THE EFFECTS OF SOME DRUGS ON AN EVOKED RESPONSE SENSITIVE TO TETRAHYDROCANNABINOLS[1]

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ABSTRACT

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The effects of several drugs were compared with those of Δ^9-tetrahydrocannabinol (Δ^9-THC) on responses evoked in frontal lobe polysensory areas, ipsi- and contralateral to the stimulus site in primary somatosensory cortex, in squirrel monkeys with post-mesencephalic or high spinal sections. Δ^9-THC augmented both the early evoked response and the late evoked response, which occurs 150 to 200 msec after the stimulus. It also frequently augmented or induced repetitive synchronous activity after the late response. In contrast, pentobarbital, ethanol and diethyl ether depressed both early and late responses, while chlorpromazine and chloralose depressed late responses without consistently affecting early responses; none of these drugs induced late repetitive activity. Mescaline had effects similar to those of Δ^9-THC on late responses, but its effect on early responses was much less. Lysergic acid diethylamide had little effect on early responses but depressed late responses at high doses. Phencyclidine also had little effect on early responses. It facilitated late responses at low doses and depressed them at high doses. Picrotoxin and pentylenetetrazol had effects similar to, but greater than, those of Δ^9-THC. Strychnine had variable, and mostly small, effects on evoked responses. Gallamine, atropine, amphetamine, levarterenol and methoxamine were essentially without effect on the responses studied. It is concluded that the effects of Δ^9-THC and mescaline on these responses in polysensory cortex are similar to those of certain convulsants but are unlike those of depressants or of amphetamine, levarterenol, lysergic acid diethylamide, phencyclidine or strychnine.

It has been previously reported (Boyd, E. S. *et al.*, 1971b) that Δ^8- and Δ^9-tetrahydrocannabinols (THCs) augment early and late cortico-cortical responses evoked in the postarcuate polysensory cerebral cortex of *encéphale isolé* squirrel monkeys and cause repetitive late activity. Pentobarbital and ethanol were found to have variable effects on early responses at low doses, to depress early responses at high doses and to depress late responses at all doses tested.

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This led to the suggestion that the augmentation of late responses and of late repetitive activity in polysensory cortex might underlie the distortions of sensory perception or of time sense caused by marihuana and THCs.

In view of this, it was of interest to compare these effects of THCs with the effects of some stimulant, depressant and psychotomimetic drugs on the evoked activity in monkey polysensory cortex. The results are reported here.

Methods

Male squirrel monkeys (*Saimiri sciureus*) were operated on under ether anesthesia. Cannulas were placed in the trachea, in the femoral artery for monitoring blood pressure and in the femoral vein for injecting drugs. The dorsolateral surface of the cerebral cortex was exposed. Either the cord was cut at the level of the first cervical vertebra or the brain stem was sectioned caudal to the mesencephalon. Late as well as early evoked activity could be recorded as long as the lesion was at the pontomesencephalic border, or further caudal. Animals were respired artificially and the expired carbon dioxide was maintained between 4 and 5% (Beckman LB-1 medical gas analyzer) by adjusting rate and volume of respiration.

In some animals an i.v. drip of methoxamine or levarterenol (3–15 μg/min) was used for short periods of time after making a spinal section in order to keep the blood pressure above 60 mm Hg, but it was usually terminated at least 1 hour before the collection of data was begun. Wounds above the neck and pressure points of the stereotaxic apparatus (used as a head holder) were infiltrated with lidocaine.

The dura was removed and a mineral oil bath was formed over the exposed cortex with the help of a piece of rubber dam cemented to the scalp. Bath temperature was maintained between 35 and 37°C and rectal temperature between 36 and 39°C. Stimulation of, and recording from, the cortical surface were by means of silver ball electrodes. The stimuli were provided by a Grass S4 stimulator, isolation unit and constant current unit. The stimuli were monophasic, 0.1-msec duration pulses ranging from a fraction of a milliampere up to 5 mA. Stimuli were delivered at the rate of 1/4 sec, a rate found to be sufficiently low so that repetitive stimulation did not produce a diminution of the responses. The postcentral forelimb-trunk area of the right primary somatosensory cortex was stimulated by means of two electrodes placed about 2 mm apart, and monopolar recordings were made from the right (ipsilateral) and left (contralateral) areas of the frontal lobe postarcuate cortex, shown by Bignall and Imbert (1969) and by Bignall and Singer (1967) to be polysensory in the squirrel monkey. The responses were amplified with Grass P 511 preamplifiers, with frequency responses set at 0.15 Hz and 2 kHz, and recorded on magnetic tape for later analysis with a LAB-8 (Digital Equipment Corporation, Maynard, Mass.) computer. One or more monopolar electrocorticograms (ECoG) were recorded from the prefrontal cortex on a Grass polygraph. The indifferent electrode for all recording was a silver wire placed either on dura that had been deflected away from the cortical surface or on occipital skull. The blood pressure was recorded by means of a pressure transducer and the polygraph. At the end of each experiment, the animal was sacrificed with an overdose of pentobarbital; the brain was fixed in formalin, and the completeness of the spinal or brain stem section was determined.

The wave forms of the early evoked responses always consisted of an initial positive wave whose amplitude was measured from the base line. The amplitude of the late response was measured from the base line or from the first positive deflection to the negative deflection. Series of 16 to 32 responses were averaged by the computer and the averaged responses were used for determinations of amplitudes. The computer calculated and displayed the standard deviation for each point. Means and standard deviations for peak values were used for statistical analyses. Differences in responses were analyzed by Student's t test and P values less than .05 were considered to indicate statistically significant changes.

As reported previously (Boyd, E. S. *et al.*, 1971a), the amplitudes of evoked responses tended to vary with the state of the animal as reflected in the ECoG records. In general, a decrease in amplitude and increase in frequency in the ECoG was accompanied by a decrease in amplitude of both the early and late evoked responses, although the opposite effect was observed occasionally. For this reason attempts were made to collect control data during periods of high-amplitude, low-frequency ECoG activity, this being the usual state of the preparation. This procedure was not usually attempted after drug administration since many of the drugs changed the state of the ECoG.

Experiments were carried out 2 to 3 hours after the termination of ether anesthesia, except that in four experiments the development of late evoked activity was recorded as the ether was cleared from the animal. Experiments were terminated if there was any marked deterioration in the background activity of the brain as recorded by the prefrontal or postarcuate electrodes or if the mean

blood pressure went below 60 mm Hg for any significant period of time.

The drugs used were 95% pure (−)-Δ^9-*trans*-tetrahydrocannabinol (Δ^9-THC) (Δ^1 in the other commonly used system of nomenclature), sodium pentobarbital (as Veterinary Nembutal), ethanol, α-chloralose, chlorpromazine HCl, lysergic acid diethylamide (LSD), phencyclidine HCl, mescaline HCl, picrotoxin, pentylenetetrazol, strychnine sulfate, *d*-amphetamine sulfate, gallamine triethiodide, atropine sulfate, levarterenol bitartrate and methoxamine HCl. Except when picrotoxin was tested, usually only one drug was given to any single animal, but to gain as much information as possible several doses of the same drug were often tested in each animal. In these cases, with the exception of pentylenetetrazol, the intervals between successive doses were always much less than the duration of action of the drug, and the dose level being tested at any particular time was expressed in terms of the total dose at that time. Where salts were used, drug doses are expressed in terms of the salt. The drugs were given i.v. over a period of at least 3 minutes to minimize cardiovascular effects, and the collection of data was started a few minutes later. The THC was administered dissolved in polyethylene glycol 400. The only consistent effect of control injections of appropriate volumes of the vehicle (up to 1 ml/kg) on any of the parameters measured was a small increase in blood pressure.

Results

The responses. Polysensory cortex responded to stimulation of the somatosensory cortex with an early response, within 5 to 10 msec, whose initial component was positive. This was followed by a late response consisting of a negative, then positive, wave form and often preceded by a distinct positive wave. The latency to the negative wave varied in different animals from about 140 to 200 msec but was very constant in any given animal. It has been previously reported (Boyd, E. H. *et al.*, 1971; Boyd, E. S. *et al.*, 1971b) that the early and late evoked responses occur together in a region of cortex extending rostrally from just caudal to the central dimple to the region of the arcuate sulcus. It was also demonstrated that both early and late responses are generated locally at the recording site and that there is a complex interaction between early and late responses. The late response can be reset, in time, by a second early response occurring between the initial early response and the late response. In this case the second early response has an increased amplitude.

The pathway for the early response has been demonstrated to run rostrally through cortical white matter and then, for the contralateral early response, to cross through the corpus callosum (Boyd, E. H. *et al.*, 1971). The pathway for the late response is still open to question. As previously reported (Boyd, E. S. *et al.*, 1971a,b), the late response disappears if the brainstem is sectioned at a mesencephalic, or higher, level. We have also demonstrated (unpublished observations) that it disappears, along with the early response, if the corpus callosum is sectioned. Studies with microelectrodes (unpublished observations) have shown that many small units, about 1.4 mm below the surface of the polysensory cortex, fire during the early and late surface responses as well as during the late repetitive surface activity caused by THC. The effects of THC and of pentobarbital on this unit firing are the same as their effects on the early and late surface waves.

Drug effects. Most of the results are summarized in table 1 and figures 1, 2, 3 and 4. For the sake of completeness, the results with Δ^9-THC, pentobarbital and ethanol include those reported previously (Boyd, E. S. *et al.*, 1971b). Early evoked activity was generally increased in amplitude by Δ^9-THC in a dose-dependent fashion. The late evoked responses, occurring 150 to 200 msec after the early responses, were also generally increased in a dose-dependent manner. There was one animal whose late responses were increased by 0.5 mg/kg but were depressed by 1.0 mg/kg. Δ^9-THC, at the higher doses given, also caused the appearance of marked, synchronous, repetitive (5–10 Hz) late waves after the cortical stimulus in five of the seven animals.

Five drugs (pentobarbital, ethanol, chloralose, diethyl ether and chlorpromazine) usually classified as central nervous system depressants had different effects on early evoked responses, but all produced a depression of late evoked responses and, with one possible exception, none of them caused the repetitive late waves seen with THCs. Pentobarbital and ethanol exhibited small and variable effects on early responses at low doses and a dose-dependent depression of early responses at higher doses. They both exhibited a dose-dependent depression of late evoked responses, with late responses often being

TABLE 1

The most usual effects of some drugs on the amplitudes of early and late evoked responses and on late repetitive activity[a]

Drug	No. of Animals	Dose Range (per kg)	Early Response	Late Response	Repetitive Activity[b]
Δ^9-THC	7	0.065–2.5 mg	↑	↑	5
Pentobarbital	9	2–20 mg	↓	↓	0
Ethanol	2	0.25–1 ml	↓	↓	0
Chloralose	2	10–50 mg	↑ or 0	↓	0
Diethyl ether	4	Recovery from anesthesia	↓	↓	(1)
Chlorpromazine	4	0.25–8 mg	0 or ↑	↓	0
LSD	5	1.25–40 μg	0	0 or ↓	2
Phencyclidine	4	0.065–3 mg	0	↑ then ↓	0
Mescaline	4	2.5–80 mg	↑ then ↓	↑	3
Picrotoxin	12	0.5–1.0 mg	↑	↑	8
Pentylenetetrazol	2	10–20 mg	↑	↑	0
Strychnine	2	0.2–1.6 mg	↑	↑	0

[a] See text for more details and exceptions.

[b] Number of animals in which drug produced or augmented late repetitive activity.

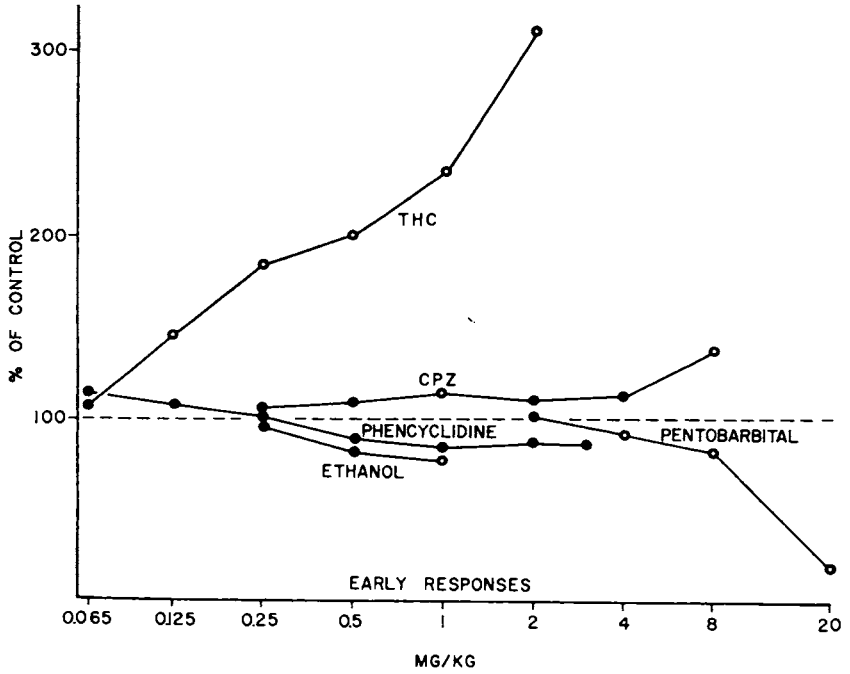

FIG. 1. Effects of five drugs on early evoked responses in monkey polysensory cortex. THC, Δ^9-tetrahydrocannabinol; CPZ, chlorpromazine. Ethanol is plotted as milliliters per kilogram. Open circles in this and subsequent figures represent differences from 100% that are statistically significant ($P \leq .05$).

eliminated at the higher dose levels. Early responses were increased or unchanged by α-chloralose. Late responses were unchanged by the lowest dose but severely depressed by the higher doses. In four animals, responses were recorded during recovery from diethyl ether anesthesia. In these animals, early responses were developed to about their maximum extent by

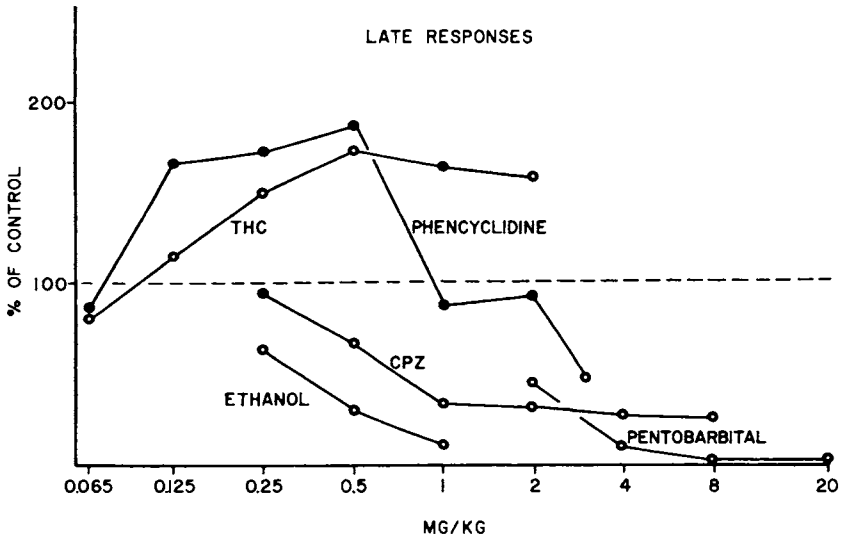

FIG. 2. Effects of five drugs on late evoked responses in monkey polysensory cortex. Abbreviations as in figure 1.

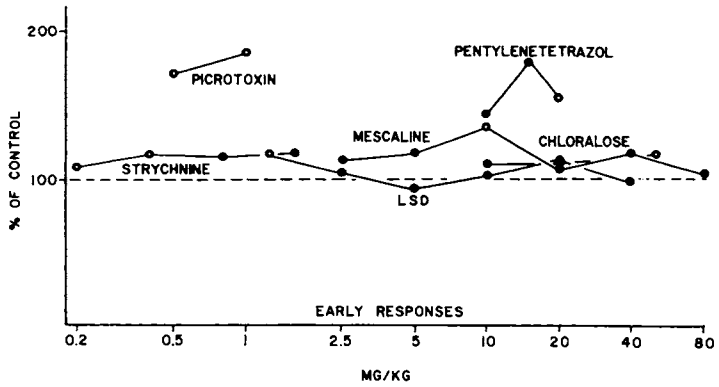

FIG. 3. Effects of six drugs on early evoked responses in monkey polysensory cortex.

the time the experimental procedure had progressed to the point where they could be examined (about 1 hour after the termination of ether administration). However, late responses were poorly developed at this time but developed over the next ½ to 1 hour. In several other experiments neither early nor late responses were present about 1 hour after ether, but both had appeared by 2 hours after ether. Thus diethyl ether appears to exhibit a dose-dependent depression of late evoked responses at doses less than those needed to depress the early evoked responses. Late repetitive activity was observed transiently in one animal during recovery from ether anesthesia. This animal is presented in table 1 by a "1" in parentheses since this was not one of the four animals whose recovery was specifically studied. Chlorpromazine had either no effect on early responses or increased them slightly, but it caused a dose-dependent depression of late responses. A typical experiment is illustrated in figure 5, where chlorpromazine at 0.25, 0.5, 2 and 4 mg/kg caused an increasing depression of the late response with little or no effect on the early response.

Unlike the depressant drugs discussed above, the psychotomimetic drugs, LSD, phencyclidine and mescaline, had effects that were similar in some respects to those of Δ^9-THC. LSD had little or no effect on early evoked responses. High doses routinely depressed late responses and in some cases eliminated them. In two of five ani-

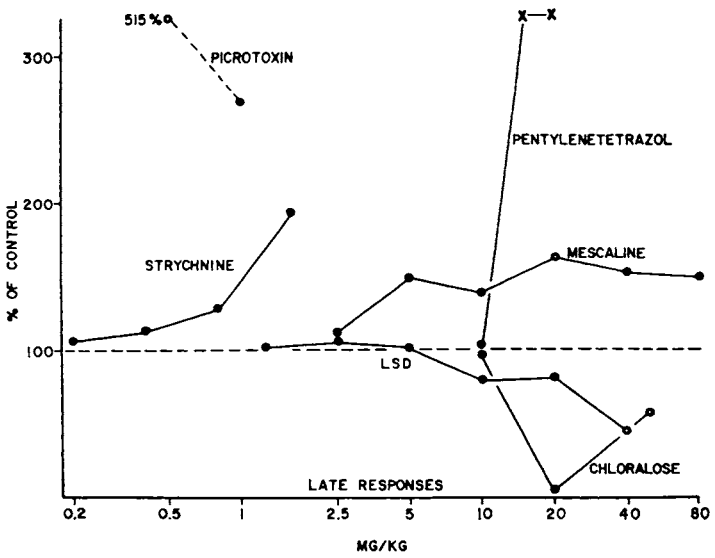

FIG. 4. Effects of six drugs on late evoked responses in monkey polysensory cortex. The last two points for pentylenetetrazol are represented by X's because they represent cases in which a late response appeared after the drug when none was detectable before the drug.

mals, it produced a significant increase in late repetitive activity.

Phencyclidine had little or no effect on the early evoked response. Low doses enhanced the late evoked response, but higher doses caused a dose-dependent depression of the late responses. Increases in late response amplitude of as much as 1000% occurred with 0.125 to 0.5 mg/kg. In none of the four experiments did phencyclidine cause repetitive late activity.

Of the three psychotomimetic drugs tested, mescaline most resembled Δ^9-THC in its effects on the system being studied. Mescaline at low doses routinely increased the amplitudes of early responses although the increases were not so great as those seen with THC, and increasing the dose tended to reverse this effect. It also produced rather dramatic increases in the amplitudes of late responses. Unlike the results with THC, where increases in late responses appeared to be independent both of stimulus intensity and of the side of the brain recorded from, the most impressive increases with mescaline were on the side of the brain ipsilateral to the stimulus and with high stimulus intensities. Mescaline was also like THC in that it caused late synchronous repetitive activity in three of four animals. In a typical experiment (fig. 6) 10 mg/kg caused increases in both early and late responses at both 2 and 5 mA stimulus intensities. Although not illustrated, these increases were first seen with the original dose of 2.5 mg/kg. Increasing the dose from 10 to 20 mg/kg had little effect on the early responses but it decreased the late response at 2 mA and increased it at 5 mA. In addition, the 10 and 20 mg/kg doses of mescaline in this animal caused the development of late repetitive activity at 5-mA stimulus intensity. An effect of mescaline on late repetitive activity as great as any found with THC was seen in another animal and is illustrated in figure 7 where it can be seen that, at the highest dose of mescaline tested (80 mg/kg), there was a facilitation of the late response on the ipsilateral side and a depression of it on the contralateral side, but both sides exhibited large repetitive synchronous waves after the stimulus.

The convulsive stimulants, picrotoxin, pentylenetetrazol and strychnine, were tested in animals that had been paralyzed with gallamine (which by itself had no effect on evoked responses). Picrotoxin was tested after the administration of other drugs or after brainstem lesions. It tended to increase the amplitudes of both early and late evoked responses and produced, or intensified, late repetitive activity in 8 of 12 animals. It was partially to fully successful in bringing back late evoked activity that had been depressed by pentobarbital (two experiments), high doses of chlorpromazine (two ex-

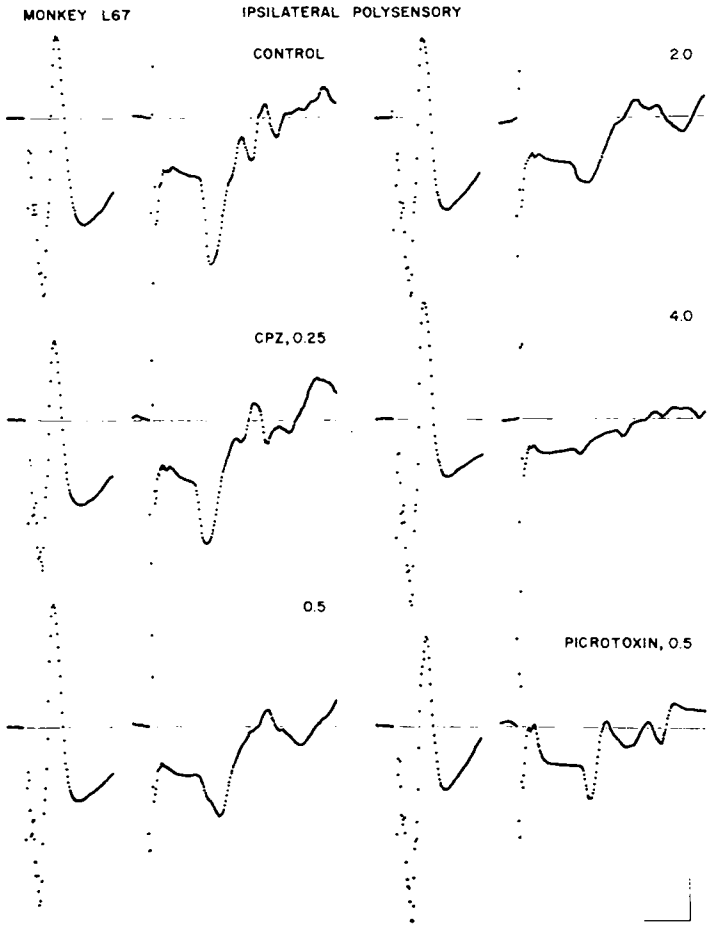

FIG. 5. Typical example of the effects of chlorpromazine on early and late evoked responses. Note the progressive decrease in the late response as the dose of chlorpromazine was increased from 0.25 to 4 mg/kg and the partial reversal of this effect by picrotoxin. Stimulus intensity, 5 mA. Calibrations represent 10 and 100 msec and 500 μV. All data in this and subsequent representations of evoked responses are computer averages of 32 responses. Here, and in figures 6 and 8, each average response is shown on two time scales: first a short time scale to show the early response and then a long time scale to show the late response, 150 to 200 msec after the stimulus. Most shock artefacts have been truncated.

periments), LSD (two experiments), phencyclidine (one experiment) or brainstem lesions (four experiments). The ability of picrotoxin to bring back late responses after their elimination by brainstem lesions will be discussed elsewhere. Its antagonism to the depressant effect of chlorpromazine on late responses is illustrated in figure 5, and its antagonism to the depressant effect of pentobarbital on late responses is illustrated in figure 8. The antagonism by picrotoxin of the depressant effects of other drugs occurred within 5 to 10 minutes of the administration of the picrotoxin—long before the effects of the other drugs could have worn off.

Pentylenetetrazol increased both early and late responses but did not produce late repetitive activity. The effects of strychnine on both early and late evoked responses were mostly small and very variable. It produced some small but statistically significant increases in the early response at low dose levels and tended to increase late responses at high doses.

In addition to the above drugs, amphetamine was tested in three animals at doses of 0.5 to 2.0 mg/kg. It produced slight decreases in both early and late responses. Gallamine in four animals at 3 to 6 mg/kg and atropine in two animals at 0.2 mg/kg had no effect on early or late responses. As pointed out previously, levarterenol and methoxamine were given as infusions to

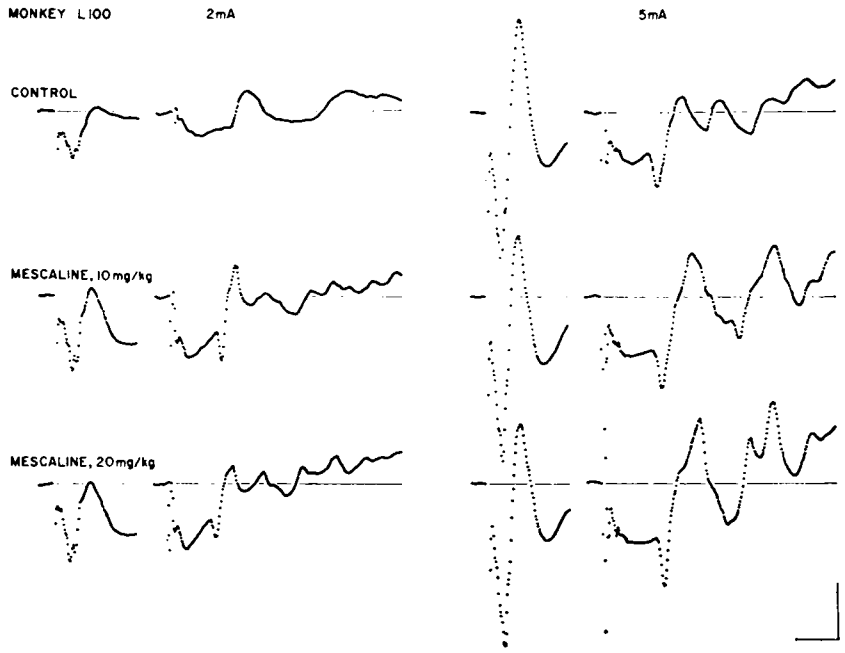

FIG. 6. Typical example of the effects of mescaline on early and late ipsilateral-evoked responses at two stimulus intensities. The increases in early and late responses peaked at 10 mg/kg at 2 mA after which the late response declined with increasing dose. At 5 mA the peak effect on both early and late responses was at 20 mg/kg. Late repetitive activity appeared at 5 mA, but not at 2 mA, with doses of both 10 and 20 mg/kg. Calibrations represent 10 and 100 msec and 500 μV.

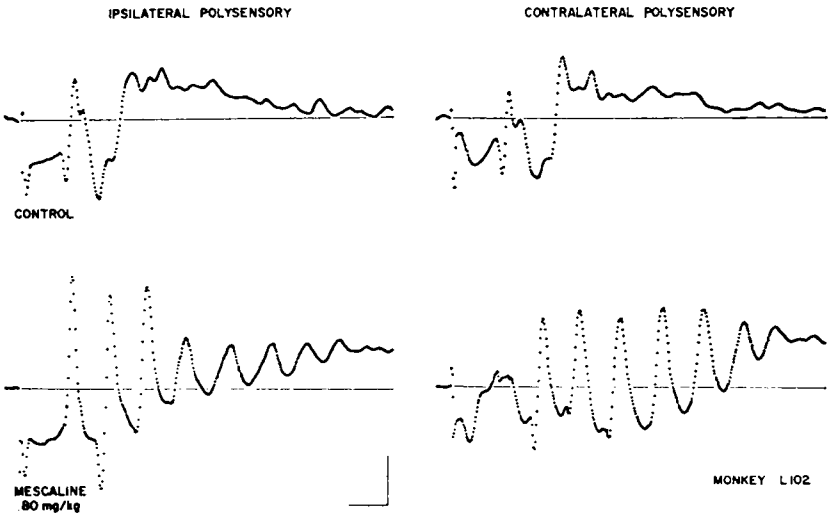

FIG. 7. The most pronounced appearance of late repetitive activity seen after mescaline. Note that this animal had a well developed second late response before drug. The repetitive late activity was maximal at 80 mg/kg, the highest dose tested. At this dose the original late response was still augmented on the ipsilateral side but was almost eliminated on the contralateral side. Stimulus intensity, 3 mA. Calibrations represent 100 msec and 500 μV.

many animals, particularly early in the experiments, to keep blood pressure above 60 mm Hg. In no case did either sympathomimetic drug appear to have any effect on evoked responses. In addition, each drug was tested once, levarterenol at 0.01 mg/min and methoxamine at 0.2 mg/min, in an animal that did not need them to maintain its blood pressure. Neither drug had

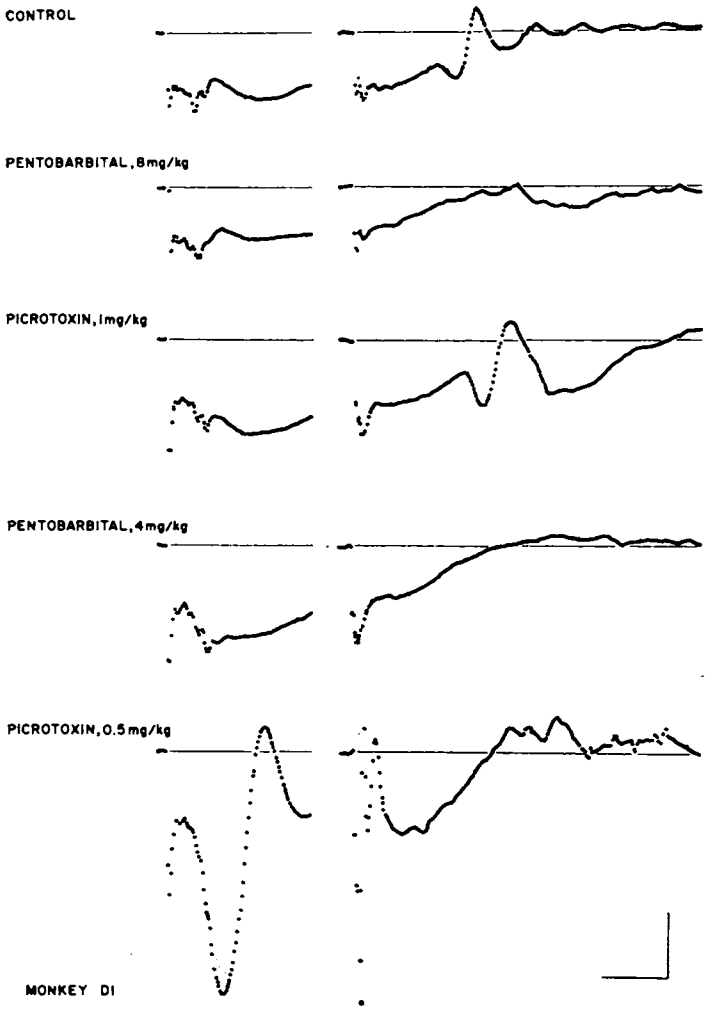

FIG. 8. An example of the antagonism between pentobarbital and picrotoxin on the late evoked response. The first dose of picrotoxin completely overcame the effect of 8 mg/kg of pentobarbital and an added 4 mg/kg of pentobarbital again eliminated the late response. A final dose of 0.5 mg/kg of picrotoxin produced a dramatic increase in the early response but had very little effect on the late response (contralateral recordings). Stimulus intensity, 5 mA. Calibrations represent 10 and 100 msec and 500 μV.

any effect on either early or late evoked responses.

Discussion

Although general depressants like pentobarbital and diethyl ether depress all levels of the central nervous system from the cord to the cerebral cortex (Heinbecker and Bartley, 1940; Eccles, 1946; Løyning *et al.*, 1964), the initial components of cortical evoked responses may be augmented by these drugs because of disinhibition due in part to depression of the reticular formation (French *et al.*, 1953; Nakai *et al.*, 1966; Borbély and Hall, 1970). However, the later components of cortical evoked responses are usually depressed by these drugs, presumably because of direct depressant actions on the cerebral cortex. In view of this, it was not surprising to find that pentobarbital, ethanol and diethyl ether depressed early responses at high doses and depressed late responses at all doses tried. The effects of chloralose were also expected since, although chloralose tends to augment early evoked responses (Winters and

Spooner, 1966), late evoked responses had not been seen under chloralose anesthesia (Boyd, E. H. *et al.*, 1971). On the other hand, the differential action of chlorpromazine in producing a dose-dependent depression of late responses, while having either no effect on, or facilitating, early evoked responses, was not expected. In unanesthetized animals chlorpromazine has usually been found to increase the amplitude, and sometimes the area of distribution, of cortical responses evoked by somatosensory stimulation in the cat (Unna and Martin, 1957), auditory stimulation in the rat (Borbély and Hall, 1970) and cat (Nakai *et al.*, 1966) and visual stimulation in the baboon (Killam *et al.*, 1967), although Preston (1956) reported no effect on the response evoked by somatosensory stimulation in the cat. It seems likely that these increases in evoked responses, where found, were the result of disinhibition by chlorpromazine and that the increases in early evoked responses sometimes seen in the present work were also due to disinhibition.

There is a large and contradictory literature concerning the effects of LSD and other psychotomimetic drugs on evoked cortical potentials. Some of the contradictions are probably due to differences in species and in the use of anesthetics, but it also seems likely that some are due to a lack of direct effects of the drugs on the systems being studied, which have usually been primary sensory systems. The field was extensively reviewed by Evarts (1957). In a more recent review, Aghajanian (1972) points out that in unanesthetized animals LSD usually either enhanced or had no effect on evoked responses. Key (1965) has postulated that effects of LSD on sensory evoked responses are not due to any direct effect of the drug but rather reflect the actions of the drug on undefined sensory integrating mechanisms. It was hoped that the present work on evoked responses in polysensory cortex might represent a step toward defining these integrating mechanisms. The relatively consistent effects of Δ^9-THC and of mescaline could indicate direct effects of these drugs on polysensory cortex. The increases in both early and late evoked responses, the increases in early and late unit firing seen with THC and the frequent occurrence of long-lasting repetitive activity caused by Δ^9-THC and by low to moderate doses of mescaline could indicate that, under the influence of these drugs, cells in this area become unduly involved in response to single inputs. Such involvement could result in intensifications of sensory perceptions and confusion in immediate memory, as previously discussed (Boyd, E. S. *et al.*, 1971b).

On the other hand, the effects of LSD and of phencyclidine on polysensory cortex were disappointing. In general, LSD did not increase early responses and it decreased late responses. It caused repetitive late activity, but the incidence was not so great as with Δ^9-THC or mescaline. Phencyclidine had a mild depressant action on early cortico-cortical responses which resembled its effects on somatosensory and visual evoked responses (Domino, 1964). It increased late responses at low doses but depressed them at higher doses, and it did not cause late repetitive activity. Thus, although the postarcuate polysensory cortex looks like a reasonable site of action for the effects of Δ^9-THC and mescaline on sensory perception, it does not look like an important site of action of LSD or phencyclidine.

The convulsant stimulant picrotoxin mimicked the actions of Δ^9-THC in that it increased the amplitudes of both early and late evoked responses and caused repetitive late activity in 8 of 12 animals tested. These effects were seen just before onset of seizure activity and after postictal depression when seizures did not start again immediately. The action of picrotoxin differed from that of Δ^9-THC or mescaline in that it often produced a very large increase in the early response (see fig. 8), a greater increase than ever seen with the other drugs. It was also capable of reversing depressions of the late response caused by other drugs and by brainstem sections. Pentylenetetrazol appeared to have actions similar to those of picrotoxin except that it did not cause repetitive late activity. However, the sample size for pentylenetetrazol is too small to make this difference very meaningful. The effects of strychnine were variable and in general unremarkable. This was not surprising since, although strychnine applied topically is useful in strychinine neuronography and can block inhibitory potentials in the cortex (Pollen and Ajmone-Marsan, 1965), inhibitory potentials high in the central nervous system seem to be resistant to i.v. strychnine (Andersen *et al.*, 1963; Crawford *et al.*, 1963; Brooks and Asanuma, 1965).

The general lack of effect of gallamine, atropine, amphetamine, levarterenol and methoxamine on either early or late evoked responses may indicate that neither acetylcholine nor catecholamines are involved in the generation of these responses.

Finally, it is worth pointing out that while it might be possible, although difficult, to study late evoked responses and late repetitive activity in polysensory cortex in animals under phencyclidine dissociative anesthesia, these responses cannot be observed in animals anesthetized with diethyl ether, chloralose or pentobarbital.

The increases in early and late evoked responses caused by THC and mescaline, the increases in repetitive late activity caused by Δ^9-THC and mescaline and the increase in early and late unit firing caused by THC in squirrel monkey polysensory cortex resemble more the effects of convulsive stimulants than the effects of sedatives and anesthetics. The magnitude and relative consistency of the effects on polysensory cortex may indicate that they are important factors in the actions of Δ^9-THC and mescaline. If polysensory cortex is involved in the integration of sensory information, and in perception, these actions of Δ^9-THC and mescaline could account for their effects on sensory perception and immediate memory. On the other hand, it seems unlikely that polysensory cortex is an important site of action of LSD and phencyclidine, although their occasional effects on polysensory cortex could contribute to their psychological actions.

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