha band manic depressives had a significantly lower mean coefficient of variation than normals in all regions. Differences for P4, P3, and T4 were significant at $p<.1$; for T3 at $p<.05$. For the "total power" band manic depressives had significantly lower coefficients of variation in the the parietal regions; for P4 at $p<.05$, for P3 at $p<.1$. Differences in the distributions of differences in the

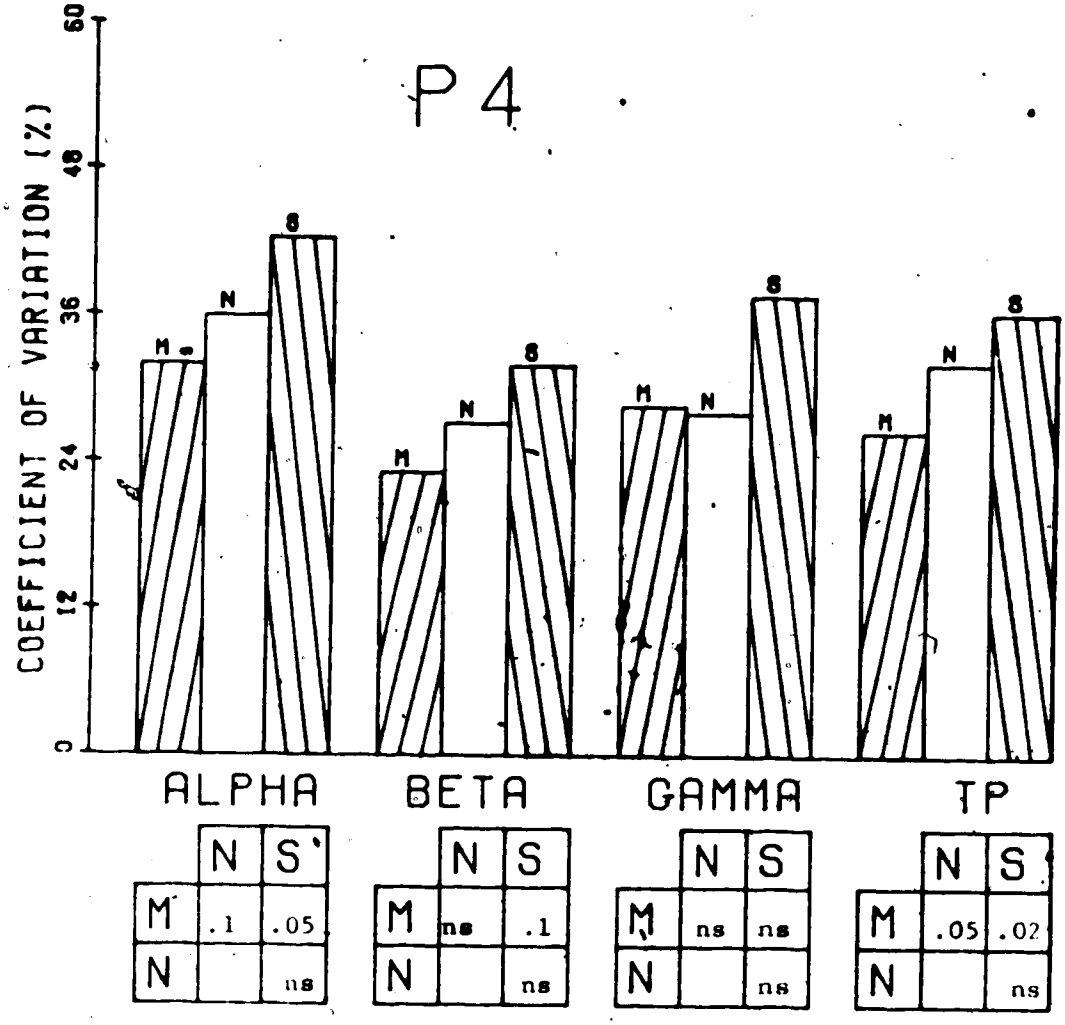


Figure 7.9(a) Average Coefficients of Variation for the Right Parietal Region

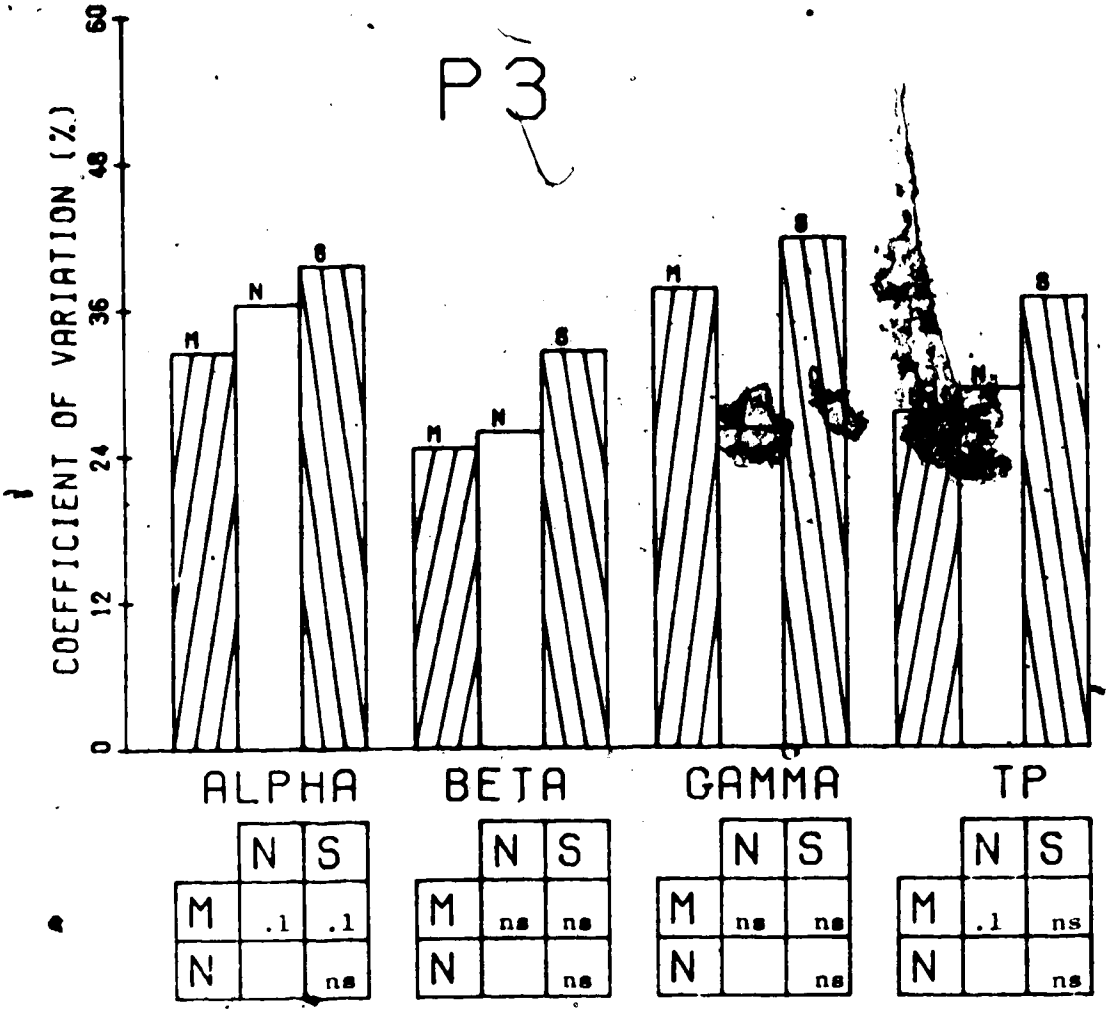


Figure 7.9(b) **Average Coefficients of Variation for the Left Parietal Region**

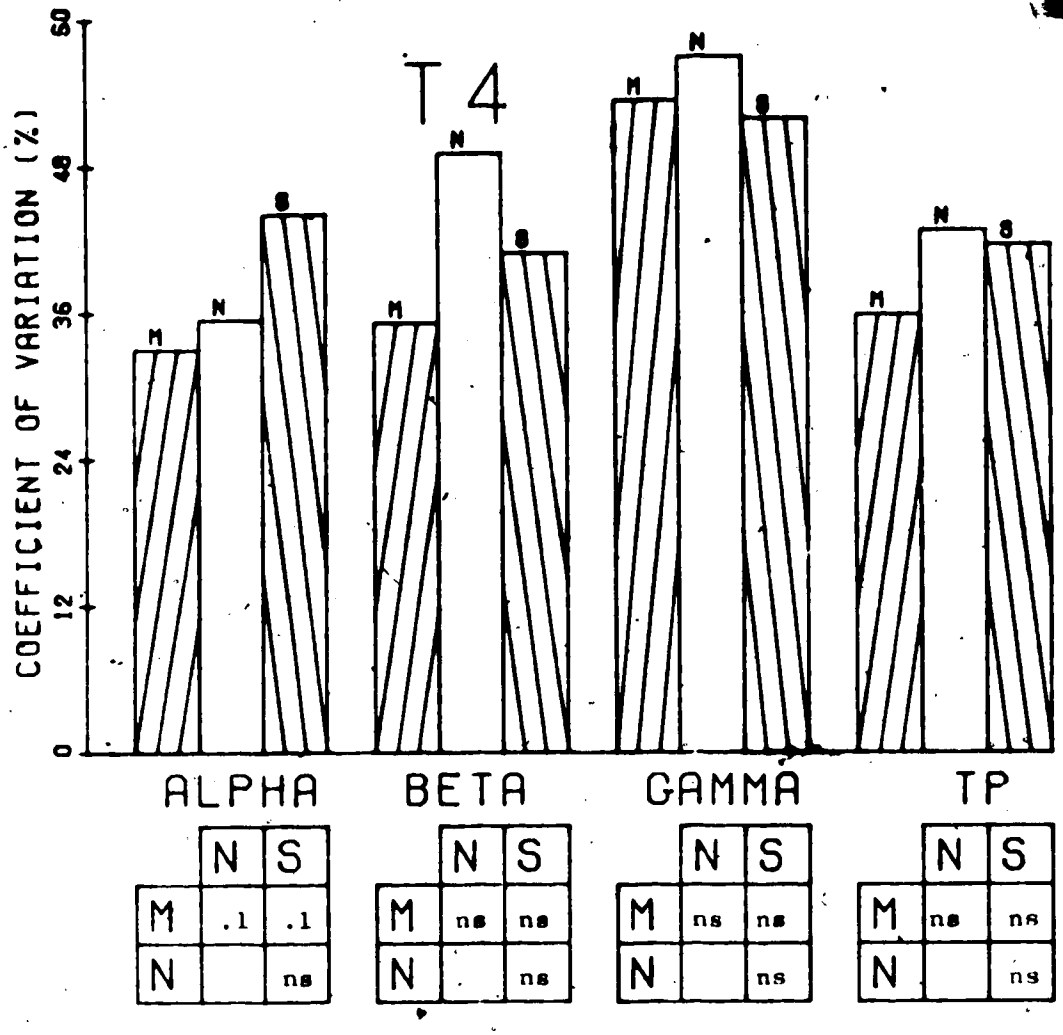


Figure 7.9(c) Average Coefficients of Variation for the Right Temporal Region

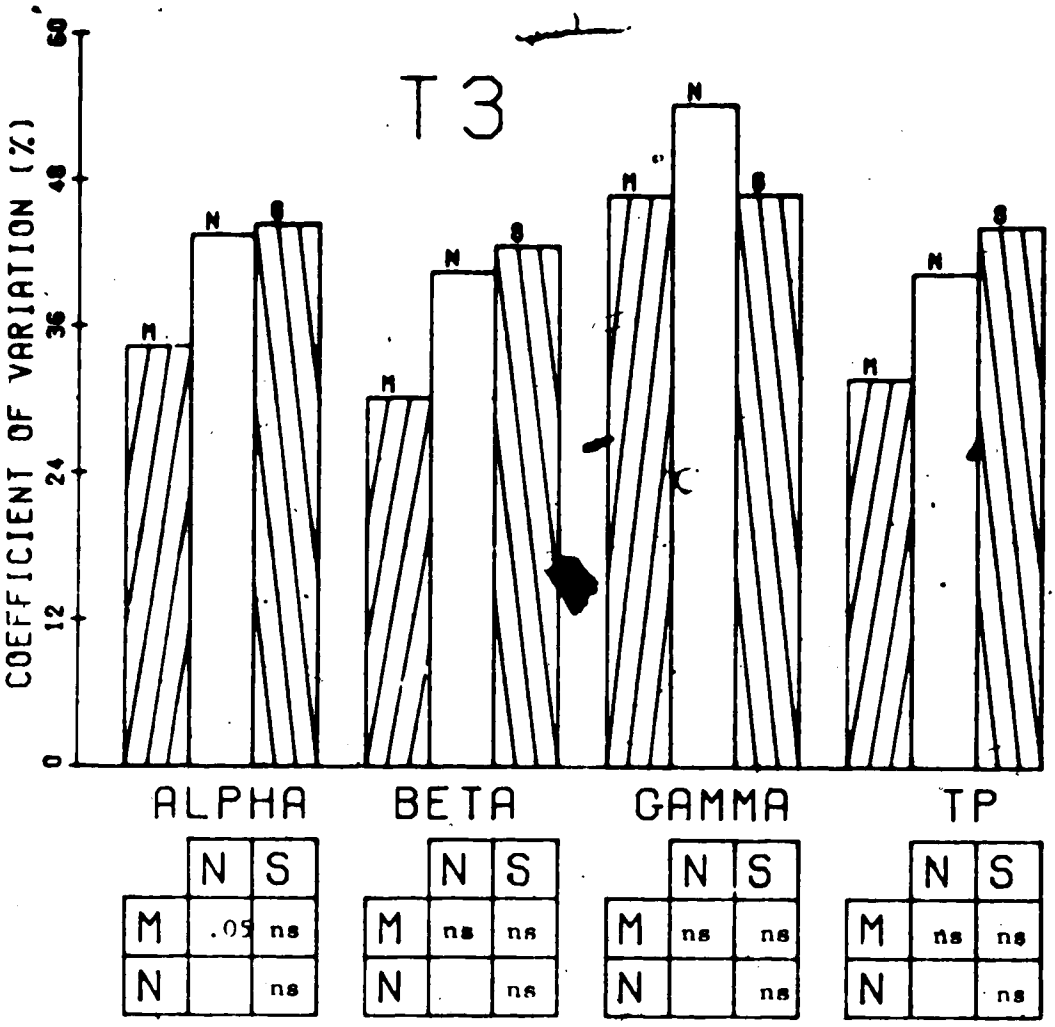


Figure 7.9(d) Average Coefficients of Variation for the Left Temporal Region

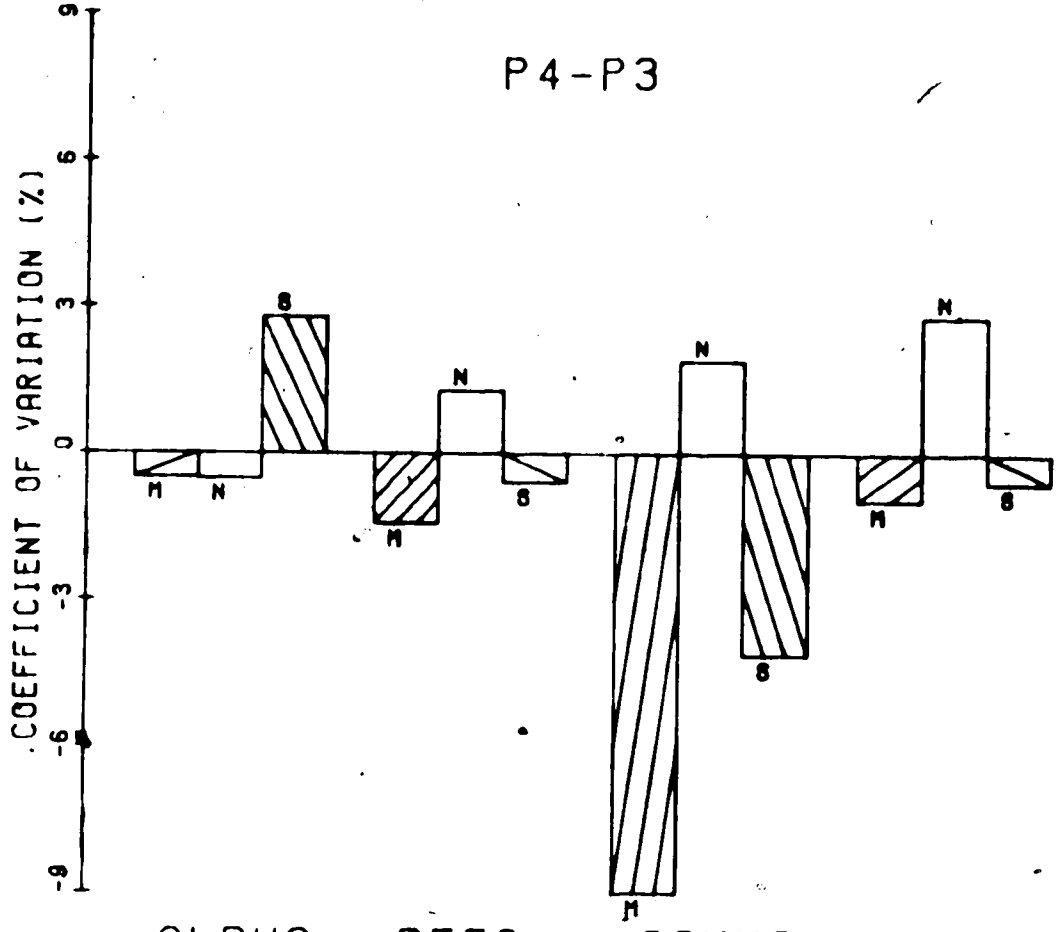
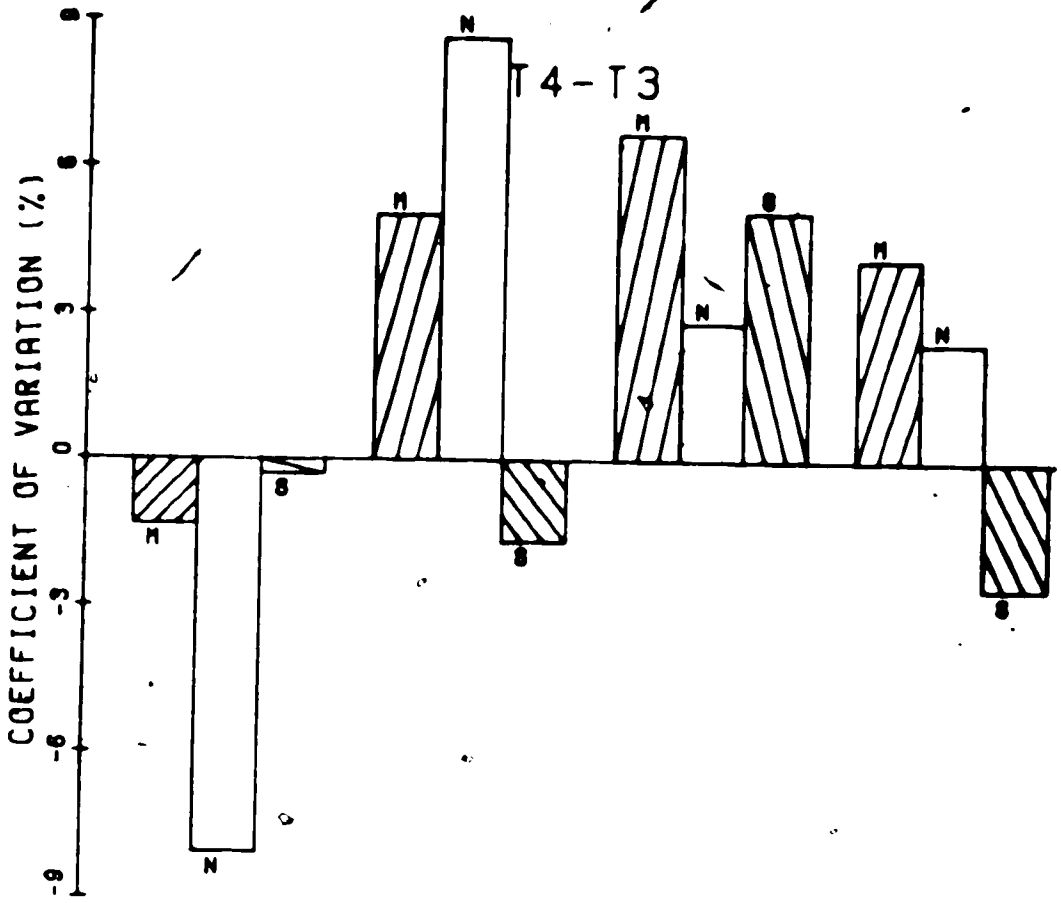


Figure 7.9(e) - Average Parietal Variability Differences



ALPHA

	N	S
M	.1	ns
N		ns

BETA

	N	S
M	ns	ns
N		ns

GAMMA

	N	S
M	ns	ns
N		ns

TP

	N	S
M	ns	ns
N		ns

Figure 7.9(f) Average Temporal Variability Differences

Table 7.4(a)

Mean C.V.

±Standard

Deviations

for Normals

BAND	P4	P3	T4	T3	P4-P3	T4-T3
α	35.9±14.5	36.4±12.3	35.4±13.3	43.4±18.6	-.53±7.5	-8.1±11.9
β	27.2±21.5	25.9±13.8	49.1±49.6	40.5±28.4	1.28±10.3	8.65±23.3
γ	28.0±19.1	26.1±13.5	57.0±64.8	54.2±52.5	1.9±8.5	2.8±20.5
T.P.	32.1±17.8	29.3±13.1	42.8±36.8	40.3±25.9	2.8±8.2	2.4±17.5

Table 7.4(b)

Mean C.V.s

±Standard

Deviations

for Manic Depressives

BAND	P4	P3	T4	T3	P4-P3	T4-T3
α	40.0±21.3	32.4±18.7	33.0±21.9	34.3±14.5	-.5±13.5	-1.33±1.8
β	23.1±8.9	24.6±13.2	35.2±18.2	30.2±17.0	-1.4±9.6	5.0±9.6
γ	28.6±12.8	37.6±45.0	53.4±37.4	46.7±33.6	-9.0±39.3	6.7±17.8
T.P.	26.5±25.0	27.4±24.7	35.9±19.2	31.7±20.7	-3.6±9.0	4.2±13.5

Table 7.4(c)

Mean C.V.

±Standard

Deviations

for Schizophrenics

BAND	P4	P3	T4	T3	P4-P3	T4-T3
α	42.4±22.8	39.6±18.8	44.1±30.3	44.4±31.0	2.8±12.3	-.29±13.8
β	31.9±18.6	32.5±26.8	40.9±29.6	42.6±30.3	-.59±21.2	-1.7±16.6
γ	37.6±41.1	41.7±51.3	52.0±40.6	46.8±40.1	-4.1±23.7	5.11±51.6
T.P.	36.2±21.5	36.8±23.3	41.6±34.4	49.2±36.8	-.59±11.9	-2.6±16.8

coefficient of variation between homologous temporal regions were significant at $p<.1$ for both the alpha and "total power" bands for manic depressives versus normals.

The coefficient of variation of manic depressives differed significantly from the coefficient of variation of schizophrenics in both the parietal and temporal regions, especially in the right hemisphere. All differences were in the direction of lower coefficients of variation for manic depressives. Alpha band differences were significant at $p<.05$ for P4 and at $p<.1$ for P3 and T4. For the beta band and "total power" bands the coefficient of variation for the right parietal region differed at $p<.1$ and $p<.02$ respectively. No significant intergroup differences were found in terms of variability differences between homologous temporal or parietal regions.

7.5 Discriminant Analysis

Univariate statistical techniques were applied to assess the significance of the results presented in the preceding sections. In this section representative results of applying the multivariate technique of discriminant analysis to (a) a given group of individuals during different tasks and (b) to different groups of individuals during performance of the same task are presented. For (a)

input variables to the discriminant analysis program were R/L alpha band ratios, temporal and parietal and the four coherences P4P3, T4T3, P3T3 and P4T4. The program attempted to discriminate individuals performing a verbal non-motor task from the same individuals performing a spatial non-motor task on the basis of these variables. Table 7.5 tabulates the results of applying the program to normals in VNM versus SNM and to psycotics in MA versus SNM. The table gives the percentage of individuals correctly classified for each task and the statistic known as Mahalanois's D-Square, a measure of the significance of the multidimensional separation of the groups analyzed. The results suggest EEG measures can successfully discriminate between verbal and spatial modes of thinking in both normal and psychotic groups.

The program was also used in a number of experimental conditions in an attempt to discriminate between normal and psychotic groups. Both a resting condition, EC, and an active condition, SNM were used for analysis. SNM was chosen over VNM since VNM differed for psychotics and normals. A non-motor task was chosen over a motor task since significant intertask coherence differences were found only for non-motor tasks. Input variables for the active condition, SNM, were the same R/L ratios and coherences used in (a) in the preceding paragraph. A separate analysis

N	GROUP	VNM	SNM	D^2
19	N	84.2	78.9	19.6
13	S	84.6	84.6	17.33
12	MD	100	100	43.98

Table 7.5 Summary of Discriminant Analysis for VNM vs SNM in Normals and MA vs SNM in Psychotics A separate Discriminant Analysis was performed for each group. The figures in the task columns give the percentage of individuals correctly classified in the VNM and SNM tasks.

compared the two psychotic groups in the mental arithmetic condition. A summary of the analysis is given in tables 7.6(a) and 7.6(b). Input variables to the discriminant analysis program for the EC condition were L/R alpha, beta, and gamma ratios and normalized auto-spectral power in the alpha,beta, and gamma frequency bands for the right and left temporal regions. The analysis was carried out for the three groups separately and also for pooled psychotics versus normals. The results appear in tables 7.7(a) and 7.7(b).

GROUP	N	S	MD
N	63.2	21.1	15.8
S	23.1	61.5	15.3
MD	20	30	50
	D^2=17.8		

Table 7.6(a) Summary of Discriminant Analysis for Normals vs Schizophrenics vs Manic-Depressives in the SNM Task. For each group analyzed the percentage of individuals classified into each diagnostic category N, S or MD are shown in the horizontal row of figures contained in the columns labelled N, S, and MD. D^2 is the value of Mahalanobis's D-Square.

GROUP	MD	S
MD	70	30
S	15.4	84.6
	D^2=9.01	

Table 7.6(b) Summary of Discriminant Analysis for Manic Depressives vs Schizophrenics in the MA Task. The interpretation of the analysis is similar to 7.6(a).

GROUP	N	S	MD
N(19)	78.9	5.3	15.8
S(28)	21.4	57.1	21.4
MD(18)	27.7	22.2	50
	$D^2=36.99$		

Table 7.7(a). Summary of Discriminant Analysis for Normals vs Schizophrenics vs Manic Depressives for the Eyes Closed Condition. The left hand column shows the three groups and the number of individuals in each. For each group the figures on the same row give the percentage of individuals in that group classified as normal (N), schizophrenic (S) or manic depressive (MD).

GROUP	P	N
P(46)	76.1	23.9
N(19)	21.1	78.9
	$D^2=24.58$	

Table 7.7(b) Summary of Discriminant Analysis for Pooled Psychotics vs Normals for the Eyes Closed Condition. For purposes of analysis schizophrenics and manic depressives were pooled into one group. The program attempted to classify individuals as normal (N) or psychotic (P).

CHAPTER 8

DISCUSSION

A number of approaches to quantification of the EEG based on auto-spectra and cross-spectra have been implemented in this study. This chapter will relate the results presented in Chapter 7 to previous reported findings and summarize conclusions to be drawn from the results. The results are discussed on a section to section basis. Suggestions for further refinements in experimental and analytic techniques are included in the discussion.

8.1 R/L Ratios

The technique of analysis used to study task dependent EEG asymmetries was based on Galin and Ornstein (13). The original intention of the study was to verify and supplement their findings in normals through an improved analytic technique and then apply the method to groups of mental patients in the hope of discovering significant group differences. Unknown to this writer a similar study on "normal" subjects was being carried out by Doyle et al (12). The results reported in 7.1 are in essential agreement with (12). Their finding of significant task dependent asymmetries appearing most consistently in the alpha

was verified. As in (12) significant task dependent asymmetries were found in the beta and gamma bands for both the parietal and temporal regions. Significant beta and gamma band comparisons in normals were found only for motor tasks though, in contrast to Doyle et al who reported significant comparisons for both motor and non-motor tasks. For the set of tasks used in this analysis only schizophrenics displayed a significant task dependent asymmetry for non-motor tasks in beta-gamma band comparisons. Conceivably an abnormal neurophysiologic concomitant to one or both of the tasks is manifesting itself here.

As results in normals indicated that the most significant task dependent asymmetries were in the alpha band, the patients analyzed for R/L ratio asymmetries were a subgroup of the total patient sample. Patients characterized by spectra not dominated by energy in the beta and gamma bands were chosen to avoid analyzing spectra with significant beta band energy in the alpha band. While the main alpha peak for most subjects is around 10 Hz with lesser energy in, say, a ± 2Hz band, the alpha band, as defined for analysis, comprised frequencies from 8-13 Hz to ensure including subjects with slower or faster alpha activity. Most subjects, therefore, have beta band contributions in the alpha band as so defined and in

subjects with records characterized by large amounts of beta band activity relative to alpha band activity R/L ratios calculated for the alpha band are more a reflection of beta band asymmetries rather than alpha band asymmetries. A strong possibility exists, however, that by excluding subjects with relatively large amounts of beta one is excluding subjects with a more acute psychosis. Indeed a large proportion of the group with records dominated by beta -gamma energy show a reversal of the asymmetry exhibited by normals. This group was not analyzed statistically though as spectra domihated by large amounts of beta -gamma enery are difficult to interpret due to the possibility of myogenic contamination in the beta-gamma bands which is difficult to distinguish from cerebral activity and is especially likely to occur during performance of an active task. Future work on subjects with high beta-gamma energy records carefully screened for muscle artifact holds promise. Such careful sreening was awkward in the present study as a shortcoming of the study was that no hardcopy readout was produced as the EEG's were recorded. The intragroup comparison of R/L ratios for various bands, while yielding no significant differences, was probably carried out on the patients whose cerebral function was the most "normal".

8.2 Coherence Asymmetries

Section 7.2 presented results pertaining to alpha band coherence asymmetries in normals, schizophrenics and manic depressives during the VNM vs SNM tasks for normals and the MA vs SNM tasks for psychotics. In all three groups the pattern of asymmetries was similar with T4T3 and P3T3 significantly greater in the verbal task than in the spatial task. P4T4 was greater for the verbal task than for the spatial task only for normals. The interpretation of the significance of the coherence differences is difficult. The fact that coherence values in all areas increase during both the VNM and MA tasks suggests a factor other than task modality may be at work. Task difficulty as well as task modality may be an additional consideration. If task difficulty were the only factor though, coherences in all lead pairs would be expected to rise similarly. The fact that coherences rose significantly only in the T4T3 and P3T3 lead pairs is compatible with the hypothesis of left hemisphere dominance for speech related faculties and right hemisphere dominance for visual spatial processing. Davis and Wada (72) measured coherence from left and right temporo-occipital lead pairs referenced to the left or right ears during both visual evoked responses and click evoked responses. Significant differences existed between corresponding visual versus click evoked response comparisons for the six possible coherences calculated from

the four lead pairs. The most interesting result was the finding of greater occipital-temporal coherences for click responses on the dominant side and greater occipital-temporal coherences on the non-dominant side for visual responses. The authors related their findings to known evidence implying lateralization of the perception and recognition of verbal stimuli to the speech-dominant hemisphere and lateralization of visual perception to the non-dominant hemisphere. In virtue of this evidence their findings seemed to suggest greater intra hemispheric coherence in the hemisphere dominant for a particular function. The findings presented in section 7.2 , while not showing an assymetry in intrahemispheric coherences for verbal and spatial tasks nevertheless show significantly higher intrahemispheric asymmetries in the dominant hemisphere for a dominant hemisphere task and significantly higher interhemispheric asymmetries in the temporal region.

8.3 Proportional Power

Section 7.3 dealt with proportional power values and R/L EEG power ratios in normals and psychotics during the eyes closed resting situation. The results considered as a whole suggest that EEG abnormalities in psychotics tend to occur in definite regions of the cerebrum, the particular region depending on the subjects diagnosis. Abnormalities in

schizophrenic subjects tended to occur more in the left hemisphere, particularly in the temporal region. Intragroup comparisons for schizophrenics reached significance for the alpha, beta, and gamma bands. There was a significantly smaller proportion of alpha power in the left temporal than on the right and a significantly greater proportion of beta and gamma band power. Corresponding comparisons for normals didn't reach significance and for manic depressives reached significance only in the temporal beta band in the opposite direction. Intergroup statistical differences suggesting a left sided EEG abnormality in schizophrenics relative to normals and manic depressives were found in comparisons involving proportional power, proportional power differences and R/L ratios. Schizophrenics had significantly less proportional power relative to normals in the alpha band for both the right and left temporal regions and the left parietal region. Temporal differences, while significant on both sides, were more significant on the left than on the right. Schizophrenics had significantly more proportional power than normals in the gamma band for the left temporal region only. Significant intergroup comparisons in proportional power differences tended to occur more often in the temporal region. Considered in conjunction with single region proportional power comparisons the significant proportional power difference comparisons suggested a left

emphasis of abnormalities. The finding of a left sided emphasis from proportional power differences was supported by the finding of significantly lower R/L ratios in the temporal beta and significantly lower ratios in the parietal and temporal gamma bands for normals versus schizophrenics. Additionally R/L beta and gamma band ratios were significantly lower in schizophrenics relative to manic depressives in the temporal region suggesting a left sided emphasis of beta and gamma band energy for schizophrenics relative to manic depressives. Certain comparisons suggested a right temporal abnormality and a left parietal abnormality in manic depressives. In terms of proportional power values manic depressives had significantly less proportional alpha power in the left and right temporal regions and significantly more proportional gamma power in the same regions. In both cases differences were more significant on the right. Temporal proportional power differences tended to be positive for manic depressives and negative for schizophrenics. Differences were significant suggesting a right emphasis of beta for manic depressives and a left emphasis for schizophrenics. The suggestion of a neurophysiological abnormality in the left temporal region in schizophrenics and in the right temporal region in manic depressives agrees with recent neuropsychological evidence reported by Flor-Henry and Yeudall et al (75) implicating

predominantly left fronto-temporal dysfunction in schizophrenia and predominantly right fronto-temporal dysfunction in the manic depressive disorder. More difficult to reconcile with neuropsychological evidence is the finding of a left parietal EEG abnormality in manic depressives. A localized neural abnormality in the left parietal region has no correlate in terms of neuropsychological impairment. The possibility exists though, that an EEG abnormality appearing in the left parietal region has it's origin in the frontal poles. Figure 8.1, from Carpenter (73), illustrates long and short association fibres in the left hemisphere. The bundle of fibres known as the superior longitudinal fascisulus passes from the frontal poles to the parietal poles. The bundle passes approximately midway between the C_z and T3 electrodes and electrical activity conducted along the bundle would likely affect both electrodes equally and appear as a common mode signal rather than a differential signal as it would between P3 and C_z. While this explanation is consistent with the observed results direct confirmation would require recording from optimally placed frontal electrodes.

8.4 Variability

A number of investigators (34), (35), (36), and (50) have reported a lower coefficient of variation in

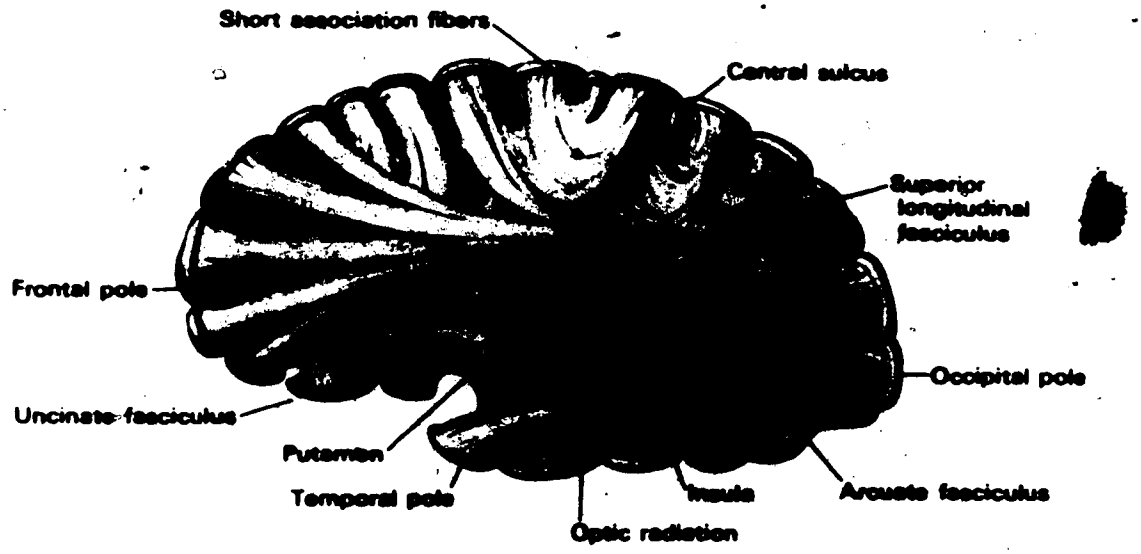


Figure 8.1. Dissection of the lateral surface of the left hemisphere to display long and short association fibers. The bundle of fibres denoted the superior longitudinal fasciculus extends from the frontal pole into portions of the parietal and occipital lobe. The figure is a reproduction of Figure 2-10 of Carpenter's Core Text of Neuroanatomy.

schizophrenic patients in comparison to normal controls. All reports of a lowered coefficient of variation were based on EEGs recorded in patients with the diagnosis of chronic schizophrenia. The results reported in section 7.4, while not showing any significant intergroup differences between the schizophrenic and normal group, are not at variance with the literature. Marjerrison (1967) studied EEG amplitude variability in chronic schizophrenics, acute schizophrenics, and normals (36). The CV of chronics was significantly lower than the CV of the normal group ($p<0.01$) and the acute group considered as a whole ($p<.05$). Acutes who reported hullucinations during the EEG recording, however, had a significantly lower CV than the acutes who didn't hallucinate. Sugerman et al 1973 (37) described a separation of schizophrenics into two major groups for research purposes suggested by Cromwell (74). The two groups, described more specifically in (74), were designated high redundancy and low redundancy and correspond roughly with the chronic acute dichotomy. To quote the authors: "Our own experience is that the chronically hospitalized patients, corresponding to Cromwell's high redundancy group, characteristically show low EEG variability, while recently admitted schizophrenics, unclassified as to high or low redundancy, may show a wide range of variability." While the group of schizophrenics used in this study included some

chronic patients the majority of the group fitted acute/low redundancy classification more accurately.

An attempt to explain the hypovariability of manic depressives in relation to normals and schizophrenics in certain power band comparisons must be made in accordance with an assumed relationship between brain function and the EEG. The relationship assumed in the following explanation is that moment to moment changes in consciousness are paralled by moment to moment fluctuations in the EEG signal. The definition of consciousness assumed in this explanation is from Eccles (18). Eccles considers consciousness as having three components; outer sense, inner sense, and pure ego. Outer sense refers to our ability to sense light, colour, sound, smell,taste, pain, and touch. Inner sense refers to consciousness of thoughts, feelings, memories, dreams, imaginings, and intentions. Pure ego is consciousness of the self. Moment to moment changes in consciousness will therefore result from an individuals response to external stimuli or changing aspects of inner sense. Manic depressives in the depressed phase are conceivably at a relatively fixed low level of consciousnous and their EEGs, as a result, are relatively invariant over the epoch length used for variability analysis. The depressed patients typical complaint of slowed or "mixed up" thinking and their lack of reactivity to external stimuli

are not inconsistent with this explanation. Manic depressives in a manic phase are conceivably at a fixed high level of consciousness. Their EEGs, as result, rapidly fluctuate from moment to moment at a relatively uniform rate but remain relatively invariant over the epoch length used for analysis. The epoch length chosen for this study, based on significant results reported in schizophrenics is likely large with respect to the period of a manics high rate of moment to moment EEG fluctuations and thus would tend to average them out. A variability analysis using a wide range of epoch lengths would have to be performed to verify this notion.

8.5 Discriminant Analysis

The results obtained by application of discriminant analysis to individual groups during performance of verbal and spatial tasks indicate that the multidimensional EEG discriminator used in the analysis can efficiently differentiate between verbal and spatial modes of thought in both normal and psychotic individuals. The use of a multivariate discriminator can potentially provide a much more efficient discriminator than a single variable. Mean R/L ratios, for example, are significantly different during verbal and spatial tasks but their separate distributions overlap considerably. Knowledge of the R/L ratio of a

subject during an unknown task would not define his mode of thinking reliably. A multivariate measure will often prove a more reliable discriminator even though the distributions of individual components of the discriminator overlap considerably. Section 14.14 of Sokal and Rohlf (67) discusses this point for a bivariate situation. While the results are promising it is worth noting that the analyses shown in tables 7.5, 7.6(a), and 7.6(b) were based on alpha band parameters only for four regions. Better discrimination could very likely be obtained by the use of more electrodes, including measures for other frequency bands, and also by devising new measures.

A reliable index for assessing the lateralization of mental processes suggests a variety of possible areas of research. Galin and Ornstein (3) discussed various possible potential uses for such an index.

The authors summarized evidence suggesting that disorders such as dyslexia and stuttering and various learning difficulties may be due to poorly developed cerebral lateralization for verbal and spatial activities; they mentioned the possible applications of an electrophysiological index of laterality in the investigation of these disorders. The possibility of studying the ontogenetic development of cerebral

specialization was also suggested and potential therapeutic uses of lateralized alpha feedback training in the treatment of disorders due to poorly developed cerebral lateralization were considered.

The results obtained by application of discriminant analysis to different groups during a given condition are shown in tables 7.6(a) and (d) and tables 7.7(a) and (b). The results depicted in table 7.6(a), while showing significant intergroup effects, indicate that considerable overlap exists in the distributions of the populations analyzed with this particular multivariate discriminator. The large percentage of individuals misclassified in each group precludes use of the discriminator in differential diagnosis. The analysis shown in 7.6(b), manic depressives versus schizophrenics in mental arithmetic misclassified 30% of manic depressives but only 15% of the schizophrenics. The fact that relatively fewer schizophrenics were misclassified in a predominantly left hemisphere task implies that schizophrenics have an EEG profile more peculiar to them in a left hemisphere task than do manic depressives. This is consistent with evidence from other disciplines suggesting left hemisphere dysfunction in schizophrenia. Table 7.7(a) and 7.7(b) summarize the discriminant analysis for the three groups in the eyes closed resting condition. Table 7.7(a) summarizes the analysis for the three groups seperately;

table 7.7(b) summarizes the analysis for pooled psychotics versus normals. As in table 7.6(a) and 7.6(b) significant intergroup differences were found although too much overlap between the groups was present to allow use of the discriminator in differential diagnosis. In table 7.7(a) relatively fewer normals were misclassified than were either schizophrenics or manic depressives. In table 7.7(b), pooled psychotics versus normals, roughly equal numbers of psychotics and normals were misclassified. On the basis of this particular multivariate discriminator it appears that a considerable proportion of psychotics have abnormal EEG's although the individual variables of the discriminator overlap considerably between the two psychotic groups.

The failure of a particular multivariate discriminator to correctly classify members of two or more groups hypothesized as disparate may be due to either: (1) the inherent inability of the discriminator to differentiate between the groups or (2) homogeneity of groups thought to be heterogeneous. The discriminator used in this analysis utilized nine EEG variables based on auto-spectral parameters for one task. Many other possibilities exist for choosing a discriminator based on both auto and cross spectral differences between groups for various regions during different tasks. An approach to the problem of an optimum discriminator similar to that applied by Sklar and

Hanley (65) is a possibility for future work. Aside from the possibility that efficient discrimination between the major psychotic groups may be impossible on the basis of the scalp EEG, the problem of misdiagnosing individuals into the different psychotic groups always exists. If an efficient discriminator were established on the basis of rigidly defined groups however, it could be applied in differential diagnosis to help prevent misclassification.

8.6 Summary

Evidence has been presented showing EEG asymmetries between predominantly left hemisphere and predominantly right hemisphere tasks and differences between normals and psychotics in terms of quantitative parameters based on EEG spectra. This section will (1) briefly outline the main significant EEG differences found between verbal and spatial tasks, in normal and psychotic subjects and (2) summarize the implications for localized cerebral dysfunction of the significant intragroup and intergroup differences in proportional power and variability.

R/L ratios were significantly higher in verbal tasks than in spatial tasks for both normals and psychotics. Significant differences occurred more consistently in the alpha band. When intertask alpha band differences were

significant in both temporal and parietal regions for both motor and non-motor tasks, differences between motor tasks tended to be more significant in the temporal region and differences between non-motor tasks tended to be more significant in the parietal region. This finding is consistent with the normal anatomical localization of motor functions in the anterior regions of the cerebrum and non-motor functions in the posterior region. Alpha band coherence values for the verbal non-motor task were significantly higher than values for the spatial non-motor task for the P3T3 and T4T3 lead pairs. Based on the subjects chosen for intergroup comparisons no significant intergroup differences were found by single classification analysis of variance for either R/L ratios or alpha band coherences.

The significant intergroup and intragroup differences found in proportional power, R/L ratios and variability in the EC resting condition support the hypothesis that EEG abnormalities in psychotic patients tend to occur in definite regions of the cerebrum. Within group and between group proportional power and R/L ratio comparisons suggested EEG abnormalities predominantly in the left temporal region for schizophrenics. Variability differences between schizophrenics and normals were not significant. Significant intragroup and intergroup proportional power comparisons suggested a bitemporal though predominantly right EEG

abnormality in manic depressives. Intergroup proportional power comparisons also suggested a left parietal EEG abnormality in manic depressives. It was suggested that the abnormality may have it's origin in activity from the frontal poles passing into the parietal region along the superior longitudinal fasciculus. In terms of EEG variability certain manic depressive vs normal and manic depressive vs schizophrenic comparisons showed a relative hypovariability in manic depressives. The most significant normal vs manic depressive comparisons occurred on the left in the temporal region and on the right in the parietal region. The most significant manic depressive vs schizophrenic comparisons occurred in the parietal region, especially in the right hemisphere. An explanation was advanced suggesting the EEG variability changes mirrored disturbances in moment to moment changes in consciousness .

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