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Acute Effects of Alcohol on Photic Evoked Potentials of Albino Rats: Visual Cortex and Superior Colliculus

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HETZLER, B. E., K. E. OAKLAY, R. L. HEILBRONNER AND T. VESTAL. *Acute effects of alcohol on photic evoked potentials of albino rats: Visual cortex and superior colliculus.* PHARMAC. BIOCHEM. BEHAV. 17(6) 1313–1316, 1982.—Photic evoked potentials were recorded from the primary visual cortex (VC) and superior colliculus (SC) of chronically implanted rats. Animals were given intraperitoneal injections of saline, 1.5 and 2.5 g ethyl alcohol/kg body weight on separate days. Evoked potentials were recorded at 5, 20, 40 and 60 min following injection. The amplitudes of all of the VC components except P2 (latency of 52 msec) were depressed to some extent by both doses of alcohol. In contrast, the amplitude of component P2 was increased by both alcohol doses. In the SC, the peak amplitudes of two individual components of the early positive complex were diminished by both doses of alcohol, as was a later negative component. A series of late oscillatory potentials recorded from the SC were minimally depressed by the 1.5 g/kg dose of alcohol, but showed a more prolonged depressant effect at the higher dose. Both doses of alcohol produced reliable increases in peak latency for the primary components in the VC and SC.

Ethyl alcohol Photic evoked potentials Visual cortex Superior colliculus Albino rats

ETHYL alcohol is a central nervous system depressant which readily crosses the blood-brain barrier and causes numerous neurological and behavioral disturbances. The acute depressant effects of ethyl alcohol on the amplitudes of evoked potentials recorded from the visual cortex (VC) of animal subjects have been demonstrated in previous studies [2, 3, 10, 16, 20]. In a recent experiment involving albino rats, we likewise reported that a moderate dose of alcohol (1.5 g/kg) depressed most of the evoked potential components recorded from the VC [8]. However, in our study, an early positive component (P2, latency of about 52 msec) was reliably increased by this dose of alcohol. This alcohol-related augmentation warrants further study, especially since an enhancement of early component amplitude has recently been reported in photic evoked potentials obtained from human chronic alcoholics [19].

In contrast to the number of studies which have to some extent examined the acute effects of alcohol on VC evoked potentials, there is currently only one study which has investigated the effects of alcohol on evoked potentials recorded from the superior colliculus (SC) of mammals [8]. In that earlier report involving albino rats, we noted a depressant effect of alcohol on photic evoked potentials recorded from the SC. However, we examined only one evoked potential component in detail. There is, therefore, a need for more complete data concerning the effects of alcohol on evoked potentials recorded from this structure.

The present study examined the effects of alcohol on evoked potentials recorded from the VC and SC of chronically implanted albino rats. Individual early and late components were examined at fixed time intervals following the administration of two doses of alcohol: 1.5 and 2.5 g/kg, IP.

METHOD

Twenty male albino Holtzman rats, weighing 375–440 g at the time of surgery, were used. The animals were implanted with recording electrodes under pentobarbital anesthesia as previously described [9]. Fourteen rats had both VC and SC electrodes, 3 had bilateral VC electrodes, and 3 had only SC electrodes. Results for the SC are reported for those 14 animals in which the lower member of the bipolar electrode pair penetrated the superficial layer of the SC, as histologically verified. For the VC, results are reported from the right hemisphere electrodes.

Animals were tested in a shielded, mirrored recording chamber following at least 2 weeks of recovery. Electrophysiological recording was computer controlled, as detailed previously [9]. A PDP-8 I minicomputer digitized the waves at a rate of 1 sample from each recording site per msec and sampled the electrical activity for 300 msec, with 20 msec of this period occurring prior to the application of the evoking stimulus. Light pulses from a Grass Model PS 22C photostimulator (intensity setting 4) were delivered with an interstimulus interval of 2 sec, for a total of 100 stimuli. Computer-averaged evoked potentials were plotted on an X-Y plotter and also listed in numeric form on a teletype printer.

Animals were given 3 days of familiarization to the testing procedures, followed by a 1 day rest, prior to data collection.

During testing, animals were injected intraperitoneally every third day with 1.5 or 2.5 g ethanol/kg body weight (20% (v/v) alcohol solution), or with equivalent amounts of physiological saline (0.9% sodium chloride). The 2 saline injections and the 1.5 g/kg alcohol dose were administered according to an individually randomized schedule. Three days after the last of these injections, the animal received the large dose of alcohol (2.5 g/kg). Photic evoked potentials were recorded 5, 20, 40 and 60 min following injection.

Evoked potentials recorded from the VC involved a sequence of alternating positive and negative waves, labelled P1, N1, P2, N2, P3, N3. The amplitude of each component was expressed as the difference between peak amplitude and a mean amplitude of 20 msec of EEG activity collected prior to the presentation of the light flash. In addition, peak latency (in msec) was calculated for the primary components P1 and N1.

An averaged evoked potential recorded from the SC involved an early positive complex containing a variable series of alternating positive and negative spikes [9]. For the first and the last positive spikes in this series, P1 and P3, both the amplitude and latency were calculated (although not for the 5 min recordings, since at this time interval the individual components were often difficult to differentiate). Amplitude and latency were computed for the succeeding negative component (N4) at all time intervals. Following component N4, there often occurred a series of low amplitude late oscillatory potentials extending to the end of the 300 msec recording interval. The total linear excursion of these oscillations was measured by tracing part of each averaged plot with a map-reading wheel [9]. Measurement began with the peak of the first positive wave following N4 and continued to the end of the plot (about 200 msec).

Data were subjected to two factor analyses of variance, involving repeated measures on both factors (i.e., alcohol dose and time). When a significant main effect was found, individual means were compared with Dunnett's test [9,12]. Statistical significance was assumed when $p<0.05$ for two-tailed comparisons. Changes in evoked potential amplitudes and latencies resulting from time-related factors were in general agreement with earlier reports [8,9], and therefore are not included. Likewise, significant alcohol × time interactions are described only in relation to the main effects of alcohol.

RESULTS

Visual Cortex

Amplitude. The VC amplitude data are contained in Fig. 1. With the exception of component P2, all other components were to some extent depressed by both doses of alcohol. Component P2 was consistently enhanced in comparison to the saline controls.

The primary components P1 and N1 were significantly depressed by alcohol, P1:$F(3,48)=11.57$, $p<0.001$, and N1:$F(3,48)=63.94$, $p<0.001$, although significant alcohol × time interactions were also present, P1:$F(9,144)=2.91$, $p<0.005$, and N1:$F(9,144)=2.70$, $p<0.01$. Component P1 was significantly depressed by the 1.5 g/kg alcohol dose at only the 5 min interval, while the 2.5 g/kg dose produced significant depression at 5, 20 and 40 min. In contrast, component N1 was significantly depressed at all time intervals by both alcohol doses. Component P2 was significantly increased by both doses of alcohol at all time intervals, $F(3,48)=27.57$, $p<0.001$. The main effect of alcohol did not reach significance for component N2, but the alcohol × time interaction was significant, $F(9,144)=6.53$, $p<0.001$. Both doses of alcohol resulted in a significant depression of this component at the 5 min interval, but this depression persisted to the 20 min interval for only the largest alcohol dose. Alcohol produced a significant depressant effect on both late components, P3:$F(3,48)=42.96$, $p<0.001$, and N3:$F(3,48)=41.37$, $p<0.001$. Although there were significant alcohol × time interactions for both components as well, P3:$F(9,144)=3.18$, $p<0.005$ and N3:$F(9,144)=3.08$, $p<0.005$, the alcohol-related depressions occurred at all time intervals for both alcohol doses.

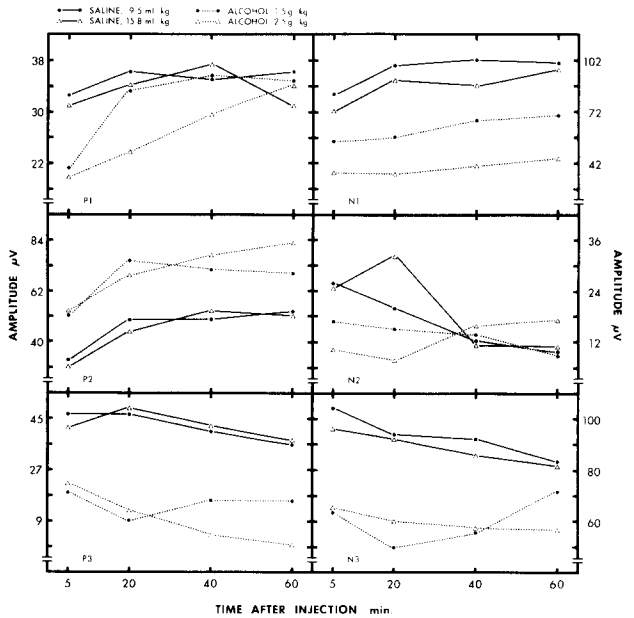

FIG. 1. Mean amplitudes of visual cortex (VC) evoked potential components at 4 time intervals following administration of saline and alcohol on separate days. Data were obtained from 17 rats.

Latency. Latency data were evaluated for the two VC primary components, P1 and N1, with baseline latencies of about 25 and 33.5 msec, respectively (data not shown). The latencies of components P1 and N1 were significantly increased by both doses of alcohol, P1:$F(3,48)=49.56$, $p<0.001$, N1:$F(3,48)=23.26$, $p<0.001$. The mean latencies of these components following administration of the 1.5 and 2.5 g/kg doses of alcohol were 26.6 and 28.0 msec for component P1, and 34.7 and 35.7 msec for component N1, respectively. However, the increase was not reliably seen at the 5 min interval for component N1 following administration of the 1.5 g/kg dose, as indicated in part by a significant alcohol × time interaction, $F(9,144)=2.35$, $p<0.025$. The alcohol × time interaction was also significant for component P1:$F(9,144)=5.76$, $p<0.001$. While these components generally demonstrated a time-related decrease in latency at the 20, 40 and 60 min intervals following saline administration, the time-related decreases in latency under the influence of alcohol were restricted to the 40 and 60 min intervals.

Superior Colliculus

Amplitude. The amplitude data from the SC are contained

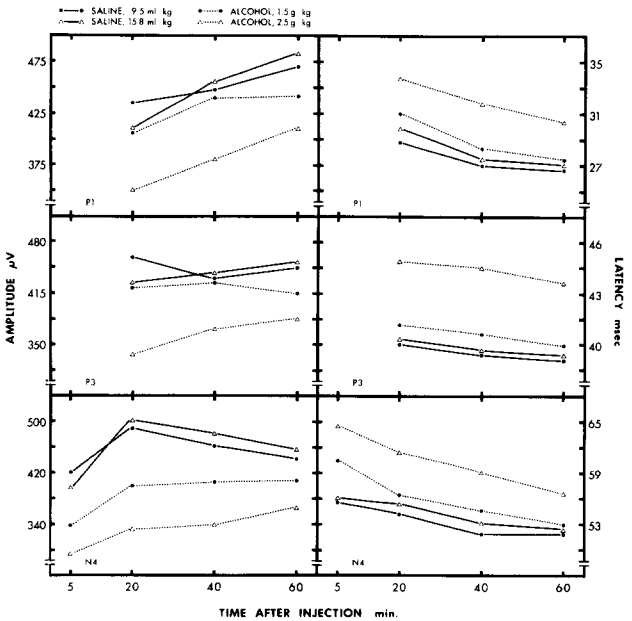

FIG. 2. Mean amplitudes (left half) and latencies (right half) of superior colliculus (SC) evoked potential components following administration of saline and alcohol on separate days. Data were obtained from 14 rats, and were analyzed at 3 time intervals for components P1 and P3, and at 4 time intervals for component N4.

in the left half of Fig. 2. The amplitudes for both components examined in the early positive complex were significantly reduced by both doses of alcohol, P1:$F(3,39)=16.67$, $p<0.001$, P3:$F(3,39)=18.13$, $p<0.001$. The alcohol × time interaction was significant for only component P3, $F(6,78)=2.79$, $p<0.025$, because the 1.5 g/kg dose of alcohol did not significantly depress this component at the 40 min recording interval. Component N4 was significantly decreased in amplitude by both doses of alcohol at all time intervals, $F(3,39)=53.13$, $p<0.001$, even though the alcohol × time interaction was also significant, $F(9,117)=5.37$, $p<0.001$.

Latency. The SC latency data are contained in the right half of Fig. 2. Both doses of alcohol produced significant increases in latency for component P1, $F(3,39)=28.26$, $p<0.001$, component P3, $F(3,39)=24.62$, $p<0.001$, and component N4, $F(3,39)=36.20$, $p<0.001$, although the effect was no longer reliable at 60 min for the 1.5 g/kg dose in the case of component N4. This was reflected in a significant alcohol × time interaction for component N4, $F(9,117)=2.51$, $p<0.025$.

Late oscillatory potentials. (Data not shown.) As was the case for the other components of the SC evoked potentials, these oscillations were reliably depressed by alcohol, $F(3,39)=13.33$, $p<0.001$. The alcohol × time interaction was also significant, $F(9,117)=2.79$, $p<0.01$. The depressant effect of alcohol was observed at the 60 min interval for both doses of alcohol, and also at the 20 and 40 min intervals for the 2.5 g/kg dose.

DISCUSSION

In the present as well as our previous study [8], alcohol produced significant changes in the configuration of evoked potentials recorded from the VC of albino rats. Both the 1.5 and 2.5 g/kg doses of alcohol produced a marked depression of components N1, P3, and N3. Two other components (P1 and N2) were less severely depressed by these doses of alcohol. In contrast to these alcohol-related depressions, the amplitude of component P2 was reliably increased by both doses of alcohol. The findings of alcohol-related depression agree in most respects with past studies of the effects of alcohol in normal non-alcoholized rats [2, 3, 4, 20]. However, these studies from other laboratories have not noted an enhancement of VC component P2. This discrepancy has probably resulted from differences in amplitude measurement. Both the present and our past study [8] employed a baseline-to-peak amplitude measurement for each component, while the other studies used peak-to-peak measures of amplitude. In effect, the peak-to-peak measurements may have masked differential effects of alcohol treatments on the individual early components. To test the accuracy of this suggestion, we have reanalyzed our VC data for component P2 in terms of the peak-to-peak amplitude between components N1 and P2. Alcohol produced a significant decrease in this peak-to-peak measure of amplitude, $F(3,48)=9.54$, $p<0.001$, with reliable depressions occurring at all time intervals for both alcohol doses, with the exception of the 5 min interval for the 1.5 g/kg dose.

The alcohol-related increase in amplitude in component P2 is especially interesting, given alcohol's depressant action. Using albino rats, Schwartzbaum and Kreinick [21] have demonstrated that the anticholinergic blocking agent scopolamine reliably augments this component in a dose dependent manner. Since alcohol is known to inhibit both the spontaneous and the electrically stimulated release of acetylcholine from cerebral cortex slices [5,11], the alcohol-induced enhancement of component P2 may have a cholinergic determinant. Unlike component N1, component P2 is not associated with intracortical cellular discharge [22], and may therefore represent inhibitory processes. It has been suggested that the excitatory effect of acetylcholine on cortical neurons with muscarinic receptors is of a modulatory nature [15], since the response to acetylcholine has a slow onset and long duration [14]. An alcohol-related reduction in acetylcholine release in this excitatory system could therefore result in an increase in amplitude of a component generated mainly by inhibitory processes.

Evoked potentials recorded from the SC were depressed by both alcohol doses employed in the present experiment. All components examined were reduced to some extent by alcohol, although the depression was most pronounced for component N4, which is in general agreement with earlier results [8]. These data are also consistent with an earlier report that spontaneous multiple unit activity recorded from the SC of rabbits is decreased following administration of low to moderate doses of alcohol [13]. Given the involvement of this structure in attention and orientation (e.g., [7]), visual-motor and visual-spatial deficits occurring as a result of alcohol intake may be in part related to the action of alcohol on this structure.

In addition to changes in amplitude, the primary components of evoked potentials recorded from the SC and VC also demonstrated significant increases in peak latency following both doses of alcohol. These results agree with a number of previous reports that acute doses of alcohol increase the latency of at least some photic evoked potential components [6, 8, 17].

We have elsewhere reported the effects of pentobarbital,

another central nervous system depressant, on photic evoked potentials recorded from the VC and SC of albino rats [9]. A major difference between the effects of pentobarbital and alcohol on VC evoked potentials in the albino rat involves the primary components. Components P1 and N1 are enhanced by pentobarbital but depressed by alcohol. On the other hand, both drugs reliably depress the later components P3 and N3, while enhancing component P2. These results are in general agreement with past studies involving other species and/or other sensory systems (see Okamato [41] for review). That is, primary specific evoked potential components recorded from the cortex are more susceptible to depression by alcohol than by barbiturates (which often enhance such components), whereas later "nonspecific" cortical potentials are reduced in amplitude by both alcohol and barbiturates.

The primary SC evoked potential component P1 responds to both alcohol and pentobarbital in much the same manner as does the VC component P1. This component is reliably depressed by moderate and high doses of alcohol, while it is enhanced by pentobarbital [9]. Interestingly, a series of late oscillatory potentials recorded from the SC are similarly differentially affected by these two drugs. These oscillations are gradually increased in amplitude with increasing doses of pentobarbital [9], but are somewhat depressed by alcohol. Since such rhythmic potentials appear to originate from the eye [1], the depressant effect of alcohol on these potentials may reflect the action of alcohol on the retina [16].

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REFERENCES

1. Anderson, K. V. and W. K. O'Steen. Single-cell responses associated with rhythmic slow-wave potentials in rat superior colliculi. *J. Neurosci. Res.* **1:** 343–351, 1975.
2. Begleiter, H., M. H. Branchey and B. Kissin. Effects of ethanol on evoked potentials in the rat. *Behav. Biol.* **7:** 137–142, 1972.
3. Begleiter, H. and B. Porjesz. Persistence of brain hyperexcitability following chronic alcohol exposure in rats. *Adv. exp. Med. Biol.* **85b:** 209–222, 1977.
4. Bierley, R. A., D. S. Cannon, C. K. Wehl and R. E. Dustman. Effects of alcohol on visually evoked responses in rats during addiction and withdrawal. *Pharmac. Biochem. Behav.* **12:** 909–915, 1980.
5. Carmichael, F. J. and Y. Israel. Effects of ethanol on neurotransmitter release by rat brain cortical slices. *J. Pharmac. exp. Ther.* **193:** 824–834, 1975.
6. Erwin, C. W. and M. Linnoila. Effect of ethyl alcohol on visual evoked potentials. *Alcoholism: Clin. exp. Res.* **5:** 49–55, 1981.
7. Goldberg, M. E. and D. L. Robinson. Visual system: superior colliculus. In: *Handbook of Behavioral Neurobiology,* vol. 1, edited by R. B. Masterton. New York: Plenum Press, 1978, pp. 119–164.
8. Hetzler, B. E., R. L. Heilbronner, J. Griffin and G. Griffin. Acute effects of alcohol on evoked potentials in visual cortex and superior colliculus of the rat. *Electroenceph. clin. Neurophysiol.* **51:** 69–79, 1981.
9. Hetzler, B. E. and K. E. Oaklay. Dose effects of pentobarbital on evoked potentials in visual cortex and superior colliculus of the albino rat. *Neuropharmacology* **20:** 969–978, 1981.
10. Himwich, H. E. and D. A. Callison. The effects of alcohol on evoked potentials of various parts of the central nervous system in cat. In: *The Biology of Alcoholism,* vol. 2, *Physiology and Behavior,* edited by B. Kissin and H. Begleiter. New York: Plenum Press, 1972, pp. 67–84.
11. Kalant, H. and W. Grose. Effects of ethanol and pentobarbital on release of acetylcholine from cerebral cortex slices. *J. Pharmac.* **158:** 386–393, 1967.
12. Kirk, R. E. *Experimental Design: Procedures for the Behavioral Sciences.* Belmont, CA: Wadsworth, 1968.
13. Klemm, W. R., C. G. Mallari, L. R. Dreyfus, J. C. Fiske, E. Forney and J. A. Mikeska. Ethanol-induced regional and dose-response differences in multiple-unit activity in rabbits. *Psychopharmacology* **49:** 235–244, 1976.
14. Krnjevic, K. Chemical nature of synaptic transmission in vertebrates. *Physiol. Rev.* **54:** 418–540, 1974.
15. Marczynski, T. J. Neurochemical mechanisms in the genesis of slow potentials: a review and some clinical implications. In: *Multidisciplinary Perspectives in Event-Related Brain Potential Research,* edited by D. A. Otto. Washington, DC: U.S. Government Printing Office, 1978.
16. Nakai, Y., Y. Takeda and S. Takaori. Effects of ethanol on afferent transmission in the central visual pathway of cats. *Eur. J. Pharmac.* **31:** 318–322, 1973.
17. Obitz, F. W., L. E. Rhodes and D. Creel. Effect of alcohol and monetary reward on visually evoked potentials and reaction time. *Q. Jl Stud. Alcohol* **38:** 2057–2064, 1977.
18. Okamoto, M. Barbiturates and alcohol: Comparative overviews on neurophysiology and neurochemistry. In: *Psychopharmacology: A Generation of Progress,* edited by M. A. Lipton, A. DiMascio and K. F. Killam. New York: Raven Press, 1978, pp. 1575–1590.
19. Porjesz, B. and H. Begleiter. Visual evoked potentials and brain dysfunction in chronic alcoholics. In: *Evoked Brain Potentials and Behavior,* edited by H. Begleiter. New York: Plenum Press, 1979, pp. 277–302.
20. Porjesz, B., H. Begleiter and S. Hurowitz. Brain excitability subsequent to alcohol withdrawal in rats. In: *Tissue Responses to Addictive Substances,* edited by D. H. Ford and D. H. Clout. New York: Spectrum, 1976, pp. 461–469.
21. Schwartzbaum, J. S. and C. J. Kreinick. Electrophysiological and behavioral reactivity to photic stimuli following septal lesions and pharmacological treatments in rats. *J. comp. physiol. Psychol.* **88:** 128–146, 1975.
22. Walker, D. R. Signs of information processing in photic evoked potentials. In: *Operant Control of Brain Activity, Perspectives in the Brain Sciences,* vol. 2, edited by M. H. Chase. Los Angeles: Brain Information Service/Brain Research Institute, 1974, pp. 145–212.