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Acute Ethanol Effects on Sensory Responses of Single Units in the Somatosensory Cortex of Rats During Different Behavioral States[1]

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CHAPIN, J. K., S. M. SORENSEN AND D. J. WOODWARD. *Acute ethanol effects on sensory responses of single units in the somatosensory cortex of rats during different behavioral states.* PHARMACOL BIOCHEM BEHAV 25(3) 607–614, 1986.—We have investigated the dose-dependence and time-course of ethanol effects on the activity of single neurons in the somatosensory (SI) cortex of behaving, unanesthetized rats. Sensory responses of neurons recorded in the forepaw area of the SI cortex were quantitatively measured by constructing post-stimulus histograms to repetitive stimulation through electrodes chronically implanted in the forepaw. Single units were isolated and held throughout a protocol involving: (1) a control period, (2) intoxication produced by a single dose of ethanol administered IP or IV and (3) recovery for 60 minutes or more. Post-stimulus histograms were generated during three standard behaviors: (1) REST, (2) IMMOBILE AROUSAL (produced by holding the animal), and (3) MOVEMENT (running on a treadmill). In pre-ethanol controls, the immobile arousal condition slightly increased both excitatory and inhibitory components of the sensory response, while the movement condition strongly inhibited them. Ethanol reduced both of these types of behavioral modulation of sensory responses by abolishing the facilitation normally seen during immobile arousal, as well as the inhibitory gating normally seen during movement. Different latency response epochs of post-stimulus histograms were also used to compare the effect of ethanol on fast vs. slow conducting pathways to the SI cortex. Ethanol at low doses (0.3 g/kg bw, IP) was found to selectively reduce the longer latency excitatory response peaks, while sparing the shortest latency response peak. At moderate doses (1.0 g/kg), however, the shortest latency response peak was also reduced. This contrasted with the effects of halothane which, at anesthetic doses, exerted a much more selective reduction of the longer latency responses. Thus, ethanol appears to disrupt normal cortical processing by reducing the normal behavioral modulation of cortical sensory responses. In a less selective manner it reduces sensory transmission through longer latency multi-synaptic pathways.

Ethanol Cerebral cortex Single units Rat Somatosensory responses

ACUTE ethanol intoxication is known to exert a powerful disruptive effect on many parameters of human performance. Among the most severely compromised tasks are those which require perceptual attention in the presence of distracting stimuli, and also those which require quick motor responses to an appropriate sensory stimulus [1, 9–12].

Unfortunately, little is known about the neurophysiological mechanisms underlying these powerful effects on higher order sensorimotor functions. The apparent specificity of the behavioral changes brought about by ethanol suggests that intoxication may selectively affect certain neural systems or processes in the brain, possibly involving the cerebral cortex and/or its afferent systems. Thus, higher order processing of sensory information may be an appropriate functional context in which to begin the search for ethanol effects on neuronal networks.

We have developed an experimental system which contains many of the elements necessary for such a study. It involves neurophysiological recording of single units in the forepaw area of the primary somatosensory (SI) cortex of unanesthetized, behaving rats. Sensory transmission through the somatosensory afferent pathways to the cortex is tested during different behaviors or drug states by stimulating at low electrical currents through electrodes chronically implanted just under the skin of the forepaw. Post-stimulus histograms, each containing several different response peaks, are generated showing the summed unit response to repetitive paw stimulation. The magnitude of the earliest of these peaks may be used as a measure of the transmission through direct subcortical somatosensory afferent pathways, while the longer latency peaks are more likely to reflect either transmission through slower afferent pathways, or telencephalic processing of the sensory information. Finally, the effects of various behavioral state changes (such as arousal and movement) on this sensory processing system may be assessed through use of this

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technique. Thus, use of this test system may allow an assessment of ethanol's effects not only on sensory transmission, but also on neurophysiological manifestations of cortical sensory processing in the context of behavior and movement (see preliminary reports [6–8]).

The results appear to demonstrate that ethanol selectively depresses certain measurable parameters of cortical single unit responses to cutaneous stimulation. These effects were behaviorally dependent, and also were dependent on dose and time course of ethanol administration.

METHOD

Techniques for preparing animals for awake single unit recording have been described in detail elsewhere [2–5]. Briefly, Long Evans (hooded) rats (200–300 g) were initially habituated to handling and treadmill running. Several days prior to experimentation the animals were anesthetized, and a small hole was drilled just over the forepaw area of the rat SI cortex. A stainless steel microelectrode drive holder (Biela Engineering, Anaheim, CA) was positioned over the hole in the skull and cemented in place with dental acrylic. For paw stimulation, a twisted pair of 8 mil, seven stranded, stainless steel teflon insulated wires (Medwire, Mt. Vernon, NY) with 0.5 mm exposed tips were implanted under the skin of the thenar eminence of the contralateral forepaw and routed subcutaneously to a plastic Amphenol plug strip fastened by dental cement to metal screws embedded in the skull.

Experimental Procedure

On the day of the experiment the animal was placed in a 16 by 36 cm recording chamber built on a motor driven treadmill. The head plug on the animal was attached to a wire harness connecting it to the amplification apparatus. A tungsten microelectrode (1–2 Megohm, Bak Electronics, Clarkesville, MD; or 5–10 Megohms, Haer Inc., Brunswick, ME) was then slowly driven into the cortex and stable single spike profiles were isolated for recording.

The procedure involved testing of the cutaneous sensory responsiveness of these cells during different behaviors, administering alcohol, and then retesting several times in the subsequent intoxication period. Standardized cutaneous test stimuli were delivered at a rate of 1 Hz through stimulating electrodes (described above) chronically implanted in the forepaw. Cells with cutaneous receptive fields on the palmar area of the contralateral forepaw invariably could be driven by low current (100–200 μA) stimulation through these electrodes.

Post-stimulus time histograms of such responses were generated with a Data General Eclipse computer. These were used to quantitate the responsiveness of the single units to peripheral activation during different behaviors. Threshold stimulus currents to obtain perceptible unit responses in the SI cortex ranged from 50 to 200 μA (single, 0.1 msec pulses were used). Definite twitches or flexion reflexes were elicited above 500 μA. To minimize these nonspecific effects, the test currents were set about 50 μA above threshold levels. At these low currents no obvious signs of evoked movement or painful reactions on the part of the animals could be observed. When such currents of skin stimulation were applied to the experimenter's finger tip with an electrode of similar tip separation and size, they produced a slight touch-tingling sensation which was not unpleasant.

Histograms of the single unit responses to these standard paw stimuli were generated first during immobile resting behavior, then during immobile arousal, and finally, movement behaviors (see the Results section for further description). An analysis program on the computer allowed calculation of precise changes in the neural responses to the paw stimuli during the different behavioral or drug conditions. The histograms were displayed on a Tektronix 4012 graphics computer terminal. The single unit firing rates (in spikes/sec) were determined during these epochs defined as: (No. of spikes/No. of sweeps) $\times$ (1000/No. of msec in epoch). Spontaneous discharge rates, in spikes/sec, were measured by making similar calculations during the time between 300 and 500 msec in which the histograms flattened. The ratio of the discharge rate during the response epoch to the spontaneous discharge rate was calculated. Values were expressed in percentages above or below spontaneous rate. Percentage scores were used, rather than absolute measures, to normalize data obtained from different cells which normally exhibited marked variations in spontaneous rate. In addition, these measurement techniques allowed quantitative comparisons to be made between magnitudes of specific response peaks during different behaviors, or drug states, when spontaneous rates often changed.

Ethanol and Control Saline Administration

Of 8 animals used in this study, 2 were implanted during initial surgery with chronically indwelling intravenous catheters in the external jugular vein. Ethanol in saline (15% v/v) was injected through a syringe attached to a 30 cm length of polyethylene tubing leading to the head-plug in the animal.

The injection was carried out slowly over a period of about 5 minutes. Six animals were administered a similar ethanol solution through intra-peritoneal (IP) injections. The possible behavioral arousal caused by handling these animals and injecting them IP was controlled for in two ways: (1) an isovolumetric saline control injection could be administered before actual ethanol injection, and any changes in the physiology caused by this alone could be monitored, and (2) since it generally took about 5 minutes for the ethanol to first begin showing its effects when administered IP, any arousal effects of the injection itself were usually gone.

IP injections were generally made with a 15% ethanol solution contained in a hypodermic syringe. By carefully lifting the hindlimb up and quickly inserting the needle into the umbilical region, such injections were finished in a matter of seconds and generally produced no major aversive reaction on the part of the animal. Control saline injections were made using the same technique. Generally 15–20 minutes were allowed to elapse between control saline and ethanol injections. After ethanol injection data was obtained continuously for 60–120 minutes. During this time the three major behavioral manipulations described in the Results section (i.e., rest, holding to produce immobile arousal, and treadmill locomotion) were alternately evoked in a sequence at about 2 minute intervals.

To prevent development of ethanol tolerance such animals were not reused until at least one week after an experiment.

RESULTS

The major goal of this investigation was to define the effects of ethanol on sensory responses of single units in the

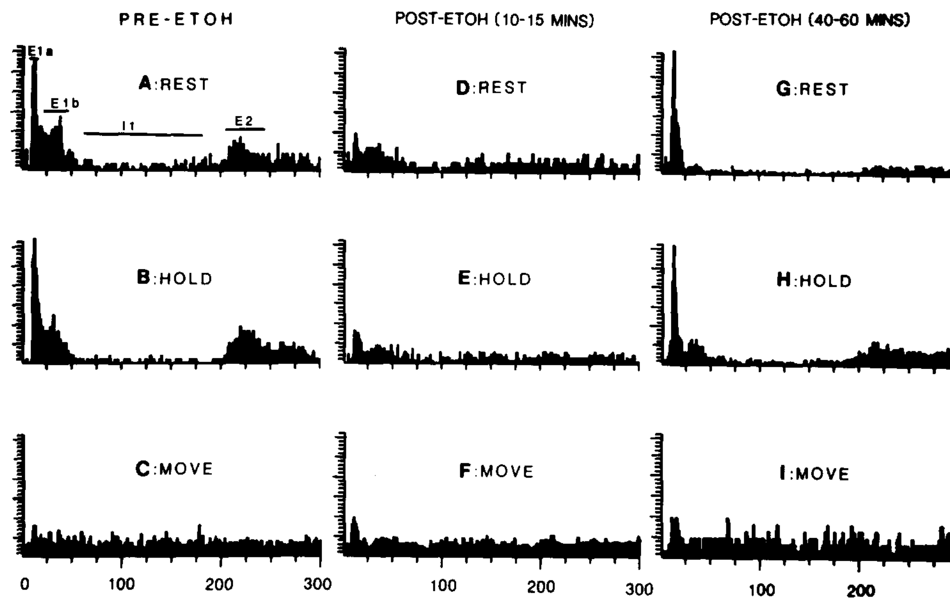

FIG. 1. Sensory responses of a single SI cortical neuron during "REST," "HOLD," and "MOVE" behaviors, before and after ethanol administration, and after 40–60 minutes ethanol recovery. All post-stimulus histograms constructed from repetitive stimulation of the forepaw (single 0.1 msec pulses delivered at 1 Hz, 200 μA, from 60–200 sweeps for each histogram). To allow direct comparison of histograms all are normalized to a constant scale of instantaneous firing rate/bin (small vertical scale ticks: 5 spikes/sec/bin; large ticks: 25 spikes/sec/bin). Histograms A–C constructed from 2–10 minutes after control saline injection, but before ethanol injection. D–F: 10–15 minutes post ethanol; G–I: 40–60 minutes post ethanol. A, D, and G: quiet resting behavior; B, E, and H: immobile arousal behavior produced when experimenter held the animal; C, F, and I: forced treadmill locomotion. Histogram A shows typical excitatory and inhibitory components of such responses: E1a—shortest latency excitatory peak (7–16 msec latency post stimulus), E1b—second excitatory peak (16–50 msec latency), I1—first inhibition (50–200 msec latency), and E2—long latency excitatory peak (200–250 msec latency). All histograms: 1 msec/bin; X-axis ticks: 25 msec.

SI cortex of unanesthetized, behaving animals. Overall, the results showed that ethanol's effects on such responses varied according to a number of factors, including: (1) the latencies of the sensory response components, (2) the ethanol dose, (3) the time after administration, and (4) the behavioral state of the animal.

Normal Components of Sensory Response Histograms

The histogram in Fig. 1A is typical of those obtained from SI cortical cells in unanesthetized rats during normal quiet resting behavior. It features several response components differentiable on the basis of latency. These include: E1a (an excitatory peak lasting from 7–16 msec post-stimulus), (2) E1b (from 16–50 msec), (3) I1 (a post-excitatory inhibition lasting from 50–200 msec), and (4) E2, beginning about 200 msec post-stimulus. In a previous report we have shown that the E1a peak is relatively resistant to the effects of anesthetics such as halothane [5] while the longer latency excitatory peaks (E1b and E2) may be completely abolished during the unconsciousness produced by these drugs (see also Fig. 4 below). These later components of the histogram are also much more variable across behaviors and from neuron to neuron in the cortex.

This investigation involved primarily an analysis of ethanol effects on these components of histograms obtained using the standardized techniques described in the Method section. Calculating the magnitudes of these response components, and expressing them in terms of percent deviations from the spontaneous firing rates of these cells (300–500 msec post-stimulus) allowed data from a group of recorded neurons in different animals to be quantitatively averaged and compared. Figure 2 contains a group of graphs generated from lumping data obtained from a sample of 11 neurons (in 5 animals) which were held for the entire procedure of experiments in which 1.0 g/kg doses of ethanol were given. This will be discussed further below.

Ethanol Effects on Sensory Responses

In general, no consistent changes in these histograms were observed after the saline-control injections. We conclude, therefore, that any arousal produced by the drug injection procedure was negligible. In some animals chronically implanted with intravenous cannulas and injected slowly over a period of 5 minutes, even these transient post-injection changes were absent.

By contrast, numerous changes in these sensory response histograms were observed after ethanol administration, varying both as a function of dose and time after administration. Figure 1D illustrates the response of a typical neuron to the paw stimulation during the period lasting from 10 to 15 minutes after administration of ethanol (1.0 g/kg; IP). The graphs in Fig. 2 show that during the first 10 minutes after ethanol injection, the spontaneous discharge rates (of the 11 cells

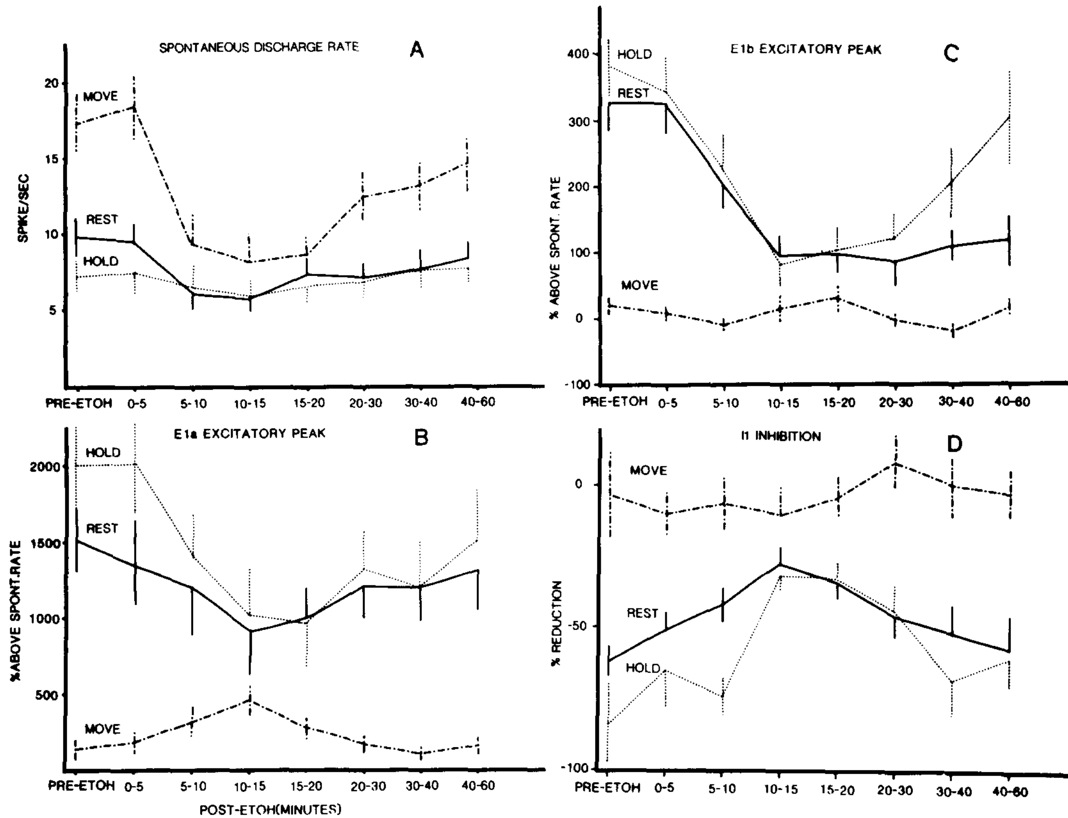

FIG. 2. Graphic analyses of behavior and ethanol effects on different response components of post-paw-stimulus histograms. Data base includes 11 neurons recorded before and at least 60 minutes after injection of 1.0 g/kg doses of ethanol (9 neurons injected IP, 2 IV). A—Mean spontaneous discharge rates (in spikes/sec; measured in 300–500 msec post-stimulus epochs of histograms from each of the 11 cells) in pre-ethanol control, and selected time intervals after ethanol injections (labelled on horizontal axis in minutes). For each time interval, histograms were constructed during each of three standard behaviors: REST, HOLD, and MOVE (see text). Vertical bars on each plotted point show standard errors (omitted on one side when they would overlap bars from adjacent plots). B—Amplitudes of E1a excitatory peaks (in percent increase in firing rate during 7–16 msec post-stimulus epoch over spontaneous firing rate). C—Amplitudes of E1b excitatory peaks in percent over spontaneous rate in 16–50 msec epoch. Data derived only from histograms from the 6 (of the total 11) neurons which possessed this peak. D—Magnitudes of I1 inhibitory responses in percent of spontaneous rate (all 11 cells used). Same histograms used for all graphs.

used in this sample) during resting behavior declined about 42% (from 9.8 to 5.7 spikes/sec), while the amplitude of the E1a peak (over baseline) declined by a similar proportion, 39% from 1502% to 922% over spontaneous discharge rate in the 7–16 msec epoch. By contrast, the E1b peak (present in 7 of the 11 neurons) declined 72% during the same period. In addition, the E2 peak (present in 4 of the 11 neurons) was essentially abolished in all cases during this stage of ethanol intoxication (not shown in Fig. 2). It is clear, therefore, that the longer latency excitatory components (E1b and E2) were relatively more strongly affected than the short latency component (E1a). Nevertheless, even the E1a was quite strongly reduced by ethanol in comparison to our previous studies with halothane [5] (see also Fig. 4).

Recovery From Intoxication

In these experiments, measurements continued to be made for at least one hour after ethanol administration. The graphs in Fig. 2 show the time course of recovery for each of the response components analyzed here (except the E2 peak). By the 40–60 minute post-ETOH period (in control resting behavior) most of these parameters had recovered to near their normal values. However, the E1b peak continued to be quite depressed, yielding histograms (Fig. 1G) somewhat similar to those seen during light halothane anesthesia (See Fig. 4D below).

Behavioral Effects of Acute Intoxication

In general, the observable behavioral effects of intoxication paralleled the time course of the neurophysiological effects, yet were apparently much weaker. After the 1.0 g/kg doses used here the animals exhibited relatively subtle signs of intoxication, including a transient increase in behavioral activation, accompanied by minor lapses in motor coordination. This pattern developed over the first 10 minutes following ethanol injection and usually reached its peak in the 10–15 minute post-ETOH period. Typically, these animals exhibited behavioral recovery from acute signs of intoxication after about 20 minutes. This was generally followed by a long period of behavioral hypoactivity. This was characterized by a reduction in spontaneous exploration and a

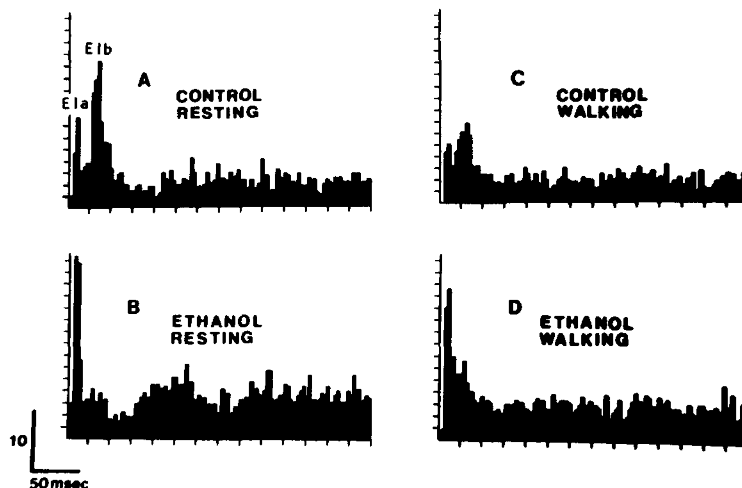

FIG. 3. Responses of a single SI cortical neuron to paw stimulation during "resting" (A,B) and "walking" (C,D) behavior before (A,C) and from 5–15 minutes after (B,D) ethanol administration (dose = 0.3 g/kg bw, IP). Bin width: 1 msec; X-axis ticks: 25 msec; Y-axis ticks: 2 spikes/sec/bin firing rate (normalized for all histograms).

tendency towards somnolence. Such signs were a normal characteristic of habituation to the testing environment, but were clearly accentuated during the ethanol recovery period.

Interaction of Ethanol With Evoked Behavioral Effects

The next major aim of this study was to compare ethanol's effects on sensory responses of histograms generated during three general types of behavioral states (REST, IMMOBILE AROUSAL, and MOVEMENT). We have previously used this simple categorization of behaviors in a study [2] which examined the effects of immobile and mobile "arousal" states on the sensory responsiveness of these SI cortical cells. In REST behavior the rat was allowed to rest quietly in the experimental chamber, but not allowed to sleep. In treadmill locomotion (the "MOVE" state) the animal ran on a treadmill moving at about 15 cm/sec. Immobile arousal was produced by holding the animal, which was associated with a characteristic rodent "freezing" response (termed the "HOLD" state). These three manipulations thus allowed measurements during a resting "control" behavioral state (REST), and two types of arousal, one mobile and one immobile. A major advantage of using these "evoked" rather than trained behaviors is that the same tests may be performed in moderately intoxicated as well as unintoxicated animals.

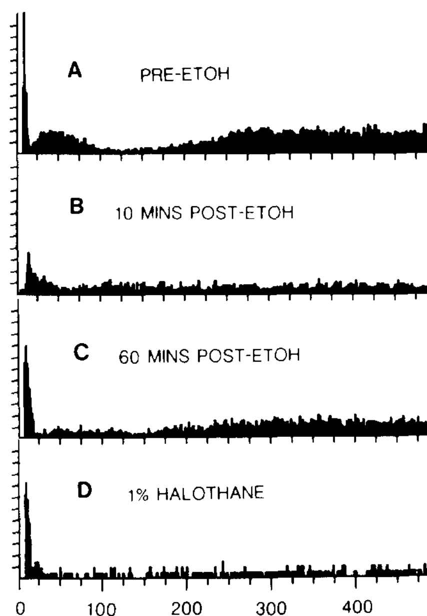

FIG. 4. Comparison of effects of ethanol and halothane on sensory responses of a single SI cortical neuron. A—Pre-ethanol response to standard parameters of paw stimulation (200 μA), B—Response 10–12 minutes after 1.5 g/kg dose ethanol injection, C—Response 60 minutes after same ethanol dose, D—Response after anesthesia with halothane (1.0% continuous inhalation in 95% Oxygen). All histograms: 1 msec/bin; Y-axis ticks: 10 spikes/sec/bin firing rate (normalized for all histograms); X-axis ticks: 25 msec.

Figures 1A, 1B and 1C illustrate the typical effects of these behavioral manipulations on sensory responses of SI cortical cells. In the HOLD condition, the cortical neuronal responses to paw stimulation typically exhibited small increases in the amplitudes of the excitatory responses, plus a deepening of the inhibitory responses and a reduction in spontaneous discharge rate. For example, in the 11 neurons in Fig. 2 the E1a peak (graphed in Fig. 2B) was 1509% over baseline during REST, but 2010% during the HOLD condition, a mean 33% increase ($p<0.01$ using paired one-tailed t-test). By contrast, during the MOVE condition the magnitude of the E1a response was sharply reduced from 1509% to 122% above baseline, while the overall discharge rate was increased from 9.8 to 17.6 spikes/sec.

In general, ethanol's effect was to reduce both of these sensory modulation effects caused by HOLD or MOVE behaviors. For example, while histograms 1A and 1B showed a

clear, though somewhat subtle difference between the REST and HOLD states, their equivalents in the 10–15 minute post-ETOH period (1D and 1E) exhibited minimal differences. Shown graphically in Fig. 2B, ethanol reduced the facilitation of the E1a responses during HOLD from a mean 33% (in the 11 neurons) in the pre-ethanol condition, to 8% in the 10–15 minute post-ethanol period. This is likely to be due to a failure of the holding procedure to produce an aroused behavioral state in the moderately intoxicated rat.

Figure 2C shows that ethanol reduced the E1b (16–50 msec) response, and also abolished the slight facilitation of the E1b response caused by the HOLD condition. Furthermore, in the 40–60 minute post-ETOH period, the E1b peak did not recover as rapidly as the E1a peak during REST. However, the HOLD condition produced a major increase in the E1b response relative to the REST condition. Since the animals generally appeared to be quite drowsy during this ethanol recovery period, the lack of a large E1b response during normal REST may have been associated with a very low level of arousal, which was reversed by the HOLD condition.

The powerful sensory inhibition normally produced during the MOVE condition (compare Fig 1A and 1C) was also reduced by ethanol. For example, the E1a peak was reduced by 91.9% during MOVE by comparison with REST before ETOH, but only by 51% in the period 10–15 minutes post-ETOH. Thus, while ethanol reduced the magnitudes of all components of the sensory responses during REST, the E1a sensory response during MOVE was actually increased from 122% above background before ethanol to a maximum of 452% above background after ethanol. This phenomenon was limited strictly to the early phase of intoxication in that the E1a peak returned approximately to pre-ethanol levels after 20–30 minutes post-ethanol.

Effects of Ethanol Dose

The neurophysiological parameters measured here showed clear dose-dependencies in their responses to ethanol. In addition to the 11 neurons recorded after 1.0 g/kg doses, 7 neurons were recorded after administration of other doses ranging from 0.3 to 2.0 g/kg. In general, these data showed a dose-dependent scaling of the same types of effects which were observed at the 1.0 g/kg doses.

One of the more significant findings of these dose-dependence studies, however, was that very clear neurophysiological changes in this system could be produced by ethanol doses which were much lower than those at which noticeable behavioral changes were observed. Figure 3 shows four histograms obtained before and after a 0.3 g/kg ethanol dose. It can be seen that even at this dose, which produced no observable behavioral effects at all, the magnitude of the E1b peak was substantially reduced. Furthermore, the magnitude of the E1a peak during running was increased after ethanol relative to the pre-ethanol condition (see Fig. 3C vs. 3D). Both these effects were clearly consistent with similar, though stronger effects measured at higher doses.

Comparison of Ethanol and Halothane Effects on Sensory Responses

An important question is whether these effects of ethanol on sensory responses of SI cortical cells are comparable with other anesthetic drugs? For example, in a previous publication [5] we have investigated with similar methods the effects of halothane on sensory response histograms of SI cortical units in rats. The major finding (from studies on 211 cells) was that halothane at anesthetic doses produced a powerful selective reduction in the longer latency excitatory response components (E1b and E2) while sparing the E1a response. By comparison, it appears that ethanol had less of a sparing action on the E1a response, in that even at moderate doses (1.0 g/kg) the E1a peak was substantially reduced (as in Fig. 2A vs. 2D).

Figure 4 illustrates a direct comparison of these two drugs' effects on the same single neuron. In this experiment, histograms were generated during REST in the following drug conditions: (4A) an initial control period, (4B) 10 minutes after a 1.0 g/kg dose of ethanol, (4C) after the animal was allowed to partially recover (60 minutes), and (4D) after an anesthetic dose of halothane (1% inhalation in 95% oxygen; see the Method section). It can be seen that, as in Fig. 1, the ethanol (Fig. 4B) produced a marked reduction of all components of the sensory response. After 60 minutes (4C) the E1a peak had recovered enough to retest with halothane (4D). While the halothane sharply lowered the spontaneous discharge rate, the E1a peak remained at about the same amplitude. Thus, ethanol's effects appeared to be much less selective than those of halothane on these response components.

DISCUSSION

The major aim of this study was to characterize ethanol's effect on different parameters of sensory information processing in the cerebral cortex. This aim was approached by measuring short and long latency responses of single units in the rat SI cortex to standardized peripheral stimulation. Overall, the findings demonstrated that ethanol had relatively small effects on the static, short latency sensory responses of the SI cortical neurons. However, it strongly depressed their more "dynamic" functions, including their longer latency sensory responses, as well as the modulation of these responses which normally occurred during behavioral state transitions.

To summarize the effects of 1.0 g/kg ethanol doses in 11 rats: (1) Ethanol reduced the shortest latency (E1a sensory responses 7–16 msec post-stimulus) of these neurons by a mean 39%, but reduced the longer latency E1b responses by 72%, and completely abolished the longest latency E2 responses. Also, the E1a response recovered more rapidly than the E1b from the intoxication effects. (2) Ethanol nearly abolished the average 33% facilitation of the E1a responses of these cells observed during control immobile arousal. (3) Ethanol sharply attenuated the inhibitory gating of the sensory responses normally observed during movement (inhibition reduced from −91% to −51%). Thus, while ethanol depressed most sensory responses by a considerable absolute amount, this reduction of inhibitory gating resulted in an absolute increase in the short latency E1a response over that normally observed during movement.

Selective Depression of Long Latency Sensory Response Components

While each of these three phenomena would seem to involve different CNS mechanisms, they may be similar in that they all presumably result from activity of higher-order, multisynaptic neural circuits. By contrast, it appears the

more ethanol resistant response component, E1a, involves sensory pathways containing few synapses. Available information suggests that this E1a response is derived from sensory volleys transmitted to the cortex via the dorsal column-medial lemniscal system (thus traversing a minimum of three synapses). This was shown directly by experiments in this laboratory (unpublished) which demonstrated that discrete lesions of the cuneate nucleus abolished the E1a, but not the E1b response, a portion of which is apparently attributable to transmission through extra-lemniscal pathways. Other portions of the E1b peak may be derived from cortical activity secondary to the afferent volleys forming the E1a response.

The origin of the E2 peak is also unclear, but is certain to involve transmission through a large number of synapses. It may in fact result largely from prolonged sensory processing activity within the forebrain, rather than slowly transmitting afferent pathways. This was suggested by the observation [5] that the presence or absence of the E2 peak was much more dependent on the behavioral state of the animal than the type of peripheral stimulus used to evoke it. In any case, the fact that ethanol selectively depressed the longer latency sensory response components of these cells is consistent with the notion that complex, multisynaptic functions are among those most sensitive to intoxication.

Ethanol Effects on Behavioral Modulation

The neural circuit mechanisms for the behavior related inhibitions and facilitations are unknown, but they appear to involve higher-order, multi-synaptic CNS functions. For example, the best available neuroanatomical and physiological evidence suggests that the inhibitory modulation or gating which is observed during movement behavior may be produced in part by axonal projections from the motor cortex to cortical and subcortical relays in the somatosensory system. We have also shown [8] that ethanol strongly reduces movement correlated activity in the motor cortex. Thus, ethanol may disrupt higher-order sensory processing by depressing normal mechanisms of corticofugal and/or cortico-cortical inhibition.

The findings of this study that low dose ethanol markedly reduces the inhibitory gating normally observed during motor behavior may be of particular interest in view of the findings in this laboratory [2–4] that this inhibition correlates highly specifically with the time-course of limb movements. We have advanced the hypothesis that this gating may serve to selectively filter the transmission of sensory information such that given cortical cells only receive such information when it is 'relevant' to the current behavioral or motor situation. Thus, if ethanol reduces this type of inhibition, it may have the effect of disrupting the high degree of control normally exerted by the brain over its sensory input.

It is possible that this disruption of the brain's normal mechanism for control and filtering of its sensory input may be relevant to ethanol's powerful effects on tasks involving selective attention and sensorimotor coordination. For example, Moscowitz and Sharma [10] have shown that ethanol has particularly potent effects on the ability of human subjects to discriminate a sensory (auditory) signal during presentation of distracting stimuli. Levine *et al.* [9] in a review of the literature concluded that such "selective attention" tasks were among the most sensitive of all psychomotor skills to the effects of low dose ethanol.

While the mechanisms of sensory discrimination and selective attention functions in humans are unknown, it is possible that they may involve similar types of cortical gating and modulation functions as those observed here at the single neuron level in the behaving rat. Further experimentation in this neurophysiological system may therefore be useful for defining the neural circuit mechanisms by which ethanol exerts such effects on cortical processing.

Comparison With Anesthetic Substances

The data obtained here also indicated major differences in the functional characteristics of SI cortical cells during ethanol intoxication as opposed to halothane anesthesia. For example, doses of halothane sufficient to cause complete anesthesia did not reduce the E1a peak as much as only moderately intoxicating doses of ethanol. Nevertheless, both drugs produced a selective reduction of the longer latency excitatory responses (E1b and E2) relative to the E1a response.

In view of the circuit model discussed above, one possible explanation for the difference between halothane and the early phase of ethanol intoxication may be that halothane produces a more selective depression of the spinal or brainstem relays carrying the E1b response to the cortex. Alternatively, the differential effects may be expressed in the cortical circuitry itself, where halothane may enhance the post-excitatory inhibition normally following the E1a response to the point where it gates out the E1b responses. Overall, it is clear from the results obtained here that any comparisons between the actions of different drugs must take several factors into account, including dose, relative effects on different response components, and time-course. It is hoped that continuing investigations of this type may help to clarify which functional systems of the brain are disrupted by ethanol.

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