From: BIOLOGICAL EFFECTS OF ALCOHOL
Edited by Henri Regleiter
(Plenum Publishing Corporation, 1980)

VISUAL EVOKED POTENTIAL CORRELATES OF INFORMATION PROCESSING DEFICITS IN CHRONIC ALCOHOLICS

B. Porjesz, H. Begleiter and R. Garozzo,

Department of Psychiatry, Downstate Medical Center, State University of New York. Brooklyn, New York

INTRODUCTION

Chronic alcohol abuse has been postulated to lead to brain dysfunction. Neuropsychological tests have indicated that alcohol affects some intellectual abilities more than others (Goodwin and Hill, 1975; Kleinknecht and Goldstein, 1972); specifically visuo-spatial and visual-motor skills are impaired, while verbal skills appear to remain intact. In addition, alcoholics are reported to have difficulty in tasks requiring abstract reasoning. They have difficulty extracting the relevant dimensions of a stimulus array, particularly if the relevance of these dimensions changes (Oscar-Berman, 1973; 1978) and hence they are known to perseverate dominant response tendencies. These characteristics have been reported in patients with frontal brain damage (Oscar-Berman, 1973; 1978; Parsons, 1975; Luria, 1966; 1973; Pribram, 1973; 1975).

The advent of computer technology has made it possible to examine the intact brains of alcoholics more closely with computer tomographic (CT) scans, as well as to study ongoing brain functioning with the use of evoked potential (EP) techniques. While the CT scan can reliably assess static structural aberrations, it is not sensitive for assessing subtle damage such as mild cortical atrophy, and/or neurological dysfunction not accompanied by overt structural changes. Furthermore, neuropsychological

techniques must necessarily rely solely on behavioral indices. These behavioral indices, in turn reflect the interaction of a number of complex factors.

There are certain advantages in using the evoked potential over other techniques in assessing the functional integrity of brain functioning, namely; it is possible to record evoked potentials to various sensory stimuli in conjunction with behavior. In addition, the various EP components have been examined with regard to their possible neural generators and the cognitive processes that they represent. Therefore, the evoked potential provides a most sensitive tool to assess the locus of brain dysfunction, as well as a direct index of functional deficit.

For the past several years, our laboratory has systematically examined electrophysiological aberrations in chronic alcoholics with the use of evoked potential techniques. One recent study (Porjesz and Begleiter, 1978) was designed to specifically investigate frontal functioning in chronic alcoholics who had been abstinent from alcohol for a minimum of 3 weeks. Frontal functioning was examined by assessing the ability of alcoholic patients to inhibit responses to irrelevant stimuli. Our most salient findings were that the visual EP late component amplitudes N120-P200 (N1-P2) were markedly reduced in the alcoholics. This depression was most significant over frontal areas, and was also significant at parietal loci. While the frontal late component amplitude in the normal control group varied as a function of task relevance, no such relationship between degree of task relevance and N120-P200 amplitude was observed in the alcoholic group.

Consequently, the results of our study with this particular experimental paradigm demonstrated cortical dysfunction in chronic alcoholics most prominently over frontal areas, and suggested possible parietal involvement as well. Because of the known neuroanatomical connections between the frontal and parietal cortices (Von Bonin, 1960) it became evident that parietal functioning should be investigated with a more appropriate experimental paradigm. Hence, the present experiment utilized a specific evoked potential component, demonstrated to be maximum

at parietal loci by a number of investigators (Ritter et al., 1968; Simson et al., 1977), namely the P300 (P3) component. The P300 component is a positive occurring deflection, so named because it occurs approximately 300 msec after the stimulus.

A P300 wave can only be elicited under rather specific conditions, namely:

1) The subject is actively attending to the stimulus sequence (discriminating targets from non-targets), and a decision or response is required (Sutton et al., 1965; 1967).

2) The targets require a different response from that made to the non-targets.

3) The targets must occur unpredictably and infrequently (Tueting et al., 1971).

We designed a P300 study to examine brain functioning in alcoholics under conditions where we would expect they would manifest maximal dysfunction: namely under conditions using visuo-spatial stimuli and tapping information processing deficits.

The experimental design permitted us to examine visual EP characteristics to relevant and irrelevant visuo-spatial stimuli in chronic alcoholics as compared to controls in a paradigm that required the subject to change sets. Stimuli that were relevant in one block were no longer relevant in another block.

More specifically, this experiment was designed to electrophysiologically assess:

1) the brain locus or loci of dysfunction in chronic alcoholics (scalp locations discriminating best between alcoholics and controls),

2) the nature of brain aberrations manifested by chronic alcoholics (which visual EP components are affected), and

3) the degree or severity of dysfunction (magnitude of EP differences between alcoholics and controls).

METHODS

Subjects

The subjects were 10 right-handed male alcoholics with a mean age of 39 and a minimum of seven years

heavy drinking history. They had been drinking heavily an average of 17.4 years. They had been abstinent from alcohol for an average of two months, ranging from a minimum of three weeks to four months maximum. Only alcoholics who were otherwise healthy and medication-free for a minimum of two and one-half weeks were accepted for the study.

Ten age- and education-matched right-handed healthy males served as normal controls (mean age 35). The control subjects were occasional "social" drinkers. The experimental and control subjects were identical with regard to eye-dominance, and did not differ significantly with regard to age or education.

In addition to participating in evoked potential procedures, all alcoholic patients were subjected to CT-scan. The results of the CT-scan, and their relationship to our EP findings goes beyond the scope of the present paper and will not be reported here.

Electrodes

Gold cup electrodes were placed at midline occipital (Oz), parietal (Pz), central (Cz), and frontal (Fz) scalp locations, as well as bilaterally at frontal locations (F3 and F4) according to the 10-20 International System. The recordings were monopolar, using the ears as reference and the nasion as ground; vertical eye leads were used to record electro-oculogram (EOG) to monitor possible eye movement contamination. The bandwidth was 0.1 to 100 Hz.

Procedure

The subject was seated in a specially treated sound attenuating enclosure, with his head resting on an adjustable chin rest, so that he was looking in the center of his visual field at a computer-generated display (on the outside of the enclosure). The stimuli consisted of two regular geometric shapes (square and triangle) and irregular geometric forms (equated for size and intensity); all stimuli were presented with an interstimulus interval randomly varying from 2 to 5 seconds.

The subject's task was to press a button only to the target stimuli, either squares or triangles.

When the square was the target, the triangle was the non-target and vice-versa, such that EPs could be obtained to the same stimulus when it served as a target or non-target. The target stimuli occurred rarely, only 8.3% of the time, as did the irregular shapes or novel stimuli, while the non-targets made up the remaining 83.3% of the stimuli. Each novel stimulus was presented only once.

The target and non-target stimuli were reversed for every block (96 stimuli), such that they alternated every other block (e.g. triangle (T), square (S), T, S or S, T, S, T. A tone indicated the beginning of a new block, and the subject had to keep track of which stimulus was target and which was non-target. Halfway through the run, the subject was given a 5-minute break.

Visual Evoked Potentials

The EPs for each of the six electrodes and the vertical EOG were sampled by a PDP 11-40 computer at 200 samples/sec for a 500 msec epoch (bandwidth .1-100 Hz). Single EPs were stored on tape for later analysis. In addition, EPs were sorted and averaged separately according to geometric shape (square or triangle), stimulus category (target, non-target or novel), subject's behavioral response (correct or incorrect), and block number (blocks 1 and 2 or 3 and 4). As the number of non-targets was so numerous (80/96 stimuli), an additional stimulus category was averaged separately by extracting only the non-target stimuli immediately preceding the target stimuli ("Preceding-Non-Targets" or PNT), thereby providing an equal number of stimuli in each of the stimulus categories. EPs were also averaged in various combinations across the different variables mentioned above (e.g. for each stimulus category separately, regardless of geometric shape and block number).

Measurement

Peak-to-peak amplitude and latency measures were obtained for all electrodes for the following peaks: P100 (70-96 msec), N120 (120-145 msec), P200 (205-230 mesc), N250 (260-310 msec) and P300 (330-380 msec). Amplitudes were measured as the perpendicular distance between peaks, namely: P100-N120, N120-P200, P200-N250 and N250-P300.

In addition to peak-to-peak measurements, Principal Component Factor Analysis with Varimax Rotation was also performed on the raw data in order to extract a small number of orthogonal components.

This paper is limited to a discussion of only the frontal and parietal leads.

RESULTS

A two-way analysis of variance with repeated measures on one factor was performed (Winer, 1962) on the peak-to-peak amplitude and latency measures. The major results were obtained in the N120-P200 and N250-P300 late components of the EP recorded at parietal (Pz).

Amplitude N120-P200 was significantly reduced in the alcoholics for all stimuli (Figure 1). This amplitude depression was significant at $p<.01$ for each of the stimulus categories: namely target (T), preceding non-target (PNT) and novel (N). As can also be seen in this figure, there were no significant differences in this amplitude across stimulus categories for either group of subjects. The same result was obtained whether the stimulus was a square or a triangle (Figure 2).

At parietal, amplitude (N250-P300) was found to be significantly larger for the control group than the alcoholic group for the target stimuli only ($p<.01$) (Figure 3). As can be seen in Figure 3, this was true regardless of the shape of the target stimulus (square or triangle).

The differences between the alcohol and control groups are most clearly illustrated when one examines the mean EPs to target stimuli calculated across subjects from the parietal lead (Figure 4). As can be seen in this figure, the points occurring between 155 and 245 msec, and the points between 315 and 435 msec were highly significant between the two groups as determined by point-for-point t-tests. These points correspond fairly well to N120-P200 and N250-P300 as measured peak-to-peak, and they were significant at $p<.01$.

Figure 5 indicates that the signifcant difference in N250-P300 amplitude between the two groups of

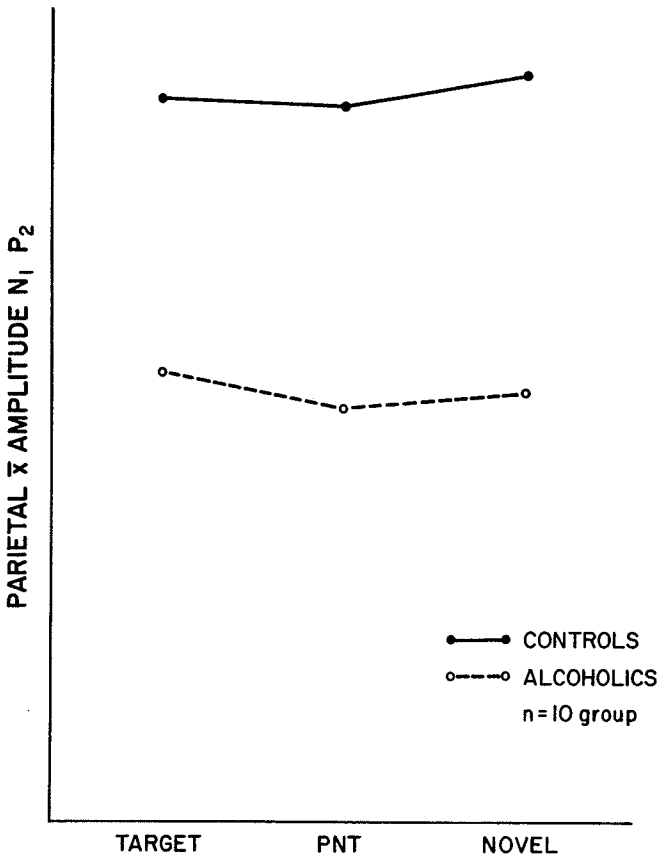

Fig. 1. Mean VEP amplitude N120-P200 (N1-P2) recorded at parietal (Pz) for target, preceding non-target (PNT) and novel stimuli for the alcoholic and control groups.

subjects was only apparent for target stimuli. As can be seen on this figure, in addition to the major amplitude differences between groups to target stimuli, the amplitude of the N250-P300 wave differed significantly across the three classes of stimuli only for the control group; it was the largest for target, next largest for novels and smallest for PNT, and was significantly different between all stimulus categories (T/PNT $p \leq .01$; T/N $p \leq .05$; N/PNT $p \leq .02$). There were no differences in this amplitude for the alcoholic subjects between any of the stimulus categories.

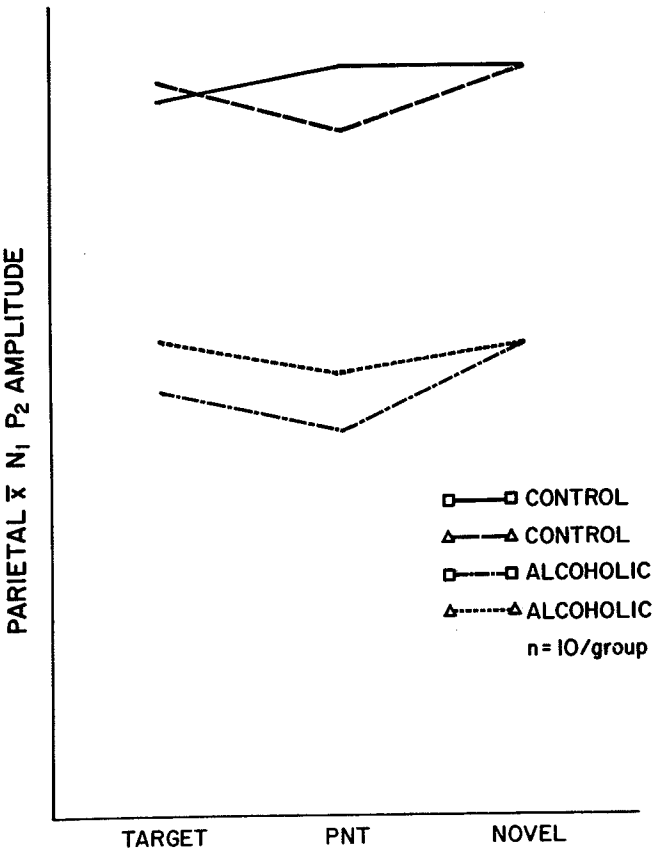

Fig. 2. Mean parietal amplitude N120-P200 (N1-P2, 130-220 msec) for each geometric shape separately, square (□) and triangle (△), when it served as target or preceding-non-target (PNT), compared to novel for the alcoholic and control groups.

This was true, regardless of the shape of the stimulus (Figure 6). As can be seen in Figure 6, there were no differences in amplitude between the two shapes per se, but rather, the differences depended on their functional utility, or whether they served as targets or non-targets.

We obtained similar but less pronounced findings at the frontal lead (Figure 7). In the control group, amplitudes N250-P300 to the relevant target

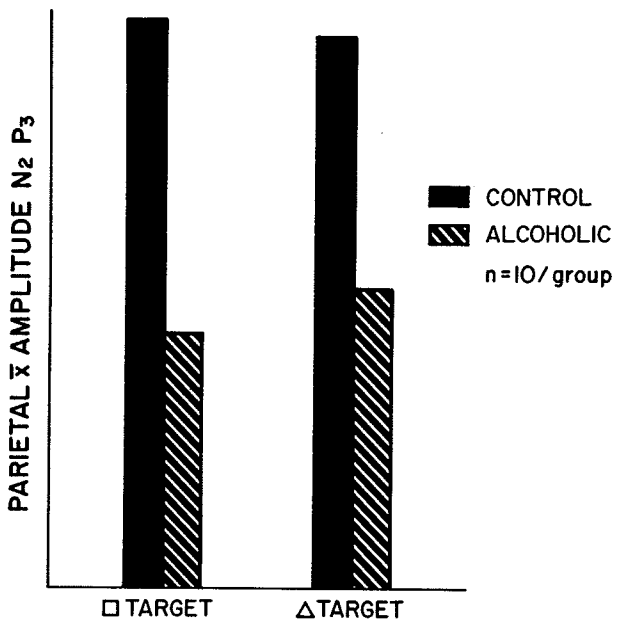

Fig. 3. Mean parietal amplitude N250-P300 (N2-P3, 275-390 msec) obtained to square target stimuli and triangle target stimuli for alcoholic and control subjects.

stimului were significantly larger than those obtained to the irrelevant PNT and novel stimuli at ($p<.01$ and $p<.02$, respectively). Amplitudes of N250-P300 remained the same over all stimulus groups for the alcoholics.

There was a large P300 amplitude difference between square T and square PNT in the control group ($p<.01$) and a negligible difference (NS) between these stimulus categories in the alcoholic group (Figure 8). As can be seen here, it was only the P300 amplitude to the target stimulus that was different between the alcoholic and control groups, while the PNT amplitudes were very similar in the two groups. This same result was obtained for the triangle (Figure 9).

The differences in P300 amplitude to the target and non-target stimuli can be clearly seen in the group

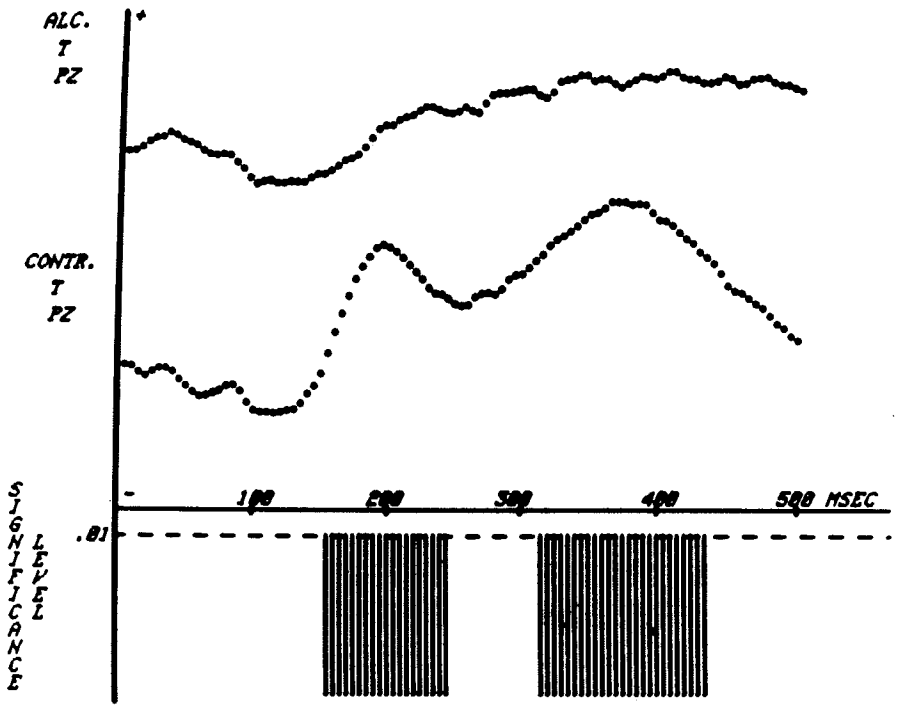

Fig. 4. Composite visual EPs obtained to target (T) stimuli only, recorded at Pz for the alcoholic (top trace) and control (bottom trace) subjects. Results of point-by-point t-tests between the two curves exceeding the .01 significance level, are displayed in the histogram below their corresponding points.

average of the control subjects (Figure 10). Notice that the late P300 component was significantly larger when the square served as a target, while the N120-P200 amplitude was the same for the two stimulus categories. As can be seen in this figure, the latency of P300 shifted depending on whether it was recorded to target or non-target stimuli; it occurred significantly ($p<.05$) earlier when the same stimulus was a non-target than when it was a target.

Principal Component Factor Analyses with Varimax Rotation were also performed on the data, and eight orthogonal factors were obtained. One factor (Factor 1) had its highest loading at approximately 300 msec

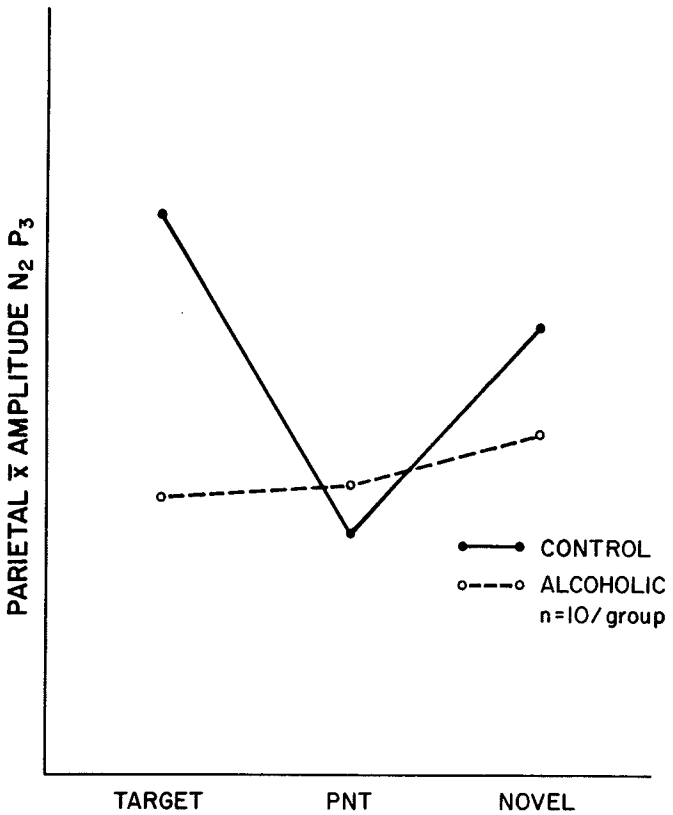

Fig. 5. Mean peak-to-peak amplitude measure of N250-P300 (N2-P3) for the alcohol and control group at parietal for the target, preceding-non-target (PNT) and novel stimuli.

(Figure 11), corresponding to the P300 component; it was most significant in discriminating between the patients and controls at the parietal lead.

Another factor (Factor 4) obtained had its highest loading at approximately 200 msec (Figure 12) and thus corresponded to the P200 component. This factor discriminated between patients and controls at all midline electrode sites.

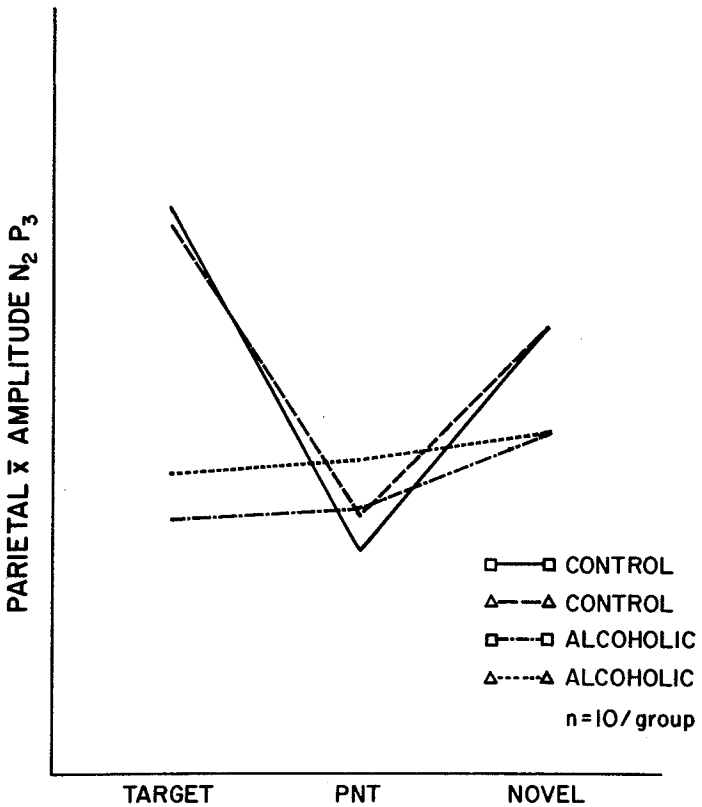

Fig. 6. Mean amplitude N250-P300 (N2-P3) for triangle and square stimuli separately when they served as targets and preceding-non-targets (PNT), as well as novel stimuli.

A detailed discussion of all 8 factors obtained, and the results of analyses of variance on these factors for all 6 electrodes goes beyond the scope of this paper.

DISCUSSION

As in our previous experiment, we found that the late components of the evoked potential were

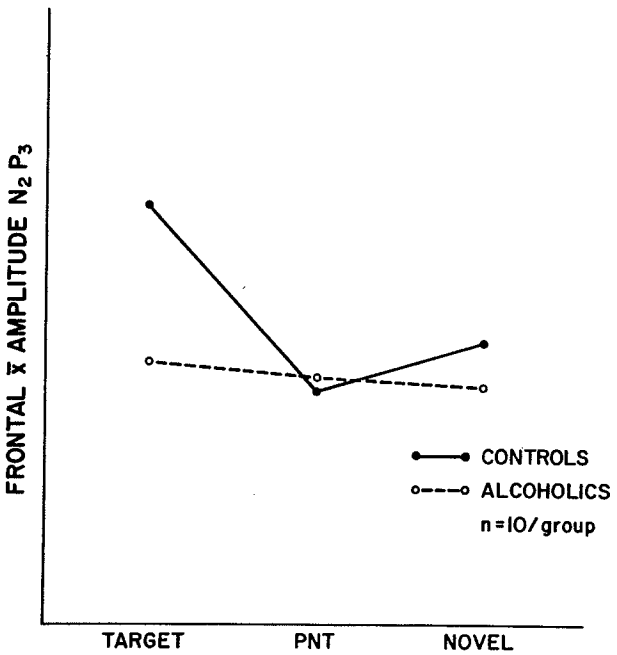

Fig. 7. Mean peak-to-peak amplitude measure of N250-P300 (N2-P3) for the alcohol and control group at frontal (Fz) for target, preceding-non-target (PNT) and novel stimuli.

significantly reduced in the alcoholics when compared to the normal controls, specifically the N120-P200 component and the N250-P300 component.

Hillyard (1978) postulates that the N120 (N1) component and the P300 (P3) component are indicative of two different stages in the selective attention process, namely sensory filtering, and cognitive or motor response selection, respectively. The earlier stage of selection, N120 (N1) differentiates between the attended and irrelevant channels (e.g. visual and auditory modalities), by being responsive only to the

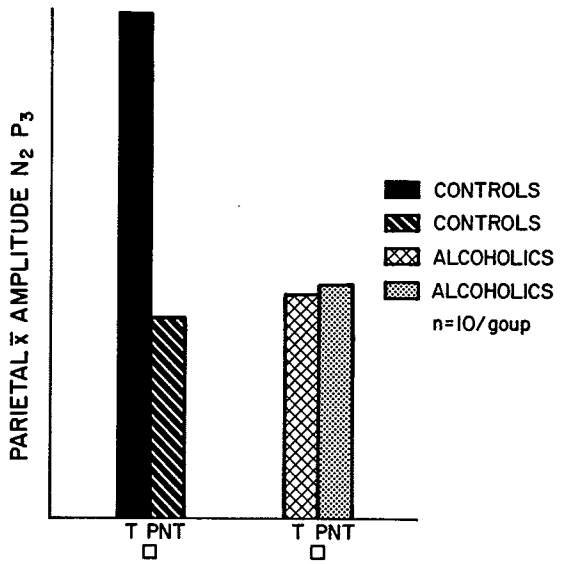

Fig. 8. Amplitude N250-P300 (N2-P3) at Pz to the square stimulus when it served as a target (T) or preceding-non-target (PNT) for the alcohol and control groups.

relevant channel and unresponsive, or rejecting of the irrelevant channels. Thus, the N120 (N1) component is taken to reflect attentional processes (Hillyard, 1978; Picton et al., 1976; Roth, 1973; Donchin, 1978), increasing with increased attention regardless of whether the stimulus is the signal or not.

The later stage, P300, on the other hand, is only responsive if the stimulus is in the relevant channel, and is the target signal. P300 is taken to reflect "stimulus evaluation" (Donchin, 1978). When a subject selects between targets and non-targets belonging to the same stimulus modality (channel), the P300 wave is differentially enhanced to the targets, while N120 (N1) is the same for both targets and non-targets. Thus, the subject must ask a series of questions in order to determine the relevance of a given stimulus as follows:

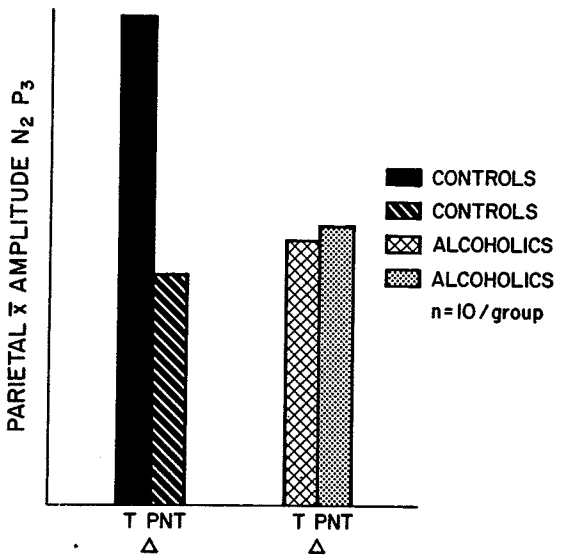

Fig. 9. Amplitude N250-P300 (N2-P3) at Pz to the triangle stimulus when it served as a target (T) and preceding-non-target (PNT) for the alcohol and control groups.

1) Is the stimulus in the relevant stimulus channel (N120), and
2) If so, is it the signal or not? (P300).

In our previous experiment (Porjesz and Begleiter, 1978), we demonstrated that alcoholics manifested a lack of appropriate "sensory filtering" mechanisms. In contrast to controls, alcoholics manifested the same N120-P200 response amplitude to flashes, regardless of whether they were in the relevant or irrelevant stimulus modality. Furthermore, amplitudes of the N120-P200 component of the alcoholics were significantly below those of the control group.

In the present experiment, the N120-P200 amplitude was also significantly reduced in the alcoholic group for all stimulus classes: targets, PNTs and novels.

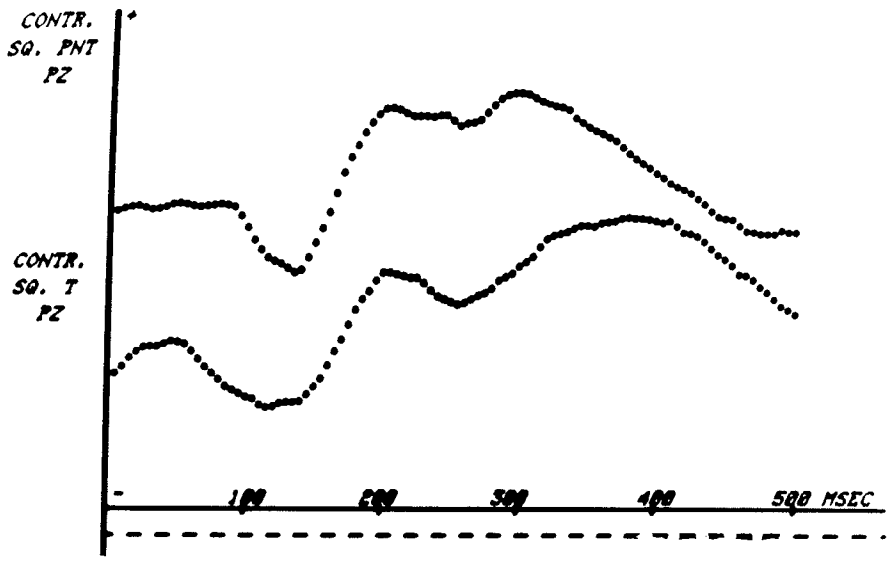

Fig. 10. Composite mean visual EPs of control group recorded at parietal (Pz). The top trace is the group average response to the square when it was a preceding-non-target (PNT), while the bottom trace is the group average response to the square when it was a target.

However, as all stimulus classes were in the relevant stimulus modality, the amplitude of N120-P200 remained the same over the three classes of stimuli for the control group as well. While this was also true in the alcoholic group, it was at significantly lower amplitude levels. Thus, on the basis of both studies it seems that sensory filtering mechanisms are impaired in chronic alcoholics.

As predicted by the P300 literature (Courchesne, 1977), for the control subjects the magnitude of P300 differed significantly depending on whether the stimulus was the target, non-target, or novel; target stimuli typically elicited large P300 waves, while non-targets did not. The alcoholics on the other hand, displayed the same low voltage P300 amplitude regardless of the stimulus class: target, novel or non-target. It is of great importance to note that even under conditions designed to optimally enhance the

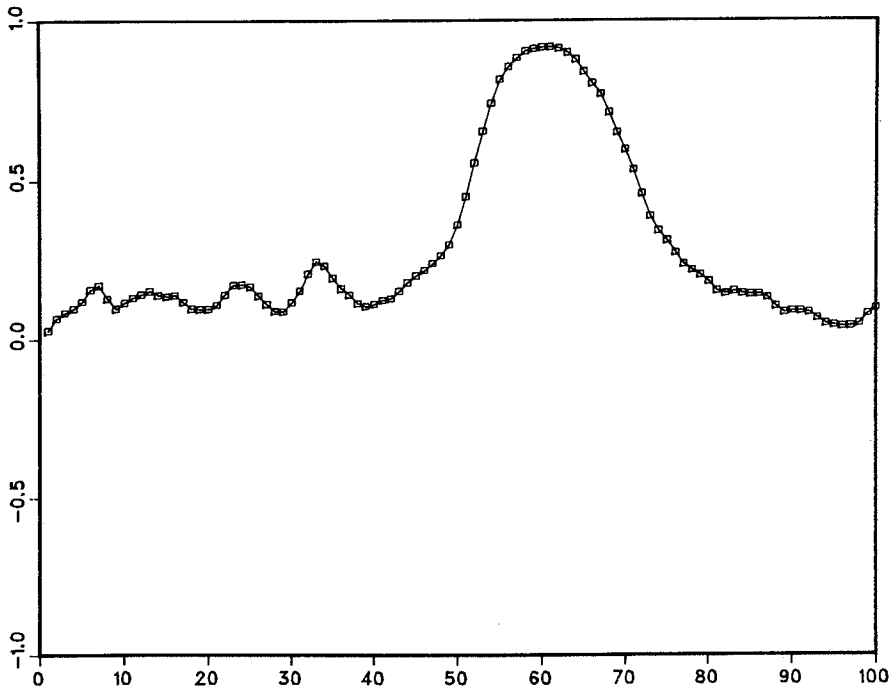

Fig. 11. The distribution of Factor 1, obtained from principal component factor analysis with varimax rotation. Each point on the curve corresponds to 5 msec, such that the total epoch is 500 msec. Note that the peak occurs at 300 msec (point #60).

magnitude of P300 waves (to rarely occurring target stimuli), the alcoholics manifested either very low voltage, or even absent P300 waves. It is unclear at this time whether the amplitude differences obtained between alcoholic and control groups are due to differences in latency jitter, signal/noise ratio or actual voltages. It has been documented that this P300 wave is maximal over parietal areas (Simson et al., 1977; Ritter et al., 1968; Goff et al., 1978; Allison et al., 1977). Thus, the absence of the P300 wave to the target stimuli in the alcoholic subjects is indicative of brain dysfunction suggesting parietal involvement.

It seems, therefore, that alcoholics manifest electrophysiological signs of brain dysfunction that

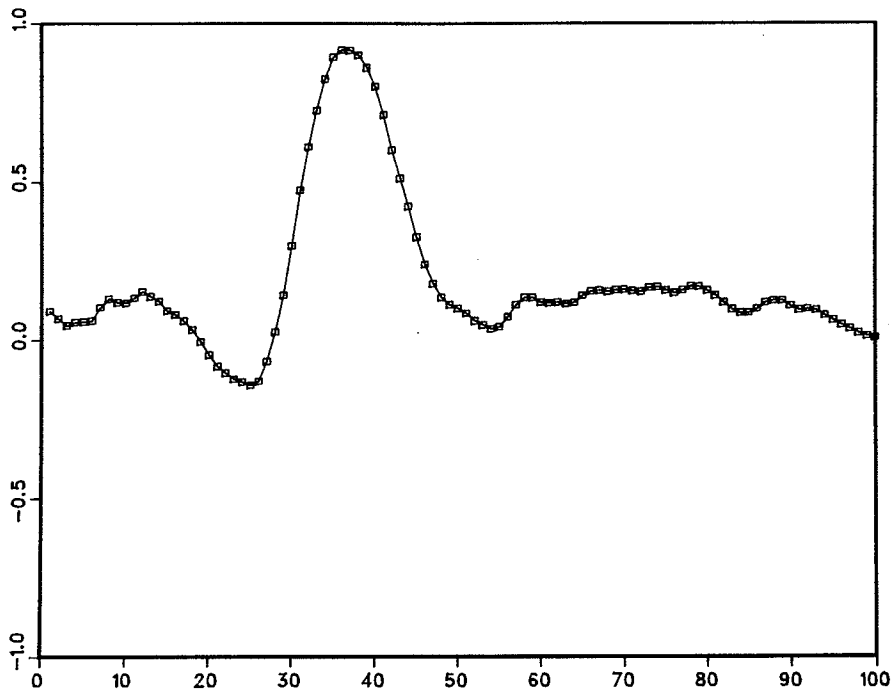

Fig. 12. Factor 4, derived from principal component factor analysis with varimax rotation. This factor reaches its highest peak at 181.25 msec.

appear to be of a higher cortical nature. Taken together, these results indicate that the alcoholics manifest a diffuse, cortical dysfunction that is not limited to one cortical area or another, but is apparent depending on the experimental paradigm designed to examine level of cortical functioning.

Support for these findings of cortical dysfunction in alcoholics comes from recent CT-scan studies (Carlen et al., 1976; Fox et al., 1976; Wilkinson et al., 1976; Bergman et al., 1977; Carlen et al., 1978) where cortical atrophy has been reported. While a recent CT-scan report by Carlen et al., (1978) indicated that CT-scan aberrations are reversible at 8 months, so far our own preliminary CT-scan results, taken as late as 4 months post-withdrawal, do not support these findings. Whether these cortical aberrations are reversible or not is still an unresolved issue and remains to be tested.

Acknowledgments

We would like to thank Lynda Herskovits for her valuable assistance. Supported by Grant No. AA02686.

REFERENCES

Allison, T., Matsumiya, Y., Goff, G.D., and Goff, W.R. The scalp topography of human visual evoked potentials. Electroenceph. Clin. Neurophysiol. 42: 185-197, 1977.

Bergman, H., Borg. S., Hindmars, R., Idestrom, C.M., and Myrhed, M. Computed-tomography of the brain and psychometric assessment of alcoholic patients: Some preliminary results. Presented at World Congress of Psychiatry, Hawaii, 1977.

Bonin, G. Von. Some Papers on the Cerebral Cortex. Thomas, Springfield, Illinois, 1960.

Carlen, P.L., Wilkinson, A., and Kiraly, L. Dementia in alcoholics: A longitudinal study including some reversible aspects. Neurology, 26: 355, 1976.

Carlen, P.L., Wortzman, G., Holgate, R.C., Wilkinson, D. A., and Rankin, J.G. Reversible cerebral atrophy in recently abstinent chronic alcoholics measured by computed tomography scans. Science, 200: 1076-1078, 1978.

Courchesne, E. Event-related brain potentials: Comparison between children and adults. Science, 197: 589-592, 1977.

Donchin, E., Ritter, W., and McCallum, C. Cognitive psychophysiology; The endogenous components of the ERP, in Callaway E., and Koslow, S.H. (Eds.) Event Related Brain Potentials in Man. New York, Academic Press, 1978, pp. 349-411.

Fox, J., Ramsey, R., Huckman, M., and Proske, A. Cerebral ventricular enlargement: Chronic alcoholics examined by computerized tomography. Journal Amer. Med. Assn., 236: 365-368, 1976.

Goff, W.R., Allison, T., and Vaughan, H.C., Jr. The functional neuroanatomy of event related potentials. in Callaway, E. and Koslow, S. H. (Eds.) Event Related Brain Potentials in Man, New York, Academic Press, 1978, pp. 1-79.

Goodwin, D.W., and Hill, S.Y. Chronic effects of alcohol and other psychoactive drugs on intellect, learning and memory, in Rankin, G. (Ed.) Alcohol Drugs and Brain Damage, Ontario, A.R.F. 1975, pp. 55-70.

Hillyard, S.A. Electrophysiological assessment of attentional processes in man, in Callaway, E. and Koslow, S.H. (Eds.) Event Related Brain Potentials in Man. New York, Academic Press, 1978, pp. 223-321.

Kleinknecht, R.A., and Goldstein, S.G. Neuropsychological deficits associated with alcoholism: A review and discussion. Quart. J. Stud. Alc., 33: 999-1019, 1972.

Luria, A.R. The Working Brain, Great Britian, Penguin, 1973.

Luria, A.R. Higher Cortical Functions in Man. Translated by Basil Haigh. New York, Basic Books, Inc., 1966.

Oscar-Berman, M. Commentary, in Callaway and Koslow, S. H. (Eds.): Event Related Brain Potentials in Man. New York, Academic Press, 1978, pp. 413-441.

Oscar-Berman, M. Hypothesis testing and focusing behavior during concept formation by amnesic Korsakoff patients. Neuropsychologia, 11: 191-198, 1973.

Parsons, O.A. Brain damage in alcoholics: Altered states of consciousness. Adv. Exp. Med. Biol. 59: 569-584, 1975.

Picton, T.W., Hillyard, S.A., and Galambos, R. Habituation and attention in the auditory system, in Keidel, W., and Neff, W. (Eds.), Handbook of Sensory Physiology, Vol. V. Auditory System, Berlin, Springer-Verlag, 1976, pp. 343-389.

Porjesz, B., and Begleiter, H. Visual evoked potentials and brain dysfunction in chronic alcoholics, in Begleiter, H. (Ed.), Evoked Brain Potentials and Behavior, New York, Plenum Press, 1978.

Pribram, K.H. The primate frontal cortex-executive of brain, in Pribram, K.H. and Luria, A.R. (Eds.) Psychophysiology of the Frontal Lobes, New York, Academic Press, 1973, pp. 293-314.

Pribram, K.H. The primate frontal cortex. Progress Report 1975. Acta Neurobiol., 35: 609-625, 1975.

Ritter, W., Vaughan, H.G., Jr., and Costa, L.D. Orienting and habituation to auditory stimuli: A study of short term changes in average evoked responses. Electroenceph. Clin. Neurophysiol. 25: 550-556, 1968.

Roth, W.T. Auditory evoked responses to unpredictable stimuli. Psychophysiolgy, 10: 125-138, 1973.

Roth, W.T., Ford, J.M., Lewis, S.J., and Kopell, B.S. Effects of stimulus probability and task-relevance on event-related potentials. Psychophysiology, 13: 311-317, 1976.

Simson, R., Vaughan, H.G., Jr., and Ritter, W. The scalp topography of potentials in auditory and visual discrimination tasks. Electroenceph. Clin. Neurophysiol., 42: 528-535, 1977.

Sutton, S., Braren, M., Zubin, J., and John, E.R. Evoked potential correlates of stimulus uncertainty. Science, 150: 1187-1188, 1965.

Sutton, S., Tueting, P., Zubin, J., and John, E.R. Information delivery and the sensory evoked potential. Science, 155: 1436-1439, 1967.

Tueting, P., Sutton, S., and Zubin, J. Quantitative evoked potential correlates of the probability of events. Psychophysiology, 7: 385-394, 1971.

Wilkinson, A., Rankin, J.G. and Kiraly, L. Organic brain syndrome in chronic alcoholism: A reversible encephalopathy? Presented at: 11th Annual Conference, Canadian Foundation on Alcohol and Drug Dependendies, Toronto, Canada, June, 1976.

Winer, B.J. Statistical Principles in Experimental Design. New York, McGraw-Hill, 1962.