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Journal
International Journal of Psychophysiology, 5(3)

ISSN
0167-8760

Authors
Sandman, Curt A
Gerner, Robert
O'Halloran, James P
et al.

Publication Date
1987-10-01

DOI
10.1016/0167-8760(87)90008-0

International Journal of Psychophysiology, 5 (1987) 215–225
Elsevier

PSP 00174

Event-related potentials and item recognition in depressed, schizophrenic and alcoholic patients

Curt A. Sandman[1,2], Robert Gerner[3], James P. O'Halloran[2] and Robert Isenhart[2]

[1] *State Developmental Research Institute, Fairview, Costa Mesa, CA 92626 (U.S.A.),* [2] *Departments of Psychiatry and Psychobiology, University of California, Irvine, CA 92717 (U.S.A.) and* [3] *Veterans Administration Hospital, Brentwood, CA (U.S.A.)*

(Accepted 4 June 1987)

Key words: Evoked potential; Item recognition; Depression; Schizophrenia; Alcoholism

Auditory event-related potentials (ERPs) to pure tones and performance on a measure of item recognition were compared in 20 controls, 14 alcoholics, 20 depressed and 21 schizophrenic patients. Compared with normal controls, P2 and N2 were delayed and of diminished amplitude in the psychopathological groups. Increased amplitude of P1 in alcoholics, diminished N1 in depressed patients, increased latencies of N1 in schizophrenics and N2 in alcoholics were pathology-specific. Unusual patterns of response in the item recognition test (elevated intercept and flattened slope) and its relationship with ERPs distinguished the diagnostic groups from the controls. Support for the preferential involvement of the left hemisphere in schizophrenia and of the right hemisphere in depression was found. Disinhibition of CNS activity in the response of alcoholics (increased P1 and delayed P3) was indicated. The findings suggested that discriminant analysis of auditory ERPs to simple, pure tones, in conjunction with psychometric data significantly differentiated pathologic groups from each other and from controls.

INTRODUCTION

As described by Shagass et al. (1978), there are two major goals of event-related potential (ERP) research in psychopathology: (1) development of reliable, "objective diagnostic indicators" and (2) characterization of possible neurophysiological deficits associated with mental illness or cognitive deficits. Discovery of such physiological deficits may yield important information regarding risk factors for psychopathology and suggest therapeutic procedures. In reviewing previously published studies, Shagass et al. (1978) noted several brain ERP signs associated with specific psychopathological disorders. In general, however, these studies have suffered from several shortcomings which have limited their application and interpretation. For example, most previous ERP studies have compared separate psychopathologic groups only with normal controls, and as a result, information related to differential diagnosis has not been forthcoming. Second, few studies have related ERP variables to established measures of cognitive integrity in these groups. Third, rarely is assessment of patients made during drug-free periods. Fourth, auditory stimuli have been used less frequently with patients than electrocutaneous or visual stimulation. This is surprising since the auditory mode permits delivery of stimulation requiring only minimal compliance, a non-trivial factor when assessing patients evidencing psychopathology, and is sensitive to lateralized differences among groups (Connolly et al., 1985). Further shortcomings of ERP studies in psychopathology are due to the variety of testing procedures that have been applied, thereby contributing to difficulties in interpreting results accross stud-

Correspondence: C.A. Sandman, State Developmental Research Institute, Fairview, Box 5, 2501 Harbor Boulevard, Costa Mesa, CA 92626, U.S.A.

ies. Tueting et al. (1984) have noted this "lack of equivalence between experimental protocol" and the problems it creates in establishing ERP/psychopathology relationships. The present study utilized perhaps the simplest possible stimuli, single frequency, repetitive tones, and did not require active responding by patients. While there have been previous auditory ERP studies, very few have relied on simple, pure tones as eliciting stimuli. Further, the present study did not require the elicitation of a performance-based long-latency component (e.g. P300), as this would introduce another level of complexity to the design and interpretation of the data, although previous studies (e.g. Roth et al., 1980; Shagass et al.,1978) have shown significant sensitivity of participation-based P300 responses in psychopathological groups. The advantages of this paradigm are its ease of application across subject groups and lack of task-related behavioral demands required in P300-type studies. Thus, this simple procedure allows waveform comparison across patient groups who may vary in their ability to comply with instructions.

The present study was a preliminary assessment of the auditory ERP and item recognition paradigm in 4 groups of drug-free patients and a control group. The goal of this study was to determine if simple auditory stimuli, without the requirement of a behavioral response, could evoke pathology-specific brain electrical responses in patients with well-defined psychopathology. In addition, a cognitive assessment, the item recognition test of Sternberg was administered, Results from the Sternberg item recognition (Sternberg, 1967, 1969, 1975) are affected in one manner (intercept) by attentional processes and in a completely different manner (slope) by memorial influences. Thus, this task permits assessment of two critical processes in psychopathological groups.

METHODS

Subjects

Right-handed subjects were identified using the Edinburgh Inventory (Oldfield, 1971) from a Veterans Administration psychiatric in-patient research ward and tested as part of the routine clinical evaluation. All patients were diagnosed by a psychiatrist according to DSM III criteria. Schizophrenics all had chronic schizophrenia and were of the disorganized or undifferentiated type. All schizophrenics previously had been chronically treated (< 6 months) with neuroleptics. None had significant concomitant medical or neurological disorders by physical exam or laboratory screening. Bipolar and unipolar depressed patients had a major depression. Alcoholics had been hospitalized continuously for 30 days for alcohol-dependence, and were documented to be free of alcohol or other drugs for 3 or more weeks prior to testing. These patients were receiving disulfiram 250 mg/day as part of routine clinical management and did not have serious concomitant medical disorders at the time of testing. The depressed and schizophrenic patients had been hospitalized and were medication-free for at least 7 days prior to testing (14 days for injection of prolixin), except for prior use of chloral hydrate for insomnia or agitation. Patients did not receive chloral hydrate during the day of testing. Normal subjects denied the use of medications, drug abuse, or a history of mental or presence of physical disorders. (Demographic parameters are given for all subjects in Table I.) Complete ERP data were collected from 75 patients and control subjects. Sixty-five of these subjects also completed the item recognition test. As is apparent from Table I, the subjects differed in age ($F_{4,70} = 6.85$, $P < 0.01$) due to the younger age of the control group (psychopathological groups alone; $F_{3,50} = 0.45$, $P > 0.05$).

ERP procedure

Subjects reclined in a comfortable chair while transducers were applied for recording EEG from each hemisphere of the brain. Grass Ag/Agcl cup electrodes were attached to the scalp overlying the right and left hemisphere of the brain according to the International 10-20 system. Monopolar placements at C_3 and C_4 were referenced to linked mastoids. The electrode sites were swabbed with acetone and the electrodes filled with Grass EEG creme and affixed to the scalp with non-flexible collodion. Pairs of electrodes with impedance of greater than 10,000 Ω were replaced, although

TABLE 1

Demographic characteristics of sample

Number of subjects completing the item recognition test is given in parentheses.

	Affective disorder				
	Normals	*Alcoholics*	*Bipolar*	*Unipolar*	*Schizophrenic*
n =	20 (17)	14 (11)	13 (13)	7 (6)	21 (18)
Females	11	1	1	1	2
age (years)	29.9 ± 9.6	43.1 ± 16.2	47.5 ± 12.4	45.4 ± 12.7	33.0 ± 9.1

impedance of less than 5000 Ω was achieved for nearly every subject. Most importantly, electrodes with differences between the left and right hemisphere of greater than 1000 Ω were corrected. The EEG signal was amplified by a Nihon Kohden JE 101A polygraph using AC preamplifiers with the low frequency filter set at 1 Hz and the high frequency filter set at 35 Hz. This could be expected to attenuate the amplitude of slower components such as the P300, but long latency waves were not the focus of this study. The subjects were fitted with headphones (Senheiser HD 400) for pure tone (600 Hz), auditory stimulation (dB adjusted from absolute threshold for each client), and were instructed to count the stimuli. This instruction was used simply as a means of directing the subject's attention without requiring an overt response to each stimulus as it was presented. This instruction resulted in small but visually evident late component (P300) activity. All subjects were studied under eyes-closed conditions so that EOG contamination of data epochs was minimized.

On-line averaging of the EEG by an Apple II computer interfaced with the amplifiers provided a refreshed, running average as well as the EEG sample from which the average was computed. The computer rejected all samples with amplitudes over 100 μV (positive or negative polarity). The ERP was analyzed by sampling the EEG at 200 Hz for 640 ms. The 500-ms post-stimulus sampling period was zeroed by averaging the preceding 140 ms (i.e. prestimulus) epoch.

Fifty ERP's to the tones were averaged for each subject. The latencies and peak-to-peak amplitudes (i.e. absolute differences) of the major components were identified. The entire ERP waveforms, including the prestimulus segments, were evaluated by a trained technician to identify the prominent peaks within specific latency windows (P1, 30–80 ms; N1, 70–150 ms; P2, 130–250 ms; N2, 180–320 ms; P3, 250–600 ms). A semi-automated scoring program displayed the ERP's on a CRT and placed cursors at the points of greatest positivity and negativity. In this program, a spectral interpolation technique was applied for measurement of the latency of waveform peaks. The waveform was approximated as a sum of sinusoids (the Fourier coefficients) resulting in unlimited temporal resolution and accurately describing components comprised of frequencies up to 25 Hz (the Nyquist frequency). Latencies in this study were rounded off to 5 ms.

Item recognition task

The Sternberg item recognition task required the subject to memorize a target set composed of one, two or four digits. The target set appeared for 0.8–1.2 s, depending on size of the target set, which varied on each trial. Subsequently, a warning signal appeared followed by a single test digit embedded in a background of distractors (letters). The subject depressed one electronic switch if the test digit was a member of the memorized set and a second switch if it was not. One half of the test digits were members of the set and half were not.

Ideally, reaction time (RT) is a linearly increasing function of the size of the memory set. Current models (Sternberg, 1975) posit that RT consists of (a) time needed to encode the test digit; (b) time needed to compare the test digit with the target set; and (c) time needed to select the response.

Attentional processes are reflected in (a) and (c) and appear as changes in the intercept. Memory is reflected in (b) and appears as changes in slope of the plot of set size versus RT.

RESULTS

Waveforms obtained using this paradigm exhibited typical, well-defined components with visually apparent differences between groups (Fig. 1). Although this paradigm was not designed to elicite a P3 component, a small, positive peak followed the N2 in these waveforms and will be referred to as P3 in the following discussion. Several analyses were conducted: (1) analysis of covariance; (2) discriminant function analysis; and (3) correlations of ERP with item recognition.

Analysis of covariance (ANCOVA) – amplitude

A relationship of age to the dependent variables was tested with bivariate analysis. A significant linear effect only was measured between age and N1. This is not surprising since age-related effects on the ERP typically are not apparent until after age 60 (Ford et al. 1979; 1982). Nevertheless, because of a significant group difference in age, a conservative covariance analysis is presented.

A 5 (group) $\times$ 2 (hemisphere of the brain) ANCOVA (with age as covariate) was computed for measures of amplitude and latency. As presented in Fig. 1, the major differences in amplitude among the groups were for P2 ($F_{4,69} = 3.29$, $P < 0.02$ beta estimate -0.03) and N2 ($F_{4,69} = 2.40$, $P < 0.05$ beta estimate -0.01). Simple effects tests indicated that the P2 differences were due primarily to the larger responses in normal subjects and the diminished response in schizophrenics ($F_{1,39} = 7.88$, $P < 0.01$). The significant effect for N2 was related to larger responses of controls compared with Bipolar depressives $F_{1,32} = 7.94$, $P < 0.01$).

Amplitude changes in early components were most powerful in differentiating among the psychopathological groups. The amplitude of P1 was significantly greater in alcoholics compared with bipolar depressed patients ($F_{1,24} = 4.58$, $P < 0.04$). Bipolar patients also had diminished N1 responses compared with schizophrenics. Thus, several measures of ERP amplitude characterized the groups. A listing of discrete values of amplitude and latency for each of the 4 diagnostic groups is given in Table II.

Latency

Measures of component latency were highly significant in separating the diagnostic groups. The latency of P2 ($F_{4,69} = 4.42$, $P < 0.01$ beta estimate 0.05) and N2 ($F_{4,69}$) = 3.04, $P < 0.02$ beta estimate 0.23) both were highly significant by analysis of covariance. The apparent difference in the latency of N1 overall was erased with covariance indicating that it was an age-related effect. However, pairwise analysis of covariance indicated that the normal groups had significantly shorter N1 ($F_{1,31} = 4.14$, $P < 0.05$), P2 ($F_{1,31} = 5.56$, $P < 0.02$), N2 ($F_{1,31} = 7.86$, $P < 0.01$), and P3 ($F_{1,31} = 4.53$, $P < 0.04$) components than the alcoholic group. Normals differed from schizophrenics in the latency of N1 ($F_{1,38} = 6.04$, $P < 0.02$) and P2 ($F_{1,38} = 9.98$, $P < 0.01$), but they did not differ on any latency measure from the affectively disordered patients. The alcoholics also had significantly longer N2 latencies than schizophrenics ($F_{1,32} = 5.59$, $P < 0.02$) and the depressed patients ($F_{1,24} = 4.86$, $P < 0.04$).

Although the overall analysis did not reveal signs of hemisphericity, 3 significant interactions between diagnosis and hemisphere of the brain were detected for pairwise covariance analyses and are presented in Fig. 2. In Fig. 2a, the lateralized difference between normals and schizophrenics for the amplitude of P1 is illustrated. The greater right hemispheric amplitude in normals is contrasted with a greater left hemisphere amplitude in schizophrenics ($F_{1,39} = 4.75$, $P < 0.04$). The right hemispheric latency of P1 in affective patients compared to alcoholics is presented in Fig. 2b ($F_{1,25} = 5.31$, $P < 0.03$). Panel 2c contrasts the left hemispheric latency of N1 in schizophrenics with the right hemispheric latency in affective patients ($F_{1,32} = 4.44$, $P < 0.04$). Thus, although not compelling, evidence of laterality related to psychopathology is suggested.

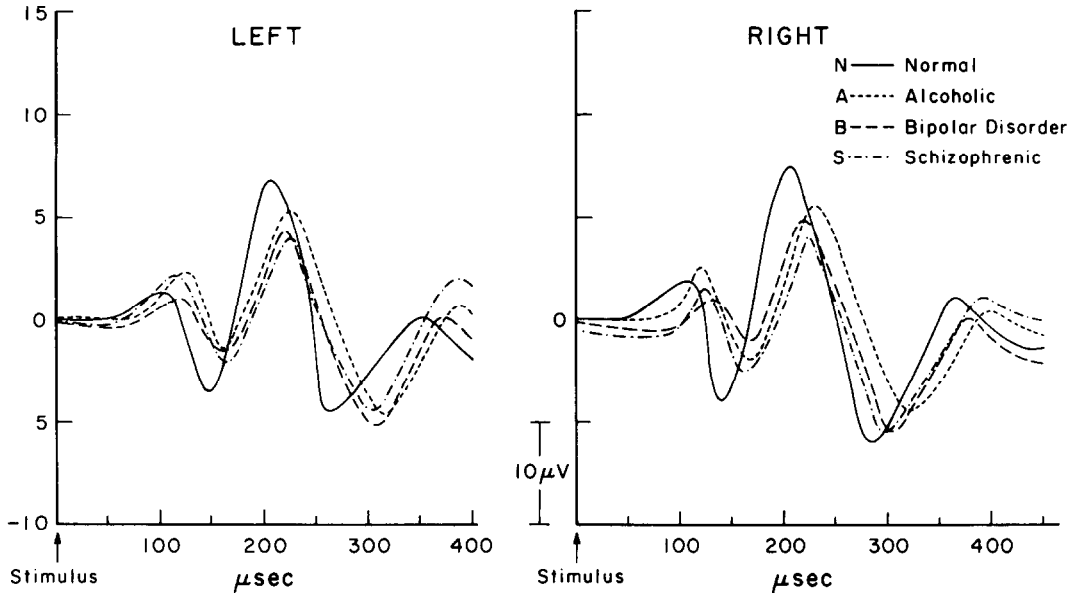

Fig. 1. Event-related potentials of the brain recorded over the left (C3) and right central hemispheres (C4) of normal volunteers, alcoholics, schizophrenics and bipolar depressed patients.

Stepwise discriminant function analysis (SWDA)

Data from 4 groups (unipolar patients were not used due to the small number of patients) were entered into SWDA to determine which variables would best separate the diagnostic classes. Two comparative analyses were conducted. The first included all of the groups including the normal controls. The second included only the patient groups. As is evident in Table III and displayed in Fig. 3, the groups were statistically distinct. Use of a jack-knifing procedure demonstrated that a high percentage of subjects/patients (39–65%) were ac-

TABLE II

Integer values of latency and amplitude for the major evoked potential components

	Normal		*Alcoholic*		*Bipolar*		*Schizophrenic*	
	Latency (ms)	*Amplitude (μV)*	*Latency (ms)*	*Amplitude (μV)*	*Latency (ms)*	*Amplitude (μV)*	*Latency (ms)*	*Amplitude (μV)*
C3								
P1	104 ± 20	1.2 ± 1.3	126 ± 42	2.3 ± 1.4	122 ± 29	1.5 ± 1.0	118 ± 29	1.9 ± 1.4
N1	145 ± 16	4.8 ± 4.3	164 ± 33	3.9 ± 2.0	161 ± 20	3.0 ± 1.4	164 ± 17	4.3 ± 2.5
P2	204 ± 20	10.5 ± 5.9	226 ± 13	6.9 ± 3.7	248 ± 9	6.9 ± 2.0	226 ± 24	6.5 ± 3.2
N2	282 ± 36	11.6 ± 5.3	313 ± 21	9.9 ± 2.3	305 ± 27	9.8 ± 1.9	300 ± 27	9.0 ± 3.8
P3	359 ± 60	9.1 ± 4.0	388 ± 43	5.3 ± 2.6	367 ± 31	5.5 ± 2.8	382 ± 37	6.7 ± 2.4
C4								
P1	104 ± 23	1.8 ± 1.3	112 ± 37	2.2 ± 1.6	127 ± 24	1.1 ± 0.7	118 ± 30	1.6 ± 1.5
N1	148 ± 21	4.7 ± 4.1	166 ± 21	3.6 ± 1.7	164 ± 14	1.2 ± 1.3	157 ± 15	4.3 ± 2.5
P2	207 ± 21	11.4 ± 5.8	224 ± 12	7.8 ± 2.9	216 ± 8	7.1 ± 2.4	224 ± 19	6.7 ± 3.4
N2	283 ± 36	13.6 ± 4.0	323 ± 20	10.6 ± 3.5	305 ± 13	10.0 ± 3	296 ± 21	9.3 ± 3.9
P3	359 ± 56	8.0 ± 4.0	393 ± 29	5.8 ± 2.4	370 ± 29	5.8 ± 26	381 ± 31	7.4 ± 2.7

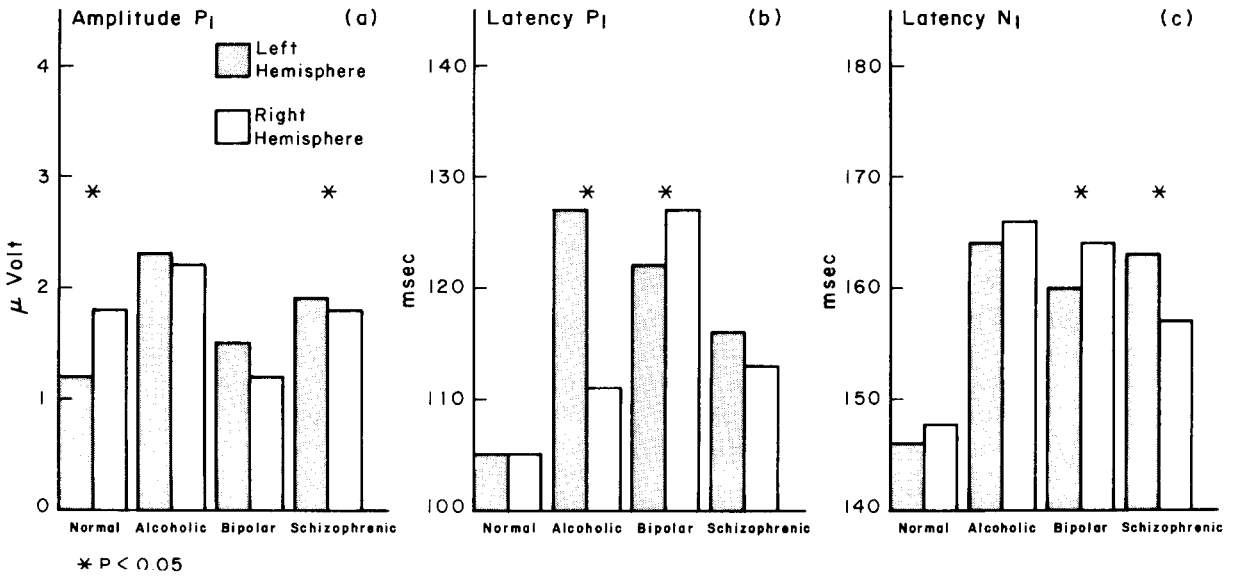

Fig. 2. The amplitude of P1 (a), the latency of P1 (b) and the latency of N1 (c) are compared in the 4 groups for the right and left hemisphere. The * indicates a significant ($P < 0.05$) interaction of group and hemisphere.

TABLE III

Classification of subject groups using the ERP by stepwise discriminant function analysis, including the variable entering, their order and significances

Jack-knifing percentages appear in parentheses; RH, right hemisphere; LH, left hemisphere.

	%Accurately classified	*Number of subjects accurately classified by analysis of the ERP*			
		Normals	*Alcoholics*	*Affective*	*Schizophrenics*
Normals	(65)	15	0	4	1
Alcoholics	(64)	1	9	2	2
Affective	(39)	1	3	7	2
Schizophrenics	(52)	3	4	2	12
Variables entering (in order)		*F*	df		
Latency N2	RH	7.13 *	3,64		
Amplitude N2	RH	6.13 *	6,126		
Latency P2	LH	5.78 *	9,151		
Amplitude P1	LH	5.35 *	12,161		
Amplitude P3	RH	4.84 *	15,166		
Classification of the patient groups only					
Alcoholics	(50)		10	3	1
Affective	(62)		2	10	1
Schizophrenic	(57)		2	4	15
Variables entering (in order)		*F*	df		
Latency N2	RH	8.93 *	2,45		
Amplitude P1	RH	5.56 *	4,88		
Amplitude N1	RH	5.23 *	6,86		
Amplitude P2	RH	4.99 *	8,84		
Amplitude P3	RH	4.49 *	10,82		

* $P < 0.01$.

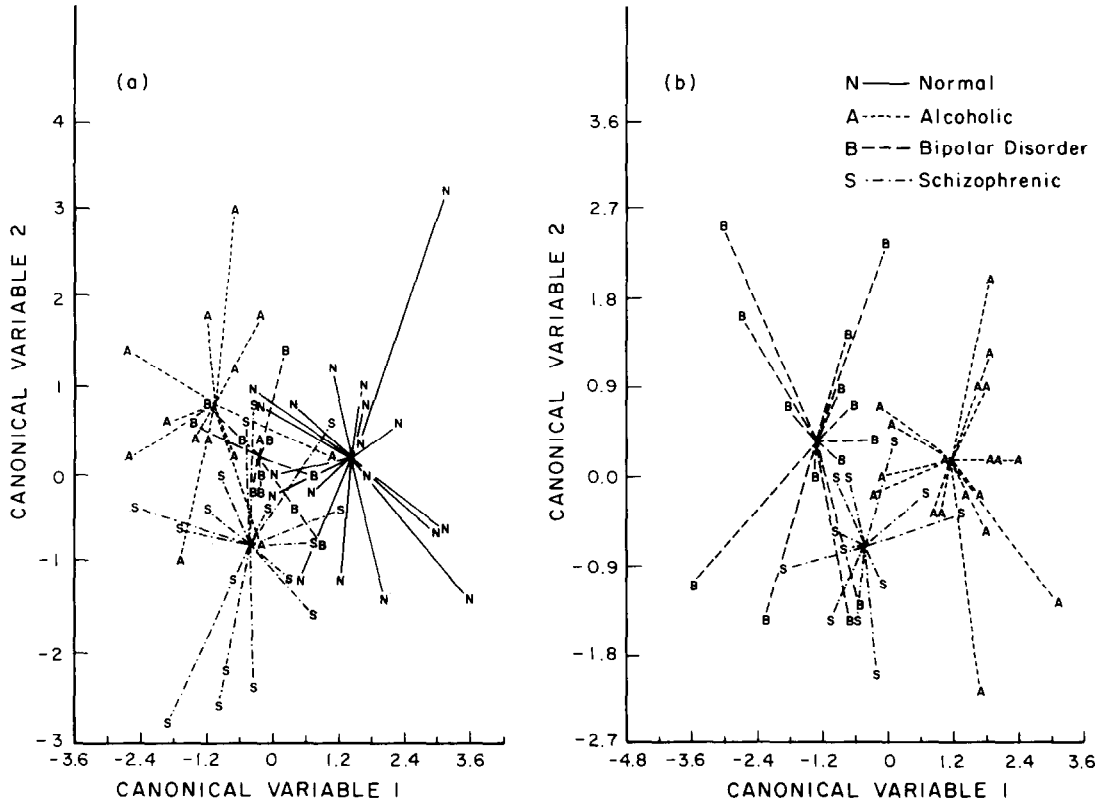

Fig. 3. Results of the stepwise discriminant analyses are presented in (a) (all subjects) and (b) (patients groups). Each point represents an individual case in 2-dimensional, canonical (linear combination of variables) space. Unique clustering of the groups was statistically reliable (see Table II).

curately classified (25% is chance in this analysis). The latency of the variables entering the equation was consistent with that found in the ANCOVA.

Analysis of the psychopathological groups alone also indicated a high (50–62%) statistical separation (33% is chance). Very few (1 each) of the alcoholics and depressed patients were misclassified as schizophrenics. The schizophrenics classification was less homogenous. All of the variables entering the discriminant equation were from the right hemisphere. Inspection of the data indicated that in every case, compared with measures from the left hemisphere, measures from the right hemisphere were of lower amplitude for early components (P1, N1) and of longer latency for later components (P2, N2, P3).

Item recognition

The reaction time for each of the memory sets, the intercept and slope function were analyzed by analysis of covariance. As is evident from Fig. 4, the intercept values (and linear functions) varied radically for the 5 groups but failed to reach acceptable levels of significance ($F_{4,60} = 2.31$, $P < 0.07$). The variability among subjects, especially acute in the alcoholic group, restricted the power of parametric statistical tests. The intercept and slope are within acceptable ranges for the control group thus validating the procedures. The most unusual finding was the inverted function for alcoholics (slope of -44 ms/memory set) and the flat slope for schizophrenics. Surprisingly, both of these groups had faster reaction times for a memory set of 2 than 4 ($F_{4,60} = 4.47$, $P < 0.01$).

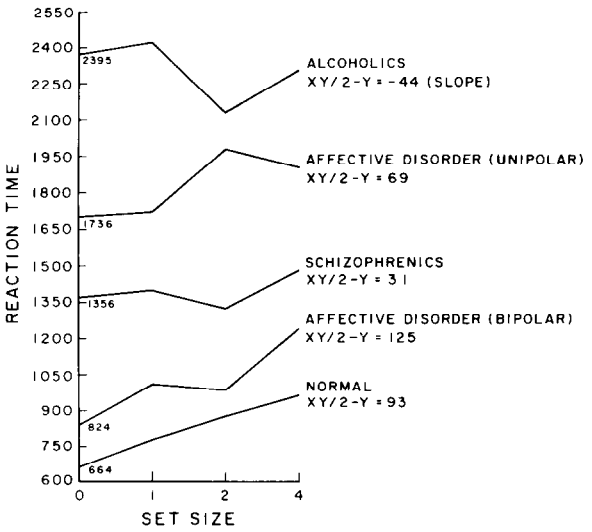

Fig. 4. Reaction times of the item recognition test for each group expressed as the intercept (ms) and slope (xy/2 − y).

ERP and RT relationship

Since ERP's and RT's in the item recognition test reflect different measures of neural efficiency, the relationship between these measures was examined with bivariate analyses. For all subjects considered together, only latency of P1 (for left and right hemisphere) correlated significantly with RT's for memory set 1, 2 and 4 and with the slope function (the range of $r = 0.29$–0.43, $P < 0.05$ with df = 64). This indicates that extended P1 latency was positively correlated with slower reaction time, suggesting that the peculiar patterns of RT observed in the patients may have neurophysiological substrates manifested in the early states of information processing (i.e. prior to long latency components).

Correlational matrices were also constructed for each group separately. The normal group displayed a positive relationship (0.47; 0.47, $P < 0.05$) between the latency of P3 (in both hemispheres) and RT in the item recognition task even though the two measures were taken sequentially. The slope of RT was positively (0.47, $P < 0.05$) related to the latency of P1 and negatively (-0.52, $P < 0.05$) related to amplitude of N1. In contrast, alcoholics had significant negative relationships between the latency of P3 (only in the right hemisphere) and RT for each of the memory sets (1 [−0.64], 2 [−0.74] and 4 [−0.66], all $P < 0.05$). Longer P3's were related to faster reaction times, in direct contrast with the normal controls. The exceedingly delayed RT's for alcoholics may have accounted for the inverted relationship.

The bipolar group displayed another distinctive pattern also localized in the right hemisphere. The amplitude of P2 was positively related to RT for memory set 1 (0.56), 2 (0.66) and 4 (0.84, $P < 0.05$). The remarkable stability of this relationship across all memory sets argues for its validity. The 0.84 correlation between P2 amplitude and set 4 RT is unusually high. The amplitude of P3 with set 1 (0.64) and set 2 (0.54) was also significant and underscores the amplitude-specific relationships of the ERP with RT in affective disorders. There were no predictable relationships between ERP variables and RT apparent for the schizophrenic patients.

DISCUSSION

The results of this study indicated that, compared with normals, patients with bipolar affective disorders, schizophrenia or alcoholism evidenced severe compromises on ERP and RT measures of neural efficiency. Later components (P2 and N2) of the ERP especially were delayed and were of diminished amplitude in the psychopathological groups.

The powerful discrimination among groups with the ERP in SWDA indicated that the amplitude and latency of waveform components, specifically in the right hemisphere, distinguished psychopathological classes from normals. Somewhat less discrimination was achieved by removing the control group, but significant discrimination was still observed. Of considerable interest in the analysis of the psychopathological groups was the exclusive contribution of measures from the right hemisphere in the 5-step analysis. The latency of N2, also the first variable to load for the contrast with the control group, combined with amplitude of P1, N1, P2, and P3 to separate, statistically, the groups. Thus, pathognomic signs of schizophrenia, depression or alcoholism may be detected in the right

hemisphere and be extracted by careful analysis.

The result of diminished amplitude of later components in schizophrenics is consistent with earlier reports (Baribeau-Braum et al., 1983; Shagass et al., 1977). However, Kadobayashi et al. (1977) reported that in their sample of Japanese schizophrenics, ERP amplitude was increased compared to normals except after a cognitive challenge. Whether or not cultural differences account for this finding is unknown. There was a trend, apparent in Fig. 1, indicating diminished amplitude for N1, a relatively invariant component across stimulus parameters (Davis et al., 1980) perhaps, suggesting that overall, the schizophrenics had dampened ERPs. Typically schizophrenics have diminished N1 in paradigms designed to elicit it (Davis et al., 1980; Buchsbaum, 1979b; Shagass et al., 1977; Baribeau-Braum et al., 1983).

The results of the cognitive test, coupled with delayed latencies of N1 and P2, reflected difficulties of encoding, response selection and memory in the schizophrenic group. These findings with a simple paradigm complement the elegant study of Baribeau-Braum et al. (1983), suggesting that schizophrenics suffer cognitive deficits related to both stimulus and response selection. Further, the present results suggested that these deficits are detectable in ERP procedures requiring only 'reflexive' responses of the nervous system.

Typically, patients with affective disorders have ERPs larger or as large as normal controls (Buchsbaum, 1979a). Even though Fig. 1 suggested significant differences in the ERP compared with controls, only amplitude of N2 reached acceptable levels of significance. These findings are not inconsistent with the results of the item recognition test as only small differences in the slope and intercept distinguished the affective patients from normals.

The findings in alcoholics of delayed latencies and diminished amplitudes were consistent with the literature (Porjesz et al., 1982). Of special interest however, was the pattern of differences between alcoholics and the depressed group. The differences of laterality mentioned above were supplemented by delayed P2 and N2 and increased amplitude of P1 in the alcoholics. In view of the extremely deficient cognitive performance, the 'hyper-responsive' P1 may reflect an alcohol-induced disinhibition of nervous system activity. The functional result may be a continuous orienting response and the inability to extract relevant information from the environment.

Further clues of differential diagnosis were provided by the relationship between brain activity and cognitive performance. Even with the successive task presentation, the normal subjects displayed the usual pattern of a positive relationship between the latency of ERP (especially late) components with RT (Marsh, 1975; Ford et al., 1979; Ford et al., 1982). The affective patients evidenced remarkably high positive relationships between late ERP component (N2 and P3) amplitudes and RT. However, only measures from the right hemisphere reached statistical significance. Affective patients with large responses tended to have longer RT's. Thus, behavioral depression (long RT's) may have trait-like relationships to measures of processing depth or cognitive capacity.

The pattern in alcoholics is the most curious. Of greatest interest is the consistent (for all RT's) negative relationship of P3 latency to RT. Alcoholic patients with delayed P3's had the fastest RT's. This effect is opposite to that seen in normals. The finding that alcoholics had extremely delayed RT's complicated the interpretation because it suggested inefficient coupling of encoding and response sequences. For instance, if, as suggested earlier, alcoholism disinhibits the nervous system (increased P1 amplitude), late components may reflect non-task-relevant responses. Thus, the P3 response in alcoholics may be simply a resonantly coupled reflection of P1. As such it may be driven by the physical parameters of the stimulus and reflect no information about cognitive process. In any case, a potentially useful model for testing brain and information theory may be generated.

Laterality and psychopathology

Several studies (Perris, 1974; Buchsbaum, 1979b; Gruzelier, 1984; Connolly et al., 1985) have suggested that schizophrenia may have a lateralized representation focused in the left hemisphere. In the present study, the greater left hemispheric amplitude of the P1 response of schizoph-

renics was contrasted with the greater right hemispheric amplitude of P1 in normals. Thus, a very early lateralized attentional/perceptual response in schizophrenics may reflect disruption of the selective attentional mechanisms specifically interfering with stimulus set attention (Picton et al., 1974; Picton and Hillyard, 1974; Baribeau-Braum et al., 1983; Connolly et al., 1985). Even in the simple task used in the present study, neurophysiological support for lateralized disregulation in schizophrenic patients was evident.

The speculation that schizophrenia is a disease of the left hemisphere and affective disorders are a disease of the right hemisphere (Gruzelier, 1984) received partial support. Contrasted with the nearly symmetrical responses in normals, affective patients had shorter latency N1 responses in the left hemisphere and longer in the right. The opposite pattern was apparent in the schizophrenics (Fig. 2b). This result is contrasted with the nearly symmetrical response in normals. A similar effect in affective patients was observed in the latency measures of P1 recorded in the left hemisphere. The perfectly symmetrical response of the controls and the nearly symmetrical response in schizophrenics is consistent with a right hemisphere "deficit" in the affective group and the left hemispheric delay in alcoholics. Thus, pathology-specific ERP effects emerged both from comparison with control subjects and with other diagnostic classes.

Limitations

The limitations of these findings are acknowledged. A consistent, meaningful drug-free interval for all subjects is a problem. Since many schizophrenics have been treated with neuroleptics with a biological half-life measured in months (even though drug half-life may only be days), and since it is difficult to test true schizophrenics who had been drug-free for weeks and in many settings it may be considered unethical to do so, most ERP/cognitive studies will be influenced by the recent or remote effects of neuroleptics. This does not mean such data are not useful (see Small, 1983). Furthermore, the report of Baribeau-Braum et al. (1983) indicated no major effects of neuroleptics on brain potentials of the latencies reported here.

Alcoholic patients raise similar issues. Certainly acute withdrawal phases may change the ERP and a completely controlled environment is the only way to be assured that the patients are not drinking. Our alcohol program lasted 30 days and patients were tested during the last week. Use of disulfiram ensures they are not drinking (an important issue) but also may produce a drug effect. However, Reilly et al. (1983) and Kelley and Reilly (1983) reported only a slight change in P80 in older alcoholics taking Antabuse.

Patterns of brain and cognitive activity differentiated normal subjects from schizophrenics, depressed and alcoholic patients. Several classically described differences were observed as well as new relationships. These data are considered a preliminary probe into the information processing capacity of psychopathological groups and may serve as a calibrator for future, more sophisticated studies of higher cognitive function in these groups.

ACKNOWLEDGEMENTS

The assistance of Sheila Tsai is gratefully acknowledged. This research was supported in part by the Scientific Advisory Council.

REFERENCES

Baribeau-Braum, J., Picton, T.W. and Gosselin, J.Y. (1983) Schizophrenia: a neurophysiological evaluation of abnormal information processing. *Science*, 219: 874.

Buchsbaum, M.S. (1979a) Neurophysiological reactivity, stimulus intensity modulation and the depressive disorders. In R. Depue (Ed.), *The Psychobiology of the Depression Disorders: Implication for the Effects of Stress*, Academic, New York.

Buchsbaum, M.S. (1979b) Neurophysiological aspects of the schizophrenic syndrome. In L. Belak (Ed.), *The Schizophrenia Syndrome*. Grune and Straton, New York.

Connolly, J.E., Manchanda, R., Gruzelier, J.H. and Hirsch, S.R. (1985) Pathway and hemispheric differences in the event-related potential (ERP) to monoaural stimulation: a comparison of schizophrenic patients with normal controls. *Biol. Psychiatry*, 20: 293–303.

Davis, G., Buchsbaum, M.S. and Bunney, W.E. (1980) Alterations of evoked potentials link research in attention dysfunction to peptide response symptoms of schizophrenia. In E. Costa and M. Trabucci (Eds.), *Neural Peptides and Neuronal Communication*, Raven, New York.

Ford, J.M., Pfefferbaum, A., Tinklenberg, J.R. and Kopell, B.S. (1982) Effects of perceptual and cognitive difficulty on P3 and RT in young and old adults. *Electroencephalogr. Clin. Neurophysiol.*, 54: 311–318.

Ford, J.M., Hink, R.F., Hopkins, W.F., Roth, W.T., Pfefferbaum, A. and Koppell, B.S. (1979) Age effects on event-related potentials in a selective attention task. *J. Gerontology*, 34: 388–395.

Gruzelier, J.H. (1984) Hemispheric imbalances in schizophrenia. *Int. J. Psychophysiol.*, 1: 227–234.

Kadobayashi, I., Nakamura, M. and Kato, N. (1977) Changes in visual evoked-potential of schizophrenics after addition tests. *Electroencephalogr. Clin. Neurophysiol.*, 43: 837–845.

Kelley, J.T. and Reilly, E.L. (1983) EEG alcohol and alcoholism. In J.R. Hughes and W. Wilson (Eds.), *EEG and Evoked Potentials in Behavioral Neurology*, Butterworths, Boston, pp. 55–78.

Marsh, G.R. (1975) Age differences in evoked potential correlates of a memory scanning process. *Exp. Aging Res.*, 1: 3–9.

Oldfield, R.C. (1971) The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychology*, 9: 97–113.

Perris, C. (1974) Average evoked responses (AER) in patients with affective disorders. *Acta Psychiatrica Scand.*, Suppl. 255: 89.

Picton, T., Hillyard, S., Krausz, H. and Galambos, R. (1974) Human auditory evoked potentials. I: Evaluations of components. *Electroencephalogr. Clin. Neurophysiol.*, 36: 179–185.

Picton, T.W. and Hillyard, S.A. (1974) Human auditory evoked potentials II: Effects of attention. *Electroencephalogr. Clin. Neurophysiol.*, 36: 191–196.

Porjesz, B., Begleiter, H. and Samuelly, I. (1982) Cognitive defects in chronic alcoholic and elderly subjects assessed by evoked brain potentials. *Acta Psychiatra Scand.*, Suppl. 286, 15: 147–154.

Reilly, E.L., Kelley, J.T., Pena, Y.M., Overall, J.E. and Faillace, L.A. (1983) Short latency brainstem and somatosensory evoked potentials in alcoholics. *Clin. Electroencephalogr.*, 14: 8–16.

Roth, W.T., Horvath, T., Pfefferbaum, A. and Kopell, B.S. (1980) Event-related potentials in schizophrenics. *Electroencephalogr. Clin. Neurophysiol.*, 48: 127–130.

Shagass, C., Straumanis, J.J., Roemer, R. and Amadzo, M. (1977) Evoked potentials of schizophrenics in several sensory modalities *Biol. Psychiatry*, 12: 221–228.

Shagass, C., Ornitz, E.M., Sutton, S. and Tueting, P. (1978) Event-related potentials and psychopathology, In E. Callaway, P. Tueting and S.H. Koslow (Eds.), *Event-Related Brain Potentials in Man*. Academic, New York.

Small, G.J. (1983) EEG in schizophrenics. In J.R. Hughes and W. Wilson (Eds.), *EEG and Evoked Potentials in Behavioral Neurology*, Butterworth, Boston, pp. 25–40.

Sternberg, S. (1967) Two operations in character recognition: some evidence from reaction-time measurements. *Perception Psychophysiol.*, 2: 45–54.

Sternberg, S. (1969) Memory-scanning: mental processes revealed by reaction time experiments. *Am. Sci.*, 57: 421.

Sternberg, S. (1975) Memory scanning: new findings and current controversies. *Q. J. Exp. Psychol.*, 27: 1–15.

Tueting, P., Kaskey, G., Buchsbaum, M., Connolly, J., Perris C. and Roemer, R. (1984) ERPs and psychopathology: II. Biological issues. *Ann. N.Y. Acad. Sci.*, 452: 523–545.