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BRIEF COMMUNICATION

Effects of Ethanol on Evoked Potentials in the Rat[1]

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Visual-evoked potentials were recorded from the visual cortex and reticular formation of chronically implanted rats. Recordings were obtained at fixed time intervals after an intraperitoneal injection of saline, 0.5, and 1.5 g/kg of ethyl alcohol. A significant depression in the evoked potentials was obtained with the high dose of alcohol, and was found to be even more striking at the visual cortex than at the reticular formation. However, no significant effect was observed with the low dosage of alcohol at either site.

INTRODUCTION

The effects of alcohol on the electrical activity of the brain in animals have been studied by many investigators, and recently reviewed by Himwich and Callison (1971). These authors conclude that alcohol in substantial doses depresses the functions of the central nervous system, while in low concentrations it appears to have a stimulating effect. We have recently reported (Branchey, Begleiter, and Kissin, 1970) that 0.5 and 1.5 g/kg of ethyl alcohol had differential effects on the sleep EEG of rats.

It has been generally accepted that central nervous system depressants markedly affect polysynaptic structures, such as the brain stem reticular formation. This is especially true of general anesthetics and other coma-producing agents like pentobarbital and ethyl alcohol (Arduini and Arduini, 1954; French *et al.*, 1953; Killam, 1962). Some workers have demonstrated that these agents depress the reticular formation more than the primary sensory receiving areas of the neocortex (Arduini and Arduini, 1954; French *et al.*, 1953). On the other hand, Himwich and Callison (1971) state that while

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alcohol affects to some degree all the functions of the brain, the functions with largest cortical components appear to be more susceptible to alcohol than subcortical structures.

To this date no data is available comparing the differential effects of alcohol on the reticular formation and primary sensory cortical areas in the rat. A study was therefore undertaken to carry out a comparative analysis of evoked responses from the visual cortex and reticular formation following the administration of two doses of alcohol.

Twelve male Sprague-Dawley rats, weighing 400-450 g, were implanted under pentobarbital anesthesia with stainless-steel screws placed bilaterally over the frontal cortex which were used as references.

Two monopolar stainless steel electrodes, covered with Teflon and exposed at the tip for 0.05 mm, were implanted. One electrode was located in the ascending reticular formation, 6 mm posterior to bregma, and 2.5 lateral to midline. The second electrode was in the right side of the visual cortex 2-3 mm anterior to the lambda, and 3-4 mm lateral to midline. Electrode placements were verified histologically at the end of the study. All leads were soldered to a miniature connector, and the assembly was fastened to the skull with acrylic cement.

The animals were allowed two weeks to recover from surgery. During the recording sessions the skull pedestal was attached to a cable connected to a mercury pool swivel, allowing the animals freedom of movement. Photic stimulation was delivered with an Iconix strobe-light located on the ceiling of the soundproof enclosure. The flash intensity used was approximately 1000 lm peak intensity; the duration was 5 msec. The stimulus was delivered regularly at a rate of 1/sec, for a total of 40 stimuli.

Evoked responses were amplified by a Grass 78-B polygraph and summed by a Mnemotron computer of average transients (CAT 1000) set to analyze electrocortical activity for 500 msec after each flash. The summed responses were plotted by a Moseley X-Y plotter.

All animals were injected on three separate days according to a counterbalanced design. They received an intraperitoneal injection of saline 0.5 and 1.5 g alcohol/kg body wt. The placebo consisted of 0.63 cc/100 g body wt of physiologic saline (0.9% sodium chloride). The alcohol doses consisted of an equivalent amount of a 10% or 30% (v/v) ethanol solution in physiologic saline. Evoked potentials were recorded at the following times after injection: 5, 15, 30, 45, 60, and 90 minutes.

Amplitude determinations were made for the evoked potentials obtained at the reticular formation and the visual cortex in accordance with criteria used by Creel, Dustman, and Beck (1970). Only the most marked and stable deflections were used to make the peak to trough measurements. In the case of the visual cortex potentials only the N_1-P_2 component occurring at approximately 50 msec was measured. With regard to the reticular formation, only the P_1-N_1 component occurring at approximately 35 msec was taken.

The findings were evaluated by the three-way analyses of variance (effect of alcohol X time X animal).

The main drug effect comparing evoked potentials obtained at the reticular formation was significant ($F(2,22) = 5.10$, $p < .05$). The time and subject effects were significant at $p < .01$. The only statistically significant interaction was the drug by subject effect at $p < .01$.

There was also a significant main drug effect for the evoked potential determinations at the visual cortex ($F(2,22) = 14.50$, $p < .001$). At the visual cortex the subject effect was also significant at $p < .01$, however the time effect was not significant. The drug X subject interaction was significant at $p < .05$.

Individual comparisons between the three experimental conditions: saline (S), low dose of alcohol (LD, 0.5 g/kg), and high dose of alcohol (HD, 1.5 g/kg) were performed with the use of the Duncan's test. At the reticular formation the HD condition was significantly different from the S condition at $p < .01$. The LD condition versus HD condition was significantly different at $p < .05$.

For the visual cortex, the comparison between HD and S was significantly different at $p < .001$. The LD and HD comparisons was significantly different at $p < .01$.

The comparisons between the low dose of alcohol and saline was not significant on either electrode position.

DISCUSSION

Our present observations confirm the notion that alcohol has a sedative effect. A dose of 0.5 g/kg body wt did not induce any significant changes in the evoked potentials recorded at the visual cortex and reticular formation. However, a larger dose of 1.5 g/kg body wt induced a significant decrease in evoked potentials recorded at both sides. These results disclose only a depressant effect of alcohol at higher doses. Masserman and Jacobson (1940) found that the responses of the hypothalamus and the somatosensory cortex to faradic stimulation in cats were somewhat increased after the local injection of low doses of alcohol, and were definitely decreased with higher doses. A similar observation was made by Horsey and Akert (1953). They found that alcohol has a biphasic effect. At very low levels there was some evidence of a slight activation, but with dosages higher than 90-100 mg per 100 cc a significant depression was observed. More recently Grenell (1971) has summarized evidence indicating that in cats, the cortical evoked response to auditory stimulation was enhanced by intravenous injection of alcohol in low dosage, but was markedly depressed by amounts higher than 146 mg per 100 g.

In the present experiment we did not observe an increased excitation with our low dose of alcohol. This finding can easily be accounted for by the

actual dosage used. We used a dose of 0.5 g/kg which is apparently higher than the ones used by those investigators who obtained increased excitability. As can be seen from Figs. 1 and 2, our low dose of alcohol induced a slight depression of evoked potentials at the visual cortex and the reticular formation. It should also be noted that the findings of increased activation have only been observed in the cat, and, we used rats in our study.

While it is highly probable that alcohol acts diffusely over the entire nervous system, nevertheless it probably does so with different intensities at different sites. Our statistical results indicate a stronger effect of alcohol at the visual cortex than at the reticular formation. These findings appear to be in agreement with those of DiPerri *et al.* (1968) who found cortical sites (association area, visual cortex) more sensitive to alcohol than subcortical

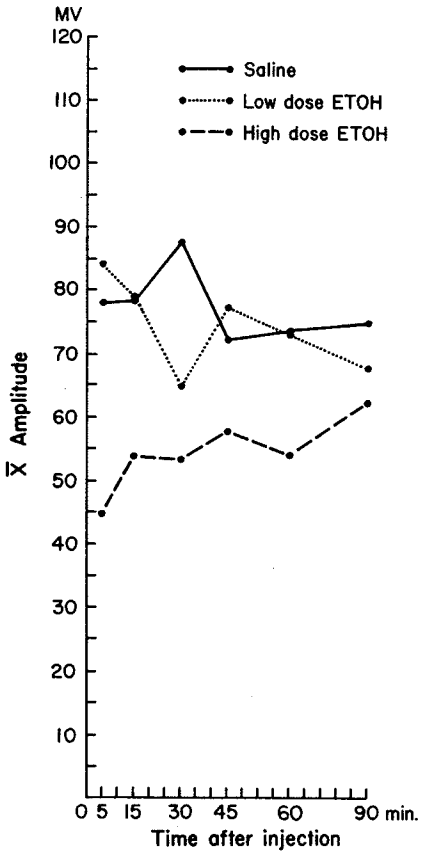

Fig. 1. Amplitude (microvolts) of evoked potential recorded at the visual cortex subsequent to the administration of saline, 0.5 g/kg and 1.5 g/kg body wt of alcohol. Recordings were taken at 5, 15, 30, 45, 60, and 90 min after injection.

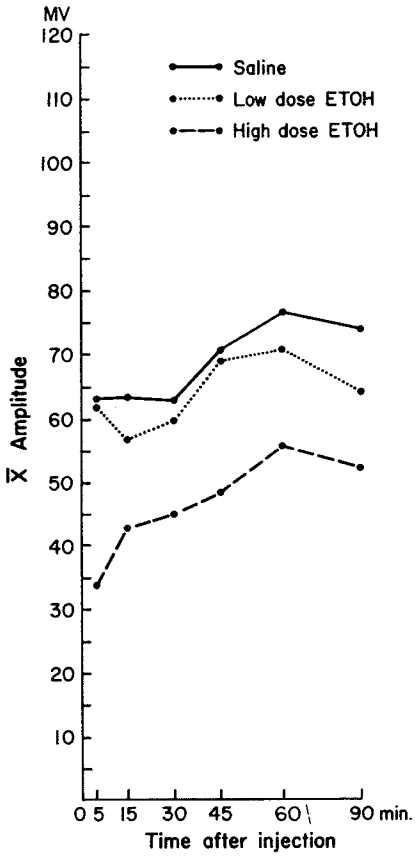

Fig. 2. Amplitude (microvolts) of evoked potential recorded at the reticular formation subsequent to the administration of saline, 0.5 g/kg and 1.5 g/kg body wt of alcohol. Recordings were taken at 5, 15, 30, 45, 60, and 90 min after injection.

structures (geniculate body, reticular formation). Furthermore, Nakai and Domino (1969) did not find any effect of ethyl alcohol on the facilitation of the visual evoked response by stimulation of the reticular formation. They state that a large number of neurons in the reticular formation are single axon cells which originate in the brain stem and send fibers to the diencephalon. Therefore, in keeping with their findings, it is not surprising that a central nervous system depressant like ethyl alcohol should have minimal effect on these monosynaptic neurons. Our present data indicate that the greater effects of alcohol are exerted on cortical rather than subcortical structures.

Inspection of Figs. 1 and 2 reveals that the onset of drug action is quite abrupt since it takes place within 5 min at the visual cortex and the reticular

formation. The recovery from the effects of alcohol seem to be more rapid at the reticular formation than at the visual cortex. This would again appear to indicate greater susceptibility of the visual cortex than the reticular formation. The fact that we did not obtain any significant drug by time interaction might be due to both the lack of a preinjection recording, and the lack of recordings past 90 min which would have shown complete recovery from the effects of alcohol.

Our present findings indicate that the greater and more enduring effects of ethyl alcohol are exerted on cortical rather than on subcortical structures. However, we realize that the behavior of an organism in response to any pharmacological agent depends in large measure on the interactions of many anatomical brain regions, and is therefore too complex to be described in terms of action upon any selected pathway or site in the brain.

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