Influence of Acute and Chronic Administration of Ethanol on Photic-Evoked Response in Rats

Elijah SOKOMBA and Gabriel OSUIDE
Department of Pharmacology, Faculty of Pharmaceutical Sciences,
Ahmadu Bello University, Zaria, Nigeria
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Abstract—The effect of acute and chronic administration of ethanol on photic-evoked response was studied in rats. Acute administration of ethanol (1–3 g/kg, i.p.) produced behavioural depression, EEG synchronization and a biphasic effect on the amplitude of the photic evoked responses (PER) recorded from the frontal cortex (FC) and optic cortex (OC), while a reduction in amplitude was observed in the midbrain reticular formation (MBRF). The amplitude of the averaged PER in the FC and OC was increased in chronic ethanol-treated rats, while in the MBRF, a reduction in amplitude was observed. Abrupt discontinuation of ethanol produced behavioural excitation and increase in amplitude of the averaged evoked responses recorded from the three brain areas studied. These observations suggest that the neural hyperexcitability that characterizes ethanol withdrawal may affect both cortical and subcortical structures.

Several studies have shown that abrupt discontinuation after chronic administration of ethanol precipitates withdrawal symptoms with which the EEG correlates (1–3). Such studies have reported seizure activity in the EEG after ethanol withdrawal in animals (2, 3). Ethanol withdrawal syndrome is often characterized by increased irritability, behavioural excitation, spontaneous and sound-induced convulsions in experimental animals (4), and this is attributed to the release of a latent state of neural hyperexcitability (1). The neural hyperexcitability is also characterized by increased amplitudes of visual evoked responses (5, 6). However, conflicting data have been reported on the evoked response changes that take place at the reticular formation during ethanol withdrawal. Some studies have reported enhancement of amplitude of the evoked response at the reticular formation, while no significant changes in amplitude were reported by others (5).

The work reported in this paper was designed to study the influence of acute and chronic administration of ethanol on photic-evoked responses from the frontal cortex, optic cortex and midbrain reticular formation in rats. Such a study may contribute to the understanding of the evoked response changes that take place in cortical and subcortical structures during ethanol withdrawal in rats.

Materials and Methods

Male albino rats (Wistar strain) weighing 150–200 g (inbred in our Animal House) were used in this study. Each rat was placed in a separate cage and provided with food ad libitum. Ethanol was administered to each rat through drinking water into which was added saccharin sodium (0.2 mg/ml) to mask the taste of ethanol according to the method of Puri and Lal (7). The starting concentration of 5% v/v was increased by 5% v/v every other day until a concentration of 20% v/v was reached. The rats were maintained on this concentration of ethanol for four weeks before withdrawal. Control rats were provided with food and drinking water containing saccharin sodium (0.2 mg/ml).

Implantation of electrodes: After chronic administration of ethanol for three weeks, the rats were implanted with electrodes using the...
following procedure: Each rat was anaesthetized with halothane (Fluothane, ICI Ltd.), and the head was held firmly in a stereotaxic apparatus. The scalp was exposed and the coordinates were taken using the bregma as the zero point. Stainless steel screw electrodes were implanted on to the frontal cortex (FC) (coordinates: Anterior-posterior, +1.9 mm; Lateral, +1.5 mm) and optic cortex (OC) (coordinates: Anterior-posterior, -9.2 mm; Lateral, -2.8 mm). Bipolar electrodes made from stainless steel insect pins, No. 00, were implanted into the midbrain reticular formation (MBRF) (coordinates: Anterior-posterior, -3.8 mm; Lateral, +2.0 mm; Vertical, -8.2 mm). Electromyograph (EMG) electrodes were made with stainless steel insect pins (No. 00) bent at the ends to make hooks. The electrodes were positioned in the proximity of the head and inserted into the spinalis capitis muscle at one side of the dorsolateral aspect of the neck. A reference screw electrode similar to those used for the cortical sites were positioned in the frontal sinus area of each rat. All the electrodes were secured chronically to the various positions with dental cement. Administration of ethanol was continued for another week before the rats were used for EEG, EMG and PER studies.

Other rats were similarly implanted and used for studying the influence of acute administration of ethanol on PER.

Recording of photic evoked response: The procedure of Osuide and Sokomba (8) was used for recording the EEG, EMG and PER.

Results

Characteristics of PER pattern in rats: Distinct averaged evoked responses to photic stimulation were recorded from the brain areas studied. In the FC, the averaged evoked response was characterized by a positive wave of high amplitude (40–70 µV). The averaged PER recorded from the OC was characterized by an initial positive wave (100–130 µV), followed by a negative component (120–160 µV). The EEG was characterized by low voltage fast activity of 20–30 c/sec frequency. In the MBRF, the averaged PER consisted of a positive component (25–60 µV) followed by a negative component of smaller amplitude, while the spontaneous activity was characterized by low voltage fast activity of 25–35 c/sec frequency. In the FC and MBRF, the evoked spikes were not visually distinguishable from the ongoing spontaneous activity, while in the OC, the evoked spikes were slightly distinct from the EEG.

Acute ethanol treated rats: Administration of ethanol (1–3 g/kg, i.p.) produced behavioural depression. The EEG was synchronized, while there was a decrease in the EMG activity. With these doses of ethanol, the amplitude of the averaged PER was initially decreased and subsequently increased in the FC. In the OC, there was an initial slight increase in amplitude of the negative component of the PER followed by a decrease, while the positive component was decreased. In the MBRF, there was a decrease in amplitude (Fig. 1).

Chronic ethanol treated rats: The rats given ethanol were usually weak and showed significant loss in weight. With a concentration higher than 20% v/v, the daily intake of ethanol decreased markedly. When ethanol administration was stopped abruptly after 4 weeks, the rats showed increased motor activity and were found irritable to touch, but did not show spontaneous or sound-induced convulsions. The EEG of the chronic ethanol treated rats were synchronized in all the brain areas studied, while the EMG activity was decreased. The amplitude of the averaged PER in these rats was increased in the FC (P<0.01) and OC (+ ve component, P<0.025), while in the MBEF, the amplitude was reduced. The withdrawal phase was characterized by desynchronized EEG and increased EMG activity. The amplitude of the averaged PER was increased in the FC (P<0.0025), OC (P<0.025) and the MBRF (P<0.005) when recorded 24 hr after withdrawal (Fig. 2, Table 1). After 48 hr of ethanol withdrawal, there was no significant change in the amplitude of the PER in the FC, OC (−ve component) and MBRF. A slight decrease in amplitude was observed in all the three brain areas when recording was done one week after withdrawal. By this time,
the rats appeared behaviourally calm and inactive.

**Discussion**

The EEG synchronization and decrease in amplitude of the PER at the FC, OC and
MBRF in acute ethanol treated rats are consistent with previous reports (9). The withdrawal signs observed after chronic administration of ethanol are similar to those reported by previous workers (10). However, in the present study, ethanol withdrawal failed to induce spontaneous or audiogenic seizures in the rats as observed by other workers (4).

Fig. 2. Effect of chronic administration of ethanol and its withdrawal on EEG, EMG and photic-evoked response in rats. A: Control (drinking water+ saccharin), B: Chronic ethanol treated (before withdrawal), C: 24 hr after withdrawal, D: 48 hr after withdrawal.
Table 1. Effect of chronic administration of ethanol and its withdrawal on amplitude of averaged photic-evoked response in rats

| Condition                        | Frontal cortex (µV) | Optic cortex (µV) | Midbrain reticular formation (µV) |
|----------------------------------|---------------------|-------------------|----------------------------------|
|                                  | Mean ± S.D.         | Mean ± S.D.       | Mean ± S.D.                      |
| Control (drinking water + saccharin) | + 59.1 ± 12.3       | -160.0 ± 22.1     | +121.41 ± 17.0                   |
| Chronic ethanol treated (before withdrawal) | + 88.09 ± 16.43     | -181.20 ± 26.34   | +155.52 ± 23.0                   |
| 24 hr after ethanol withdrawal   | +100.71 ± 18.6      | -201.0 ± 31.22    | +189.3 ± 24.0                    |
| 48 hr after ethanol withdrawal   | + 70.93 ± 13.1      | -179.53 ± 22.0    | -150.0 ± 17.74                   |

* is significantly different from the chronic ethanol treated (before withdrawal) and represents P<0.0005.

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