VISUAL EVOKED POTENTIALS AND BRAIN DYSFUNCTION IN CHRONIC ALCOHOLICS

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Chronic alcohol abuse is known to lead to brain dysfunction
(Begleiter and Platz, 1972; Rankin, 1975). In an effort to ascer-
tain some parallel between acute and chronic alcohol intake, the
effect of single doses of alcohol on normal brain functioning is
being studied. Extensive research has been conducted in order to
investigate the effects of acute doses of alcohol on the normal
human evoked potential. This has been examined with the auditory
evoked response (AER) (Gross et al., 1966), the somatosensory evoked
potential (SEP) (Lewis et al., 1970; Salamy and Williams, 1973;
Porjesz and Begleiter, 1973), and the visual evoked potential (VEP)
(Lewis et al., 1969, 1970; Porjesz and Begleiter, 1975; Rhodes et
al., 1975), P_3 amplitude (Roth et al., 1977), the contingent negative
variation (CNV) (Kopell et al., 1972; Roth et al., 1977), and the
amplitude-intensity gradient (Spilker and Callaway, 1969).

Taken together, the results of these single dose alcohol studies
with normal subjects concur that:
1) alcohol depresses the amplitude of the EP late components
(Lewis et al., 1969; Salamy and Williams, 1973; Porjesz and Beg-
leiter, 1975; Rhodes et al., 1975);
2) alcohol produces its maximal amplitude depression over
association areas, as opposed to primary receiving areas (Salamy
and Williams, 1973; Porjesz and Begleiter, 1975);
3) there is an inverse relationship between the dose of alcohol,
the blood alcohol level, and the evoked potential amplitude (Salamy
and Williams, 1973);
4) this EP amplitude depression represents decreases in single

EP amplitudes, rather than increased latency variability (Salamy, 1973);

5) alcohol depresses right hemisphere responses of visual evoked potentials to a greater degree than left (Lewis et al., 1969; Porjesz and Begleiter, 1975; Rhodes et al., 1975);

6) alcohol dissipates hemispheric asymmetry, where present prior to alcohol ingestion (Lewis et al., 1969; Porjesz and Begleiter, 1975; Rhodes et al., 1975).

The sites of action of single, acute doses of alcohol are important in that they may provide a clue as to the possible locus or loci of brain dysfunction resulting from prolonged, chronic alcohol abuse. However, there is a paucity of evoked potential experiments in alcoholics who are abstinent from alcohol for long periods of time, and are medication-free.

A study in Beck's laboratory (Schenkenberg, Dustman and Beck, 1972) reported that while normal subjects manifested VEP amplitude asymmetry at central locations (with $C_4 > C_3$), alcoholic subjects did not. Furthermore, they also reported lower VEP amplitudes in their alcoholic samples at all electrode locations, namely frontal, central and occipital. In a recent dissertation from the same laboratory (Cannon, 1974), it was reported that late component occipital amplitudes of alcoholics were smaller than those of normal controls. Alcoholics also manifested delayed late component latencies for central and occipital locations.

In our laboratory, we have studied the electrophysiological concomitants of withdrawal following cessation of chronic alcohol intake in animals (in rat: Porjesz et al., 1976; Begleiter and Porjesz, 1977; and monkey: Begleiter et al., 1978) as well as in humans (Begleiter et al., 1974). In one study (Begleiter et al., 1974) we examined the recovery function of somatosensory evoked potentials in alcoholics during intoxication and withdrawal and found increased CNS excitability during withdrawal. In all our studies, alcohol withdrawal was found to be accompanied by marked increases in the late component amplitude. This we postulate to be the result of brain hyperexcitability. Similar results were recently obtained by Coger et al. (1976), who examined the effects of alcohol withdrawal on the amplitude-intensity gradient.

Taken together, the results of studies dealing with evoked potentials and chronic alcohol abuse suggest that:

1) late component EP amplitudes are reduced in alcoholics;
2) alcoholics manifest less EP hemispheric asymmetry than normal controls;
3) alcohol withdrawal is accompanied by marked increases in late EP amplitude.

Consequently, it seems that the same EP components that are most sensitive to single doses of alcohol in the normal brain, are most susceptible to more permanent deficits in the chronic alcoholic. Specifically, alcoholics seem to manifest electrophysiological deficits in the late components of the EP, and show less hemispheric asymmetry than normals (right hemisphere more affected than left).

Alcohol seems to affect some intellectual abilities more than others; specifically, visual-spatial and visual-motor skills are impaired, while verbal skills remain intact. Results of neuropsychological tests have led to two major hypotheses regarding the sites of action of alcohol in the brain, namely: 1) that right-hemispheric functioning is affected (Parsons, 1975; Butters and Cermak, 1976) and 2) that there is frontal impairment (Jones and Parsons, 1971; Parsons, 1974; Tarter, 1975).

Evidence implicating the right hemisphere comes from neuropsychological tests, where alcoholics' scores on spatial tasks are more impaired than on verbal tasks, and their performance on spatial tasks is similar to performance of patients with right hemisphere lesions. In addition, they exhibit more impairment on manual tasks requiring the use of their left hand (Parsons, 1975).

Chronic alcohol abuse has also been shown to produce an impaired ability to process relevant dimensions of visual stimuli (Oscar-Berman, 1973). In a study of the ability of Korsakoff patients, alcoholics, and normals to adopt and modify problem solving strategies, Oscar-Berman found that once a Korsakoff or alcoholic patient adopts a particular response strategy, he perseverates this hypothesis despite the reinforcement contingencies. These results suggest that perhaps a general information processing deficit may account for many of the Korsakoff and alcoholic patient's cognitive difficulties.

Evidence is accumulating that demonstrates a deficit in cognitive performance in chronic alcoholics, resembling aberrations observed in frontal lobe brain damaged patients. Independent studies by Fitzhugh et al. (1960, 1965) and Parsons and his co-workers (Jones and Parsons, 1971) have found that alcoholics perform more similarly to brain damaged subjects than normal controls on the Halstead Category Test. The performance deficit of the alcoholics has been found to be related to the number of years of drinking, independent of age (Jones and Parsons, 1971).

In a more recent study, Tarter (1973) reported that alcoholic patients admitting to a history of alcoholism of greater than ten years were impaired in set persistence, set shifting, and error utilization compared to normal controls, while those subjects who describe themselves as alcoholics for a period of less than ten years, were deficient only in set persistence. In order to

ascertain whether the brain dysfunctions reported were a function
of socioeconomic class, Smith et al. (1973) studied alcoholics of
upper socioeconomic status. He demonstrated the same incidence of
impaired ability on the Halstead Category Test in these alcoholics
as exhibited by alcoholics of low socioeconomic status.

Thus, it seems from the foregoing brief literature review that
alcoholics have two general characteristics that interfere with
their conceptual performance: 1) they make numerous perseverative
errors, and 2) they show an inability to persist with correct cog-
nitive sets.

These difficulties are typical of patients with frontal lobe
damage (Luria, 1973). Another typical characteristic of frontal
lobe patients and animals is their difficulty with inhibitory con-
trol. A study by Parsons et al. (1972) demonstrated that alcoholics
were impaired in their capacity to inhibit their own behavior.

There is also a growing body of evidence suggesting that alco-
hol has direct neurotoxic effects. Postmortem studies by Courville
(1955) indicated neuropathology of chronic alcoholics in the dorso-
lateral aspects of the frontal lobe, with atrophy as its main
characteristic. Similar results have been reported from other
laboratories using pneumoencephalography (Tumarkin et al., 1955;
Feuerlein, 1970; Brewer and Perrett, 1971). Most recently, CAT-Scan
techniques have demonstrated cortical atrophy in alcoholics compared
to normal controls (Carlen et al., 1976; Fox et al., 1976; Wilkinson
et al., 1976; Bergman et al., 1977; Tenner, Begleiter and Porjesz,
unpublished observations).

Thus, the evidence seems to implicate possible impaired right
hemisphere and frontal lobe functioning in alcoholics. In the pres-
ent experiment, we investigated possible frontal lobe dysfunction
in alcoholics by testing their ability to change "sets". Most
evoked potential experiments with alcoholics use responses to blank
flashes that do not require the subject to be actively engaged in
any task (Sutton, 1968). The present design requires the subject
to shift attentional sets. Stimuli that are relevant in one run,
become irrelevant in another run.

The present study was designed to assess:
1) VEP differences between alcoholics and normal controls in
terms of brain loci that manifest the greatest aberrations in al-
coholics;
2) dysfunction with regard to shifting attentional "sets" in
alcoholics;
3) the degree and type of evoked potential aberration.

METHODS

Subjects

The subjects were 14 right-handed adult male alcoholics with
a mean age of 35 and a minimum of eight years of heavy drinking
history. They had a mean duration of heavy drinking of 13.4 years.
They had been abstinent from alcohol for a minimum of three weeks,
and were medication-free for at least 2.5 weeks.

Fourteen age and education matched right-handed males served as
normal controls (mean age 32). The control subjects were occasional
"social" drinkers. All subjects were tested for eye-dominance and,
in addition, a complete medical history was obtained. The experi-
mental and control subjects did not differ significantly with respect
to eye-dominance, age or education.

The same alcoholic subjects who participated in the present VEP
experiment were also tested on a battery of neuropsychological tests,
as well as sleep EEG patterns (in collaboration with B. Kissin and
A. Wagman). The results of those scores and their relationship to
the VEP data, goes beyond the scope of the present paper and will be
published elsewhere.

Electrodes

Gold-cup electrodes were placed bilaterally at frontal (F_3 and
F_4), central (C_3 and C_4), parietal (P_3 and P_4), and occipital (O_1
and O_2) scalp locations according to the 10-20 International System.
All recordings were monopolar, using the ears as references and
nasion as ground. Resistances were maintained below 5000 ohms be-
tween brain loci and references. Interaural resistances were kept
below .5 ohms.

Procedure

Each subject was seated in a sound-attenuated IAC enclosure,
with his head resting on an adjustable chin rest, so that he was
looking directly into a viewing hood. He was instructed to fixate
in the center of his visual field at all times. A Grass PS-2 photo-
stimulator, set at an intensity of 2, was mounted 50 cm from the
subject on the other side of a one-way mirror. All subjects were
dark-adapted and then habituated to blank flashes (10 msec in dura-
tion and delivered at a regular rate of 1/2.5 sec, for a total of
64 flashes).

The experiment consisted of three types of runs, manipulating
the subject's attentional set, namely "no set" (NS), "flash-task-
relevant" (FTR), and "flash-task-irrelevant" (FTI), respectively.

Stimuli

     The stimulus sequence consisted of a series of interspersed
visual and auditory stimuli presented in random order at a random
rate varying between one and five seconds apart. Interspersed among
64 single flashes were 10 double flashes, with an interstimulus
interval (ISI) of 80 msec. The auditory stimuli consisted of 64
lower frequency tones and 10 tones of a higher frequency.

     Each subject was presented with the identical stimulus sequence
in all three of his runs, and this order of stimulus presentation was
randomized across subjects. In addition, the order of presentation
of the three experimental conditions (NS, FTR and FTI) was counter-
balanced for both the alcoholic and normal control subjects. There
was a five-minute break between runs throughout the experiment.

                       EXPERIMENTAL CONDITIONS

No Set (NS)

     During the NS condition, the subject was instructed to sit very
still, look into the center of the viewer, and attend to all the
stimuli. The randomized sequence of high and low tones, and single
and double flashes, was then presented to the subject.

Flash-Task-Relevant (FTR)

     During the FTR condition, the subject's task was to count the
number of double flashes to himself and report his answer at the end
of the run. The double flashes were fairly difficult to detect and,
in order to ensure that the subject was able to discriminate between
the single and double flashes, a training procedure preceded the
actual run. Once the subject achieved the criterion of 5 correct
consecutive discriminations, the run began. The subject was in-
structed to look into the center of the viewer and to sit as still
as possible. The identical stimulus sequence as during the "no set"
condition was then presented to the subject.

Flash-Task-Irrelevant (FTI)

     During the FTI run, the subject was instructed to silently
count the number of infrequent high tones while looking at the
flashes. The subject reported his answer at the end of the run.
A training procedure also preceded this run and after 5 correct
discriminations, the run commenced. Again, the identical stimulus
sequence was delivered.

Visual Evoked Potentials (VEP's)

     Evoked potentials were obtained only to the 64 single flashes
in all runs. They were amplified by means of a Grass model 78-B

Polygraph with a band width between .1 and 100 hz, and a gain setting of 5 μ/V mm. The VEP's for each of the 8 electrodes were sampled by 8 A/D converters in a PDP 11/40 computer for on-line signal averaging of a 500 msec epoch (resolution 2 points/msec).

In order to minimize any possible differences between amplifiers and A/D converters, halfway through each run, the amplifier and A/D converters for each pair of bilateral brain locations were interchanged (such that the right-hemisphere and left-hemisphere recordings were switched).

The vertical electrooculogram (EOG) was recorded and averaged in all subjects so that possible contamination from ocular artifacts was ruled out.

Measurements

Peak-to-peak amplitude and latency measures were obtained from all leads by means of a display program developed in our laboratory. Amplitude measures were taken as the perpendicular distance (in μ/V) between successive peaks, while latency measures were taken as their time of occurrence (in msec). This paper will be limited to a discussion of the frontal and parietal results only. Occipital and central results will be reported elsewhere.

RESULTS

A two-way analysis of variance with repeated measures on one factor was performed (Winer, 1962). The major amplitude difference between the alcoholic and normal control samples is that the late component of the VEP (110-190 msec) is significantly larger in the normal controls, particularly under the FTR condition. This is true for all four electrode placements (Figure 1). This effect is greatest over the right frontal area ($p < .01$). It is significant at $p < .05$ for all other electrode placements.

In addition, the control group manifests hemispheric asymmetry with regard to this component over the frontal area, with the right hemisphere late wave being of a significantly larger amplitude than that simultaneously recorded over the left hemisphere (Figure 2). Dependent t-tests performed on differences between hemispheres revealed that this is highly significant for all tasks in the control group ($p < .01$, $p < .025$, and $p < .005$ for FTR, FTI, and NS, respectively). The alcoholics, on the other hand, exhibit no hemispheric asymmetry at all (not significant for any task).

Furthermore, the amplitude of this late component of the frontal VEP bears a direct relationship to the degree of task-relevance only in the normal controls (largest for FTR, next for FTI, and smallest
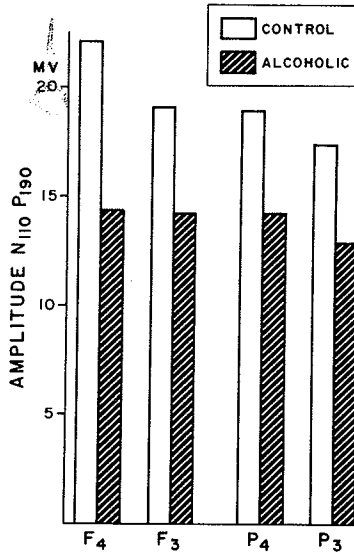
Figure 1.   Amplitude N_{110}-P_{190} for all electrodes during the FTR
            task.   Amplitude values are based on group means
            (n=14/group) of peak-to-peak measurements.   Notice that
            the control group manifests a larger late component
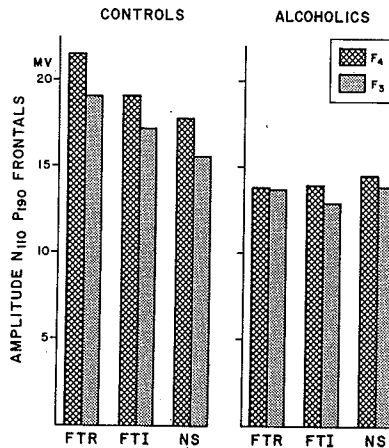   amplitude than the alcohol group.

Figure 2.   Group mean amplitude N_{110}-P_{190} for left and right frontal
            leads for all tasks separately.   Hemispheric asymmetry
            of amplitude (F_4>F_3) is displayed only by the control
            group, while the alcoholic group does not manifest any
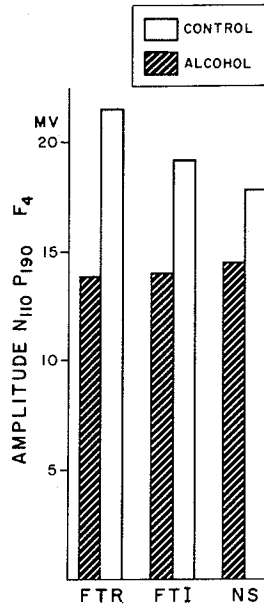   hemispheric asymmetry.

Figure 3.   Amplitude $N_{110}-P_{190}$ for the right frontal placement under
the three experimental conditions: FTR, FTI and NS.
This amplitude is larger in the control group, and is
directly related to the degree of task relevance
(FTR>FTI>NS). The amplitude remains the same across
tasks in the alcoholic group.

Figure 4.   Mean amplitude early component ($N_{60}-P_{80}$) recorded over
left frontal scalp locations under the three experimental
conditions (N=14/grp). This early component amplitude is
larger for the alcoholics than the normal controls for
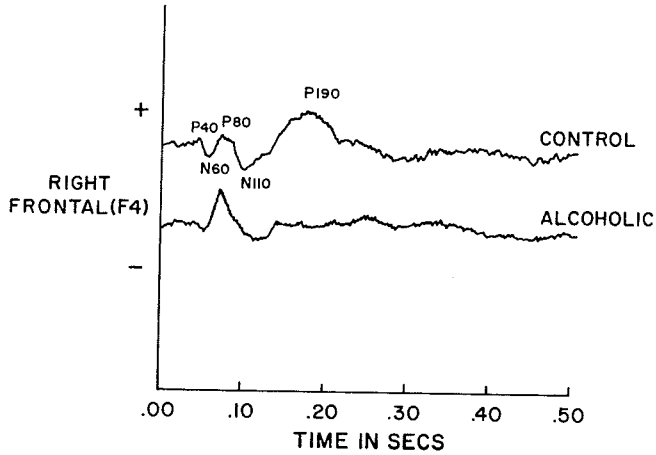all tasks, particularly under the FTI condition.

Figure 5. This illustration contains examples of VEP's recorded at
the right frontal electrode under an attention condition
(FTR), for one control subject (top trace) and one alco-
holic subject (bottom trace). Notice the reduced late
component amplitude ($N_{110}-P_{190}$) in the alcoholic subject
as compared to the control, and the markedly enhanced
early components $N_{60}-P_{80}$ and $P_{80}-N_{110}$. As can be seen
in this illustration, the waveform is quite different in
the alcoholic and normal control subjects at frontal
locations. Typically, normal controls exhibit much
larger late components in comparison to their early
components, while the alcoholics manifest the reverse
waveform--with their early components being considerably
larger than their late components.

for no-set) (Figure 3). No relationship exists between degree of task relevance and late component amplitude in the alcoholics; in fact, this amplitude remains almost identical across tasks for them. This is true for both the right frontal electrode placement as well as the left. The slope of the amplitude measures taken across tasks indicates that the late component parallels the degree of task relevance only for normal control subjects. This relationship is significant not only for amplitude N_{110}-P_{190} (Tukey test, p <.05) but also amplitude P_{80}-N_{110} at frontal leads (Tukey test, p <.05, F_4; p <.01, F_3), only for the normal controls.

The early components, on the other hand, are of a larger amplitude in the alcoholics than the normal controls. This can be seen in amplitude N_{60}-P_{80} over the frontal area, particularly for the FTI task (p <.01) (Figure 4). For the normal control group, it can be seen that there is a larger difference in amplitude between the FTR and FTI conditions, but not for the alcoholics.

The waveform of the frontal recordings are quite different for the alcoholic and control subjects (Figure 5). The alcoholic subjects manifest reduced late component amplitudes (N_{110}-P_{190}) and enhanced early component amplitudes (N_{60}-P_{80} and P_{80}-N_{110}) when compared to the controls. The morphology of the frontal VEP for control subjects typically consists of a late component that is much larger than the early component. The alcoholics, on the other hand, typically exhibit the reverse waveform, where the early components are considerably larger than their late components.

The results obtained are illustrated in Figure 6, which is a schematic composite waveform, based on mean amplitude and response times of F_4, during the FTR task for both groups. Note the reduced late component amplitude in the alcoholic group (N_{110}-P_{190}) and the enhanced early components (N_{60}-P_{80} and P_{80}-N_{110}).

The early component P_{80}-N_{115} is also enhanced in the alcoholic group at parietal locations for all tasks. This is true for both the right and left parietal recordings, where it is significant at p <.05 for all tasks (Figure 7).

This component recorded at parietal leads shows hemispheric asymmetry of amplitude, where the right hemisphere has a larger amplitude than the left (Figure 8). This hemispheric asymmetry is highly significant for the control group at p <.005 for FTR, p <.05 for FTI, and p <.01 for NS. Hemispheric asymmetry is also present in the alcoholic group (at parietal) significant at p <.05 for all tasks. However, while this asymmetry is present in both groups, it is of a larger magnitude in the control group under the FTR and NS conditions.
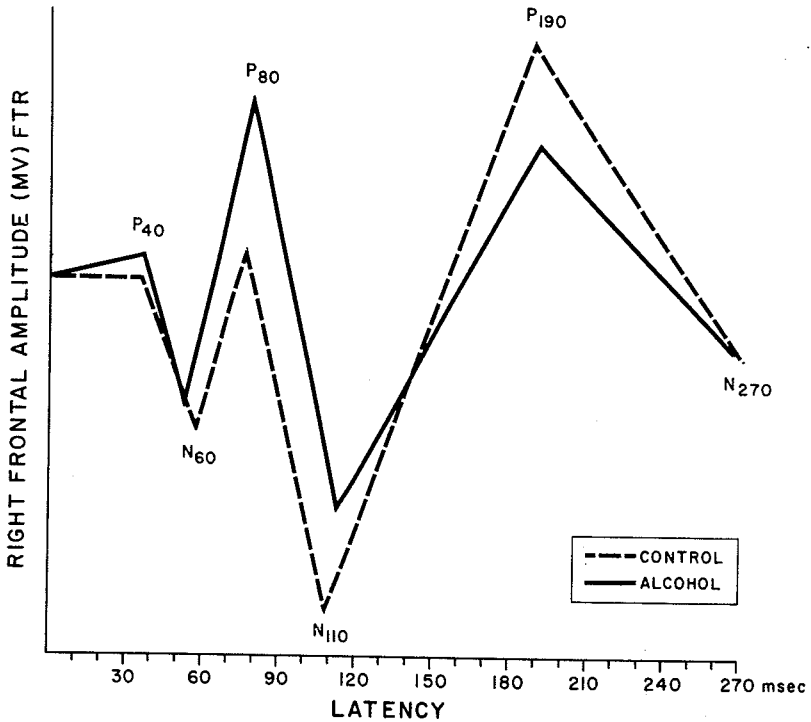
Figure 6. This is a schematic composite right frontal waveform,
based on the mean amplitudes and response times of all
subjects combined for each group (N=14/grp). The curves
were obtained during the flash-task-relevant (FTR) task,
where the subject is attending to the flash. Note the
decreased late component amplitude (N_{110}-P_{190}) in the
alcoholic group, and the increased early component
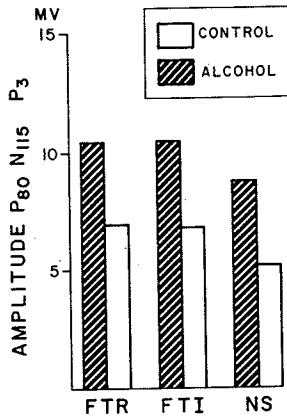(N_{60}-P_{80} and P_{80}-N_{110}).

Figure 7.   Mean amplitude early component (P_{80}-N_{115}) recorded at left parietal placements (N=14/grp). Note that this component is larger for all tasks in the alcoholic group.
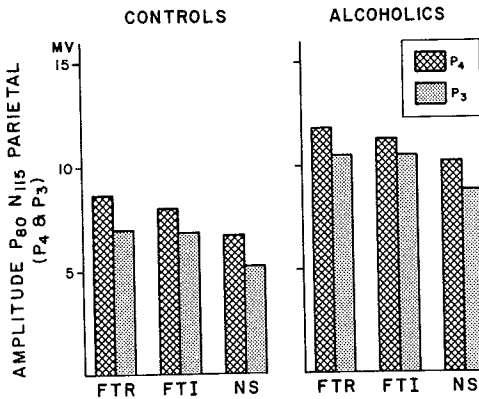

Figure 8.   Bilateral recordings of P_{80}-N_{115} over right and left parietal areas comparing each homologous pair for each group separately, under the three experimental conditions. Note the amplitude hemispheric asymmetry P_4>P_3) in the control group, and to a lesser degree in the alcoholic group for this amplitude.
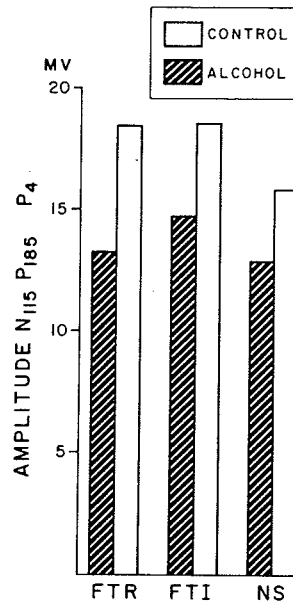
Figure 9. Group means for right parietal amplitude N_{115}-P_{185} for
the alcoholic and control groups for the three experi-
mental tasks. Note the strikingly larger amplitude of
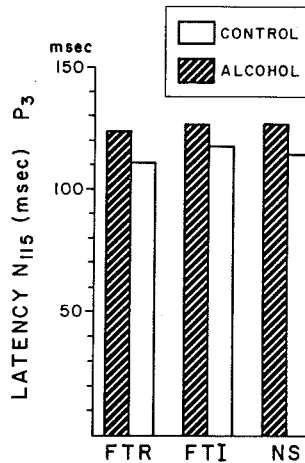this late component in the control group.

Figure 10. Mean latencies (N_{115}) for each group for each of the
three tasks. Note that the alcoholics' latency occurs
later than those of the normal subjects.
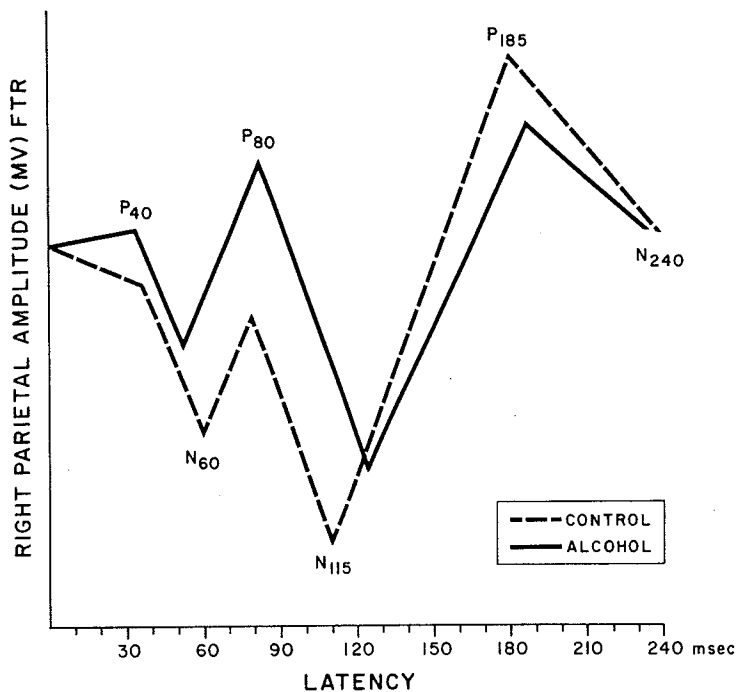
Figure 11. This is a schematic illustration of the right parietal waveforms based on the mean amplitudes and latencies for the two groups, under the FTR task. The late component (N_{115}-P_{185}) is reduced in the alcoholic group, while the early component amplitude (P_{80}-N_{115}) is enhanced. Also note the latency shifts in the late components for the alcoholics (N_{115} and P_{185}), occurring later in the alcoholic group.

As with the frontal leads, the late component of the parietal areas is also significantly larger for the control group than the alcoholic group, particularly under the FTR condition. This is true for both the left and right parietal recordings at $p < .05$, and is illustrated for the right parietal in Figure 9.

The time of occurrence of this late component, typically beginning around 115 msec occurs significantly later in the alcoholic group than in the controls. This significantly longer latency in the alcoholic group is most apparent during the FTR condition. This is true for both hemispheres (Figure 10).

Figure 11 is a schematic illustration of the right parietal results during the FTR task, based on the mean response amplitudes and latencies for the two groups. The late component ($N_{115}-P_{185}$) is reduced in the alcoholic group while the early component ($P_{80}-N_{115}$) amplitude is enhanced. Also note the latency shifts in the late components for the alcoholics (N_{115} and P_{185}) occurring later in the alcoholic group.

DISCUSSION

After many extensive attention experiments performed by Hillyard and his co-workers (Hillyard, 1977), Hillyard concludes that N_1 (approximately N_{110} in the present paper) is indicative of the selection of target or non-target stimuli while later peaks (P_3) reflect memory-related cognitive or motor response selection.

In the present experiment, we found that the alcoholic subjects exhibited reduced late component amplitudes at all electrode sites. Furthermore, in the alcoholic sample, we found no difference in amplitude of the late component across different attentional tasks. Applying Hillyard's conclusions to the present experimental results, it can be hypothesized that the alcoholics are more impaired in the later stages of attentional processes. Information processing reaction-time experiments support this contention. Recent studies (Rundell et al., 1973; Tharp et al., 1974, 1975) have found that stimulus pre-processing and encoding are unaffected by alcohol, while alcohol affects the more central (output) stages of information processing, namely response selection and organization.

Similarly, support for this hypothesis comes from EP studies in many laboratories where acute doses of alcohol are administered to non-alcoholics (Lewis et al., 1970; Salamy and Williams, 1973; Porjesz and Begleiter, 1975; Rhodes et al., 1975). These studies report that alcohol primarily depresses the late components of the EP, while the early components are very resistant to its depressant effects. In addition, the maximal amplitude depression has been obtained over association areas of the brain.

The early components of the EP are generally taken to reflect sensory input. Hillyard maintains that in attentional processes they represent the selection of the target or non-target stimulus modalities or "sensory filtering." The human perceptual system is capable of rejecting or _filtering_ irrelevant input at an early stage of processing.

In the present experiment, the high amplitude early component (N_{60}-P_{80}, P_{80}-N_{110}) manifested by the alcoholics in comparison to the controls, may be indicative of inappropriate filtering of sensory input (for example, for the N_{60}-P_{80} component at frontal leads, the FTR and FTI responses had the same amplitude in the alcoholic). Perhaps this indicates a lack of selective-inattending to the irrelevant stimuli in alcoholics.

Nataanen (1975) postulates that an early amplitude enhancement of his N_1 peak (occurring at approximately 60-70 msec) indicates increased excitability or impulse activity related to preparation for a difficult discrimination (in his case pitch discrimination). According to Nataanen, the subjects must ask a series of questions in order to determine the relevance of a given stimulus, namely,
     1)   Is the stimulus task-relevant or not?
     2)   If task-relevant, is it a signal or not?

Using Natannen's approach to the present experiment, all stimuli are relevant in the attention and distraction runs in that they are necessary to make the decision. On the other hand, all our VEP's were obtained only to an _irrelevant_ stimulus, namely, the single flash. However, its _degree_ of relevance varied across the tasks. For the FTR task, the single flash was in the relevant stimulus modality; however, it was the non-signal (the signal being the double flash). In the FTI condition, not only was the flash the irrelevant signal, but it was also in the irrelevant stimulus modality.

Thus, the undifferentiated enhanced early component in the alcoholics is in response to irrelevant stimuli, and hence represents an inability to inhibit irrelevant input. This hypothesis is strengthened by the additional result that alcoholics differ most from normal controls for this component with regard to the flash-task-irrelevant condition. The control subjects' responses for the FTI condition are appropriately attenuated, as predicted by Hillyard's model.

The greatest late component difference between alcoholics and normal controls was found over the rightfrontal electrode placement. In addition, we found that while normal controls display hemispheric asymmetry with regard to this late component over the frontal area, alcoholics do not, and also manifested some loss of lateralization over parietal leads. This finding is in agreement with

studies from Beck's laboratory (Schenkenberg et al., 1972; Dustman et al., this volume), indicating that hemispheric asymmetry typically manifested by normal subjects is not present in alcoholics. Similarly, studies with acute doses of alcohol administered to college students, in both his laboratory and ours, indicate that single doses of alcohol abolish hemispheric asymmetry when present and maximally depress responses from right central areas (Lewis et al., 1970; Porjesz and Begleiter, 1975; Rhodes et al., 1975). Taken together, these findings implicate possible impairment of right hemispheric functioning in chronic alcoholics.

Thus, it seems that the results of the present study with chronic alcohol ingestion, parallel results obtained with acute intake--suggesting that brain functioning that is impaired by acute alcohol doses is also more permanently impaired in the chronic alcoholic.

The results of the present experiment, that alcoholics exhibit an increased early component and decreased late component and delayed latencies, parallel the results obtained with samples of elderly people in Beck's laboratory (Cannon, 1974; Dustman et al., this volume).

It has been hypothesized that alcohol accelerates the aging process of the brain. Evoked potential studies of the aging process have demonstrated that the early components remain fairly stable until senescence, at which time amplitude increases occur. With aging, the amplitudes of the late components of the visual evoked response increase until adolescence, and progressively decrease thereafter. Furthermore, evoked potential latencies (VEP, SEP) decrease until adolescence and increase through old age. The VEP characteristics of the alcoholic patients in the present experiment resemble those obtained with elderly patients; namely, they have larger early components, smaller late components, and delayed late component latencies.

Similarities between alcoholics and elderly normal individuals have been independently found in neuropsychological (Fitzhugh et al., 1960; 1965) and neuroanatomical studies (Courville, 1955). Autopsy examinations between these two groups have revealed similarities in cortical atrophy and diffuse cell loss (Courville, 1955). It is interesting to note that at autopsy, chronic alcoholics exhibit progressive atrophy of the frontal lobes, particularly the dorsolateral convolutions. With senescence, cell loss has been found mainly in the superior temporal gyrus and the frontal cortex, with the smallest loss at the post-central gyrus (Brody, 1970).

A recent experiment by Loveless and Sanford (1974) examined changes in preparatory set in elderly patients and contingent negative variation (CNV). They found that elderly subjects exhibited poor performance at long predictable foreperiods, accompanied by a

substantial difference in the form of the CNV. This is less sugges-
tive of the impaired ability to maintain a state of preparation than
of difficulty in controlling a sequence of psychological processes
so as to initiate preparation at an appropriate time. Luria (1966)
suggests that a breakdown in the ability to follow through a series
of previously specific actions is a good indication of diffuse
frontal lobe damage.

The hypothesis that chronic alcoholism promotes the aging pro-
cess of the brain has been proposed by a number of sleep researchers.
Extreme sleep disturbances in chronic alcoholics were first recog-
nized by Gross and his co-workers (1966). More recently, Johnson
et al. (1970) examined sleep (EEG patterns) in a group of alcoholic
patients withdrawn from alcohol for several days, who had been ex-
cessively drinking for 17 years. They found that alcoholics had
fragmented sleep manifested by frequent awakenings, frequent changes
of EEG stage and, most importantly, found no slow wave sleep. The
records revealed that the frequency of sigma spindles was low and
the frequency of well-formed K-complexes was considerably below
that found in normal subjects. Generally, the sleep patterns of
alcoholic patients in Johnson's study resembled those of elderly
subjects. Confirmation of these results has been reported by Lester
et al. (1973), who also found that alcoholics did not manifest any
stage 4 sleep. They concluded that chronic alcoholism may impair
the cortical mechanisms necessary for spontaneous generation of high
voltage, slow-wave activity, and in that sense be associated with
premature aging of the brain.

At present, there is some reason to suppose that the generators
for such EEG phenomena are located in the frontal cortex. In 1961,
Jouvet found that in the decorticate cat, only REM sleep occurred,
and the absence of SWS was quite striking. Clemente and Sterman
(1967) reported that low frequency stimulation in certain basal and
cortical forebrain regions produced immediate sustained and diffuse
cortical synchronization. Bilateral low frequency stimulation of
forebrain sites resulted in drowsiness and sleep within an average
of 30 seconds. They conclude that the more frontal regions, together
with certain limbic and thalamic sites may constitute a critical
system capable of responding to conditions favoring behavioral in-
hibition and acting to bring the nervous system in line with the
physiological requirements at any instant.

The degree of reversibility (or lack of it) of electrophysio-
logical changes produced by alcoholism is still an unresolved issue.
It is not clear whether the EEG aberrations reported in alcoholics
are withdrawal concomitants (which would be expected to dissipate
once the withdrawal symptomatology disappears) or whether they rep-
resent more long-lasting brain damage. EEG abnormalities have been
reported to show their greatest improvements following the disappear-
ance of delirium and withdrawal symptomatology (Raffauf, 1974;

Mildovanska and Kukladziev, 1975); however, Bennett et al. (1956) have reported some improvements in abnormal EEG records as late as two months post-withdrawal. In our own laboratory (Porjesz, Begleiter, and Hurowitz, 1976; Begleiter and Porjesz, 1977) we have found that visual evoked responses of rats who had been chronically intubated with alcohol were no different from those obtained from naive rats following an abstinence period of two weeks. However, the two groups of rats responded very differently to a challenge dose of alcohol administered at that time.

Similarly, there are conflicting reports on the question of whether neuropsychological impairment in chronic alcoholics is permanent or reversible. Goodwin (Goodwin and Hill, 1975) claims that there is little or no evidence for permanent brain damage in alcoholics, unless coupled with nutritional deficits. Indeed, improvements have been reported in short-term memory (Jonsson et al., 1962; Weingartner et al., 1971), abstract thinking (Smith et al., 1971; Page and Linden, 1974), verbal understanding (Smith et al., 1971; Page and Linden, 1974), and perceptual-motor and psychomotor co-ordination (Long and McLachlan, 1974; Tarter and Jones, 1971; Templer, 1975).

However, major improvements in neuropsychological test scores have been reported to occur during the first 2-3 weeks of testing, with no further recovery over an 8-month abstinence period thereafter (Page and Linden, 1974; Page and Schaub, 1977). Despite these improvements in neuropsychological tests, abstract reasoning scores and visual-spatial skills remain below average (Jonsson et al., 1962; Smith et al., 1971; Page and Linden, 1974; Page and Schaub, 1977).

Thus, the issue of whether CNS aberrations observed in alcoholics are reversible or not, is still an unresolved issue and remains to be tested.

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