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The Effects of Intravenous Lidocaine on Optic Evoked Potentials in Light and Darkness

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The effects of lidocaine on optic evoked potentials (OEP) of the cat's visual cortex in response to electrical stimulation of the optic nerve in light and in darkness were investigated. EEG, ECG, and blood pressure were recorded simultaneously in barbiturate-anesthetized as well as in immobilized cats. In light, less than 1 mg/kg had no effect in anesthetized cats, but 1 mg/kg facilitated OEP, whereas in darkness, with OEP at naturally lower levels, both 0.5 and 1 mg/kg facilitated OEP, and the magnitude of facilitation was greater than that in light. In light, as much as 8 mg/kg was necessary for facilitation of OEP in immobilized cats, but twice that dose had no detectable effect. In darkness, with OEP naturally lower, 8 mg/kg lidocaine not only facilitated OEP in immobilized cats, but the magnitude of facilitation was greater than that in light, and 16 mg/kg also facilitated OEP. In darkness, the difference between 8 and 16 mg/kg was that with the latter dose facilitation was more predictable and longer-lasting. Facilitation of OEP by lidocaine was unrelated to its effects on blood pressure, ECG, or EEG. It is suggested that lidocaine-induced convulsions are due to a dissociation in neuronal integration that results from depression of the active inhibitory inputs of the neuronal circuitry, that darkness induced depression of OEP is an active inhibition and that barbiturate anesthetization spares quantitatively greater inhibitory processes and thereby alters the process of homeostasis. (Key words: Lidocaine; Optic evoked potential (OEP); Disinhibition.)

THE EXCITATORY EFFECTS of intravenously administered lidocaine and other local anesthetics on the central nervous system are well known,[1-6] although the mechanism of such effects is poorly understood. Some authors[7,8] have suggested that excitation is due to a selective depression of inhibitory neurons, while others have questioned this view.[9] The present study was undertaken using a complex CNS sensory system, the visual system, in which the receptor cell activities in the retina in light and in darkness and their facilitatory and inhibitory influences on geniculate and cortical cells are well known.[10-12] The effects of lidocaine on visual cortical responses to optic-nerve stimulation were measured in light and in darkness because optic evoked potentials are at a low level in darkness[13,14] as a result of a tonic inhibitory effect of the retina on the central visual system.[14-18] The effects of lidocaine on EEG, ECG, and blood pressure were also measured (some of these results have been reported in preliminary form[19,20]). Data were collected from anesthetized as well as from immobilized adult cats of either sex.

Methods

Anesthetized Cats

Twelve cats were individually anesthetized with allobarbital (Dial), 0.7 ml/kg, ip, and placed in a stereotaxic instrument. After exposure of the skull, a Hess electrode was inserted through burr holes, aiming at the optic nerve at the level of the optic chiasma. The stimulus, consisting of a brief pulse (0.01 msec, 2–4 v, 0.5 Hz), was delivered through an isolation unit from a Grass (S-4) stimulator. Unipolar recordings of the evoked responses were made from the exposed surface of the ipsilateral visual cortex, which was covered with mineral oil. The indifferent electrode (silver wire) was buried in the neck muscle. After appropriate amplification (Tektronix, 122-preamplifier), the evoked responses were displayed on an oscilloscope for visualization as well as recorded on magnetic tape with an FM recorder for computer analysis.

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The recording electrode (floating silver wire) of the visual cortex as opposed to the neck and a screw electrode buried in the right suprasylvian gyrus as opposed to the frontal sinus permitted monopolar EEG recordings. The cats were also prepared for blood pressure (femoral artery) and ECG (chest lead) recordings, as well as with an indwelling cannula for intravenous (femoral vein) administration of the drug. EEG, ECG, and blood pressure were recorded on paper with an ink-writing polygraph (Grass 5). The animals breathed spontaneously. Body temperatures were maintained at 36–37 C by means of a heating pad.

Immobilized Cats

The tracheas of 16 cats were intubated under ether anesthesia. The head was fixed to the stereotaxic instrument. Placement of stimulating and recording electrodes, EEG and ECG electrodes, and cannulation of the vein and artery were carried out as described above. After operation, lidocaine ointment (5 per cent) was applied to all wounds to alleviate discomfort. Ether was discontinued and the cat was immobilized with gallamine (Flaxedil), 20 mg iv, and maintained on gallamine (3 mg/kg/hour, as a single intravenous injection), with artificial respiration (15/min with stroke volume adjusted so that pupils were constricted). All conditions were similar to those of the anesthetized cats except that 5–15 v were used because higher voltages were necessary to elicit visual cortical responses.

Usually, after completion of preparations the optic nerve was stimulated for about an hour in the anesthetized cats and about two hours in the immobilized cats before control recordings were made and lidocaine effect investigated. Graded doses of lidocaine were administered intravenously at hourly intervals unless otherwise specified. In the immobilized cats gallamine injection always preceded lidocaine injection by half an hour. Lidocaine hydrochloride (0.5, 1, 2, 5, and 10 per cent solutions) was diluted with physiologic saline solution (*p*H 6.8) so that the desired dose (0.0625–1 mg/kg in anesthetized cats and 0.25–16 mg/kg in immobilized cats) in 0.5–1 ml with 1 ml saline wash could be administered intravenously. A continuously-shining 7.5-watt white light was placed about a foot from the eyes for studies in light. When the effect of lidocaine in darkness was being investigated, the animals were first dark-adapted for 10 minutes by turning off the light (room was not absolutely dark), control data were recorded in the dark, and the effects of lidocaine on these control values were recorded for 4–5 minutes, after which the light was turned on.

In every instance (in light and darkness as well as in immobilized and anesthetized cats) 16 control evoked responses were recorded on magnetic tape. Lidocaine was then administered and an additional 112 to 128 such responses were recorded. These data were analyzed in groups of 16 with a LINC computer, using an averaging program, and were stored on LINC data tape. The stored averages of the evoked potentials were plotted on an x–y plotter (x = time). Amplitude from the peak of the positive to the peak of the negative component of the primary visual evoked response complex was measured. The induced changes were calculated as ratios of control. The mean ± SE of the changes was calculated and tabulated as a function of time. The stored averages were also displayed on an oscilloscope and pictures were taken with a Grass camera.

Results

In anesthetized cats lidocaine, 0.0625–0.25 mg/kg iv, induced no appreciable change in the magnitude of the primary visual cortical responses to electrical stimulation of the optic nerve in the presence of continuously shining white light. In darkness (after 10 min of dark-adaptation), before administration of lidocaine the magnitudes of the primary visual cortical responses were less than those of responses to the same stimuli in light (fig. 1), and similar doses of lidocaine (0.0625–0.25 mg/kg) did not alter these responses appreciably (table 1). However, higher doses of lidocaine (0.5 and 1 mg/kg) affected the evoked responses in light and those in darkness differently. In light, 0.5 mg/kg induced effects similar to those induced by lower doses, whereas 1 mg/kg facilitated the evoked responses consistently even though the absolute

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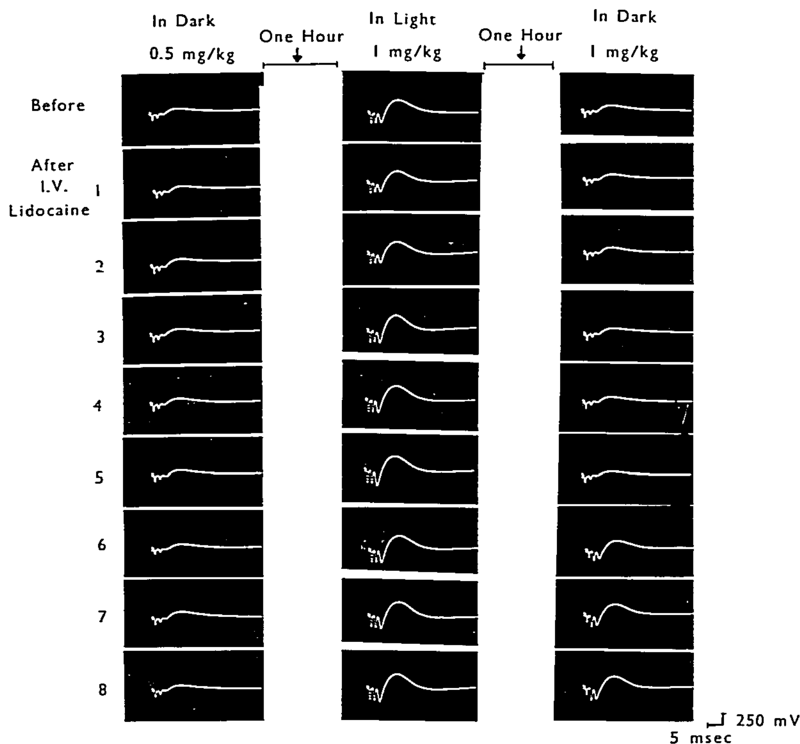

FIG. 1. LINC averages of optic evoked potentials (OEP) at the ipsilateral visual cortex in response to stimulation of the optic nerve in light and in darkness in the allobarbital-anesthetized cat and effects of intravenous lidocaine. Note the slight facilitation of OEP by 1 mg/kg lidocaine in light (3–8) as opposed to the marked facilitation caused by the same dose of lidocaine in darkness (6–8), when OEP are inhibited in darkness (Before, Light *vs.* Dark), showing unmasking of the excitatory phenomenon by masking the inhibitory effect of darkness, in this example specifically, by 1 mg/kg. In this and the following figures the optic nerve was stimulated at the level of the chiasma with square-wave pulses of 0.01 msec, at 0.5 Hz, with suitable voltage. "Light" = OEP in the presence of 7.5 watts of white frosted bulb shining continuously about a foot from the eyes; "dark" = OEP recorded 10 minutes after turning off the light (i.e., 10 min dark-adaptation). "Before" = immediately prior to injection of lidocaine; "after" = eight subsequent traces immediately following lidocaine injection of identical volumes but different doses. The intervals between "before" and "after" were about 30–40 seconds, whereas the intervals between traces were 32 seconds. Each trace is the average of 16 OEP; downward deflection signifies positivity.

magnitude of facilitation was minimal (table 1; fig. 1, column 2). On the other hand, in darkness both 0.5 and 1 mg/kg of lidocaine facilitated the optic evoked potentials, and this was dose-related in terms of absolute magnitude (table 1) and incidence (fig. 1).

Lidocaine in doses of 0.0625–0.25 mg/kg did not affect the EEG, but higher doses (0.5

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and 1 mg/kg) caused synchronization. There was no difference between EEG patterns in darkness and in light, and no difference between lidocaine effects in the two situations. Lidocaine, 0.0625–1 mg/kg, did not affect either blood pressure or ECG.

In the immobilized cats, lidocaine, 0.25 and 0.5 mg/kg, invariably depressed the visual cortical responses in the presence of light, whereas 1–4 mg/kg increased the variability of the visual cortical responses only. In contrast, in darkness lidocaine in identical doses (0.25–4 mg/kg) increased the variability of the visual cortical responses only (table 2). Lidocaine, 8 mg/kg, facilitated the optic evoked potentials in both light and darkness, but in darkness the facilitation was more pronounced in terms of both duration and magnitude (fig. 2; table 2). In light 16 mg/kg had the same effect on the evoked potentials as 1–4 mg/kg, whereas in darkness 16 mg/kg facilitated the evoked potentials (table 2). The facilitatory effect of 16 mg/kg in darkness was more predictable and longer-lasting than that of 8 mg/kg. The predictability was evident from the small standard error with the former dose, although the absolute magnitude of facilitation at times was considerably less (*cf.* 8 and 16 mg/kg (D), table 2). Even though the effect of lidocaine in darkness has been defined in terms of facilitation only, for the sake of simplicity, in reality it is a reversible masking of the darkness induced depression of the evoked potentials (fig. 3).

Lidocaine, 0.25 and 0.5 mg/kg, had no effect on EEG, ECG, or blood pressure, but 1–4 mg/kg induced spindle activity which often lasted 5–7 minutes without affecting blood pressure or ECG. Lidocaine, 8 mg/kg, immediately desynchronized the EEG concomitant with pupillary dilation, and also induced a biphasic change in blood pressure which consisted of an initial transient decrease followed by a compensatory increase, without affecting the ECG. However, 5–7 min after administration of lidocaine the EEG showed spindle activity which often lasted as long as 10 minutes. Lidocaine, 16 mg/kg, induced immediate desynchronization of the EEG, with reduced frequency concomitant with pupillary dilatation; blood pressure and ECG rate decreased immediately but gradually (15–20

TABLE 1. Effects of Various Doses of Lidocaine (Intravenous) on Optic Evoked Potentials in Light (L) and in Darkness (D) in Allobarbital-anesthetized Cats

Dose of Lidocaine (mg/kg)	Number of Cats	Change (Ratio*) in Amplitude† (Mean ± SE) of Evoked Potentials as a Function of Time, in Seconds after Lidocaine							
		32	64	96	128	160	192	224	256
0.0625 (L)	2	0.05 ± 0.08	0.10 ± 0.05	0.12 ± 0.02	0.09 ± 0.00	0.08 ± 0.00	0.02 ± 0.05	0.06 ± 0.04	— —
0.0625 (D)	2	−0.02 ± 0.01	−0.08 ± 0.02	0.01 ± 0.04	−0.03 ± 0.02	−0.12 ± 0.04	−0.01 ± 0.08	−0.06 ± 0.02	— —
0.125 (L)	7	−0.09 ± 0.05	−0.05 ± 0.03	−0.05 ± 0.02	−0.06 ± 0.04	−0.10 ± 0.02	0.03 ± 0.06	— —	— —
0.125 (D)	7	0.02 ± 0.03	0.05 ± 0.05	−0.01 ± 0.05	−0.01 ± 0.05	−0.04 ± 0.05	−0.01 ± 0.08	0.03 ± 0.10	— —
0.25 (L)	11	−0.05 ± 0.08	0.08 ± 0.09	0.01 ± 0.10	0.03 ± 0.09	0.11 ± 0.12	0.19 ± 0.12	0.09 ± 0.09	0.17 ± 0.16
0.25 (D)	11	0.05 ± 0.02	0.08 ± 0.04	0.08 ± 0.04	0.07 ± 0.06	0.02 ± 0.03	0.06 ± 0.02	0.04 ± 0.07	0.10 ± 0.04
0.5 (L)	10	−0.04 ± 0.06	0.06 ± 0.08	0.06 ± 0.09	0.10 ± 0.09	0.06 ± 0.07	0.04 ± 0.06	0.01 ± 0.05	0.07 ± 0.05
0.5 (D)	10	0.09 ± 0.07	0.18 ± 0.08	0.20 ± 0.09	0.19 ± 0.09	0.14 ± 0.10	0.24 ± 0.15	0.30 ± 0.11	0.25 ± 0.13
1.0 (L)	7	0.04 ± 0.04	0.10 ± 0.04	0.20 ± 0.06	0.17 ± 0.06	0.21 ± 0.04	0.29 ± 0.06	0.26 ± 0.08	0.22 ± 0.08
1.0 (D)	7	0.03 ± 0.04	0.23 ± 0.13	0.22 ± 0.11	0.20 ± 0.11	0.20 ± 0.09	0.38 ± 0.15	0.59 ± 0.14	0.57 ± 0.08

* Ratio of the change over the control. † Depression of amplitude is indicated by a negative value.

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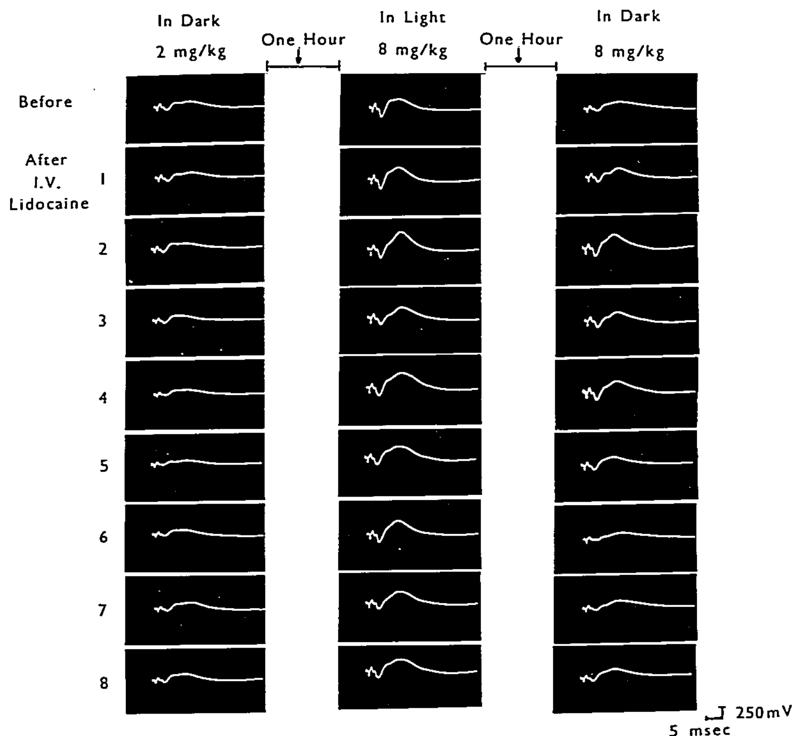

FIG. 2. LINC averages of optic evoked potentials (OEP) from the ipsilateral visual cortex in response to optic nerve stimulation in light and in darkness in the gallamine-immobilized, artificially ventilated cat and effects of intravenous lidocaine. Note the failure of 2 mg/kg lidocaine to facilitate OEP in darkness even though 8 mg/kg in darkness caused facilitation (2–4) which was not only longer-lasting but also of greater magnitude than the corresponding value in light (2) caused by the same dose of lidocaine. Although as presented the effect of lidocaine in darkness appears to be facilitation, in reality it is a reversible masking of the darkness induced depression of OEP. This is clearly brought out in fig. 3.

min) recovered to control levels without a compensatory increase in pressure or frequency. Furthermore, after a latency period of 5–7 min, complex spike activity which often lasted 20–30 min developed on the visual cortical lead only. Light and darkness did not influence the effects of lidocaine on EEG, ECG, or blood pressure.

Discussion

In view of the results presented, it is clear that higher doses of lidocaine effectively inhibit the depressant effect of darkness on visual cortical responses and unmask facilitation in anesthetized as well as in immobilized cats. That this is due to the specific effect of higher doses of lidocaine is evident from the fact that

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TABLE 2. Effects of Various Doses of Lidocaine (Intravenous) on Optic Evoked Potentials in Light (L) and in Darkness (D) in Immobilized and Artificially Respired Cats

Dose of Lidocaine (mg/kg)	Number of Cats	Change (Ratio*) in Amplitude† (Mean ± SE) of Evoked Potentials as Function of Time, in Seconds							
		32	64	96	128	160	192	224	256
0.0 (L)	16	0.04 ± 0.04	0.09 ± 0.09	0.10 ± 0.11	0.06 ± 0.11	−0.03 ± 0.06	0.04 ± 0.11	0.10 ± 0.08	0.05 ± 0.03
0.25 (L)	4	−0.01 ± 0.11	−0.01 ± 0.10	−0.12 ± 0.08	−0.04 ± 0.09	−0.15 ± 0.12	−0.19 ± 0.08	−0.18 ± 0.09	−0.11 ± 0.18
0.25 (D)	4	0.12 ± 0.11	−0.01 ± 0.01	−0.11 ± 0.11	−0.13 ± 0.12	−0.16 ± 0.13	0.05 ± 0.13	0.01 ± 0.06	−0.10 ± 0.15
0.5 (L)	3	−0.07 ± 0.03	−0.10 ± 0.06	−0.09 ± 0.09	−0.06 ± 0.17	−0.09 ± 0.25	−0.11 ± 0.22	−0.25 ± 0.16	−0.07 ± 0.12
0.5 (D)	3	0.24 ± 0.20	0.13 ± 0.13	0.04 ± 0.10	−0.04 ± 0.08	0.03 ± 0.02	0.04 ± 0.04	−0.10 ± 0.10	−0.04 ± 0.04
1.0 (L)	4	0.13 ± 0.03	0.15 ± 0.12	0.16 ± 0.23	0.04 ± 0.14	0.11 ± 0.10	0.15 ± 0.12	0.24 ± 0.15	0.16 ± 0.09
1.0 (D)	3	0.16 ± 0.10	0.16 ± 0.10	0.15 + 0.13	0.16 ± 0.18	0.01 ± 0.03	0.05 ± 0.05	0.19 ± 0.12	0.10 ± 0.13
2.0 (L)	4	0.43 ± 0.41	0.12 ± 0.10	−0.09 ± 0.12	0.00 ± 0.09	0.02 ± 0.07	0.24 ± 0.33	0.11 ± 0.21	−0.08 ± 0.08
2.0 (D)	3	−0.06 ± 0.10	0.22 ± 0.18	0.09 ± 0.10	−0.04 ± 0.10	−0.15 ± 0.08	0.01 ± 0.08	−0.19 ± 0.09	−0.08 ± 0.01
4.0 (L)	6	0.05 ± 0.04	0.16 ± 0.07	0.15 ± 0.10	0.08 ± 0.04	−0.03 ± 0.03	−0.13 ± 0.04	−0.03 ± 0.10	0.04 ± 0.11
4.0 (D)	5	−0 10 ± 0.06	−0.06 ± 0.07	−0.10 ± 0.07	−0.09 ± 0.06	−0.08 ± 0.10	0.07 ± 0.12	−0.06 ± 0.11	−0.07 ± 0.10
8.0 (L)	8	0.29 ± 0.13	0.63 ± 0.23	0.09 ± 0.15	0.06 ± 0.12	0.14 ± 0.16	0.10 ± 0.08	−0.16 ± 0.07	−0.08 ± 0.02
8.0 (D)	7	0.34 ± 0.22	0.95 ± 0.18	0.42 ± 0.23	0.48 ± 0.31	0.25 ± 0.31	−0.09 ± 0.09	−0.05 ± 0.15	0.00 ± 0.10
16.0 (L)	4	0.00 ± 0.05	0.30 ± 0.17	0.12 ± 0.09	0.09 ± 0.16	0.08 ± 0.23	0.13 ± 0.25	0.09 ± 0.22	−0.01 ± 0.20
16.0 (D)	3	0.03 ± 0.08	0.31 ± 0.06	0.40 ± 0.10	0.68 ± 0.18	0.53 ± 0.09	0.31 ± 0.06	0.01 ± 0.01	0.0 ± 0.0

* Ratio of the change over the control.
† Depression of amplitude is indicated by a negative value.

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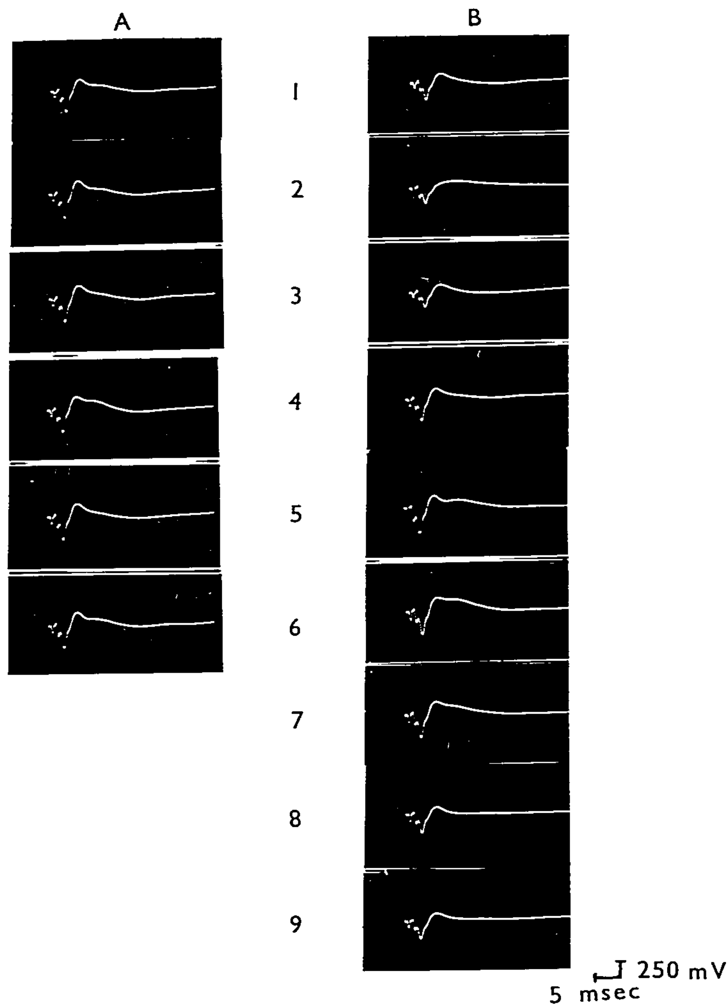

FIG. 3. Six consecutive LINC-average traces of ipsilateral visual cortical responses to stimulation of the optic nerve in light immediately prior to adaptation to darkness (A) and its depression by 10 minutes of adaptation to darkness (1, B). Traces 2–9 (B) are eight consecutive traces immediately following administration of lidocaine, 16 mg/kg, iv, in darkness. Note that traces 5–7 (B) show a complete reversible masking of the darkness induced inhibition of visual cortical responses by lidocaine, 16 mg/kg, iv. However, traces 5–7 (B) also show that in darkness lidocaine, 16 mg/kg, iv, facilitates the visual cortical responses.

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in lower dose(s) under identical conditions, in anesthetized as well as in immobilized cats, lidocaine does not facilitate visual cortical responses. A detailed discussion of the effects of light and darkness on the retina and subsequently on the central visual system is not feasible here, but it is known that in darkness the rods inhibit the cone function, and the so-called "lateral inhibition" is known to be present in the cat.[10] It is also well known that local anesthetics interfere with ionic permeability and thereby alter cellular excitability.[21] Since the retinal depressant influence on the central visual system in darkness is an active process,[14-18] it is likely that relatively active cells are the first to be affected by local anesthetics. However, in a bimodal system the net result should be a relative gain of the opposite sign. In fact, this is the exact pattern of the lidocaine effect, which explains the relative difference between potencies in darkness and in light in both anesthetized and immobilized cats (tables 1 and 2). Similarly, it is possible to speculate that the relatively lesser facilitation of the visual cortical responses in light than in darkness in anesthetized cats [1 mg/kg, (L) *vs.* (D), table 1] and in immobilized cats [8 mg/kg, (L) *vs.* (D), table 2] may be due to masking of the inhibitory inputs into the visual system and thus, unmasking of the excitatory events.

In anesthetized cats disinhibition was observed without any effect on blood pressure, but in immobilized cats a similar disinhibition took place with an unavoidable effect on blood pressure, indicating that these two phenomena are unrelated. Moreover, in anesthetized cats comparatively lower (⅛ to 1/16) doses of lidocaine caused facilitation of the optic evoked potentials in darkness or in light, which suggests that barbiturate anesthetization results in the sparing of quantitatively greater inhibitory processes. Against this view it could be said that higher voltages were necessary to elicit visual cortical responses in immobilized cats than in anesthetized cats. This can be negated, however, on the basis that it is not the inhibitory processes *per se* but rather their involvement in the process of excitation which governs the end result. This is supported by the demonstration that removal of the eyes does not reverse the darkness induced depression of the geniculate evoked potentials,[13] whereas retinal ischemia does indeed reversibly block this phenomenon[14] or lidocaine in dose-dependent fashion masks it (figs. 1 and 2), thereby suggesting the importance of the retina in this regard. However, such a view, *i.e.*, barbiturate anesthetization spares quantitatively greater inhibitory processes than gallamine immobilization, would presuppose the involvement of the inhibitory processes in homeostasis. As can be seen from the finding that in immobilized cats facilitation lasts only as long as 192 seconds [8 and 16 mg/kg (D), table 2], in contrast to the longer-lasting facilitation in anesthetized cats [1 mg/kg (D), table 1], this in itself supports the above-mentioned hypothesis. Also, the finding that in immobilized cats less than 4 mg/kg lidocaine induces only random variation into the system, in spite of the possibility that the variation could in part be due to volume artifact, in both light and darkness, would lend further support, because these doses may not be effective enough either to maintain a state of disinhibition or to counteract the consequence of disinhibition. That both are possible is evident from the finding that in immobilized cats lidocaine, 8 mg/kg, facilitates the optic evoked potentials, which reach a maximum by 64 seconds, whereas 16 mg/kg induces no distinguishable facilitation, and certainly induces less than 8 mg/kg [*cf.* 8 and 16 mg/kg (L), table 2].

Although lidocaine, 1 mg/kg, in anesthetized cats effectively inhibits the depressant influence of darkness and thereby causes facilitation of the optic evoked potentials, it is known that in low doses lidocaine acts as an anticonvulsant.[22] Thus, inhibition of the depressant influence of darkness by lidocaine in anesthetized cats is not directly related to its convulsogenic effect. However, in cats, more than 10 mg/kg iv lidocaine is a convulsant dose.[6] Therefore, the fact that in immobilized cats lidocaine, 16 mg/kg, effectively inhibits the depressant influence of darkness and thereby causes facilitation of the optic evoked potentials [fig. 3; table 2, 16 mg/kg (D)] clearly demonstrates that convulsogenic doses of lidocaine effectively unmask the excitatory phenomenon by inhibiting the depressant influence, and supports the contentions of those

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who have reached such a conclusion based on indirect evidence.[7,8,23] Even though lidocaine, 16 mg/kg, effectively inhibits the depressant influence of darkness but in light the effect of such an inhibition is not reflected on the visual cortical responses in the form of facilitation [16 mg/kg (L), table 2], perhaps this may explain the failure of Prince (cited by Wagman *et al.*[9]) to detect any changes with intracellular recordings. Thus, lidocaine-induced convulsion probably is due to a dissociation in the neuronal integrative processes resulting from depression of the active inhibitory inputs of the neuronal circuitry.

No generalization should be made from the mechanisms of the CNS excitatory effects of lidocaine to those of cocaine, because even though both are classed as local anesthetics, cocaine possesses the unique property of interfering with the reuptake of neurotransmitters.[24] Similarly, it might be futile to attempt to rationalize about the differences between the EEG effects of convulsant doses of lidocaine in immobilized cats and in chronic cats, because in immobilized cats not only is the neuromuscular blocking agent present, but also the animals may lack drive for the respiratory adjustment because of forced ventilation. Nevertheless, EEG effects of lidocaine, 16 mg/kg, consisted of immediate desynchronization with reduced frequency and complex spikes in the visual cortical lead only, which originated after latency of 5–7 minutes and lasted as long as 20–30 minutes.

Chang[13] accidentally discovered the depression of the visual cortical responses of barbiturate-anesthetized cats in darkness and suggested that this was due to removal of the excitation caused by light rays falling on the retina. However, in the course of years others have presented arguments against such a view and have suggested, alternatively, that the phenomenon first observed by Chang was due not to removal of excitatory events but rather to an active inhibitory input into the central visual system.[14] The results presented in this paper support the latter view, because lidocaine, a membrane stabilizer, otherwise could not have facilitated visual cortical responses in darkness when darkness alone had depressed the responses.

It is suggested that lidocaine-induced convulsions are due to a dissociation in neuronal integration resulting from depression of the active inhibitory inputs of the neuronal circuitry, and that darkness induced depression of optic evoked potentials is an active inhibition. Since in anesthetized cats comparatively lower doses of lidocaine were effective in facilitating optic evoked potentials in darkness, it is also suggested that anesthetization results in the sparing of quantitatively greater inhibitory processes.

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sure indicated that the directions of decrease in PBV and in P_d coincided in all 11 cases, although there was considerable variation in the magnitude of these changes.

In Group II, although there was a significant decrease in heart rate and a significant increase in cardiac index, LVEDP did not change significantly. No significant changes were found in LA or PA mean pressures, in P_d, or in pulmonary blood volume. Hence, if digitalization has no effect on left ventricular dynamics, it apparently has no significant effect on the pulmonary vessels. In Group II—as in Group I—calculated pulmonary vascular resistance was unchanged.

Controls: In eight additional patients the injection of saline solution instead of acetylstrophanthidin resulted in no appreciable hemodynamic changes. (*Murphy, G. W., and others: Effects of Acute Digitalization on the Pulmonary Blood Volume in Patients with Heart Disease, Circulation 43: 145 (Jan.) 1971.*) EDITOR'S COMMENT: The authors note that pulmonary vascular resistance may not accurately reflect the vasoactive effects of drugs, since resistance measurements are affected by pulmonary arterial, left atrial, and airway pressures, and also by changes in cardiac index. In their Group II patients who showed no significant changes in cardiac output and LA and PA pressures after digitalization, there was no change in calculated pulmonary arterial resistance. In the Group I patients in whom changes in the hemodynamics of the left heart and pulmonary vessels did occur following digitalization, the pulmonary distending pressure (P_d) was decreased consistently (9/9), whereas the changes in pulmonary vascular resistance were inconsistent (four increased, seven decreased) and varied from as little as 16 to as much as 162 dyne-sec cm^{-5}. One wishes that the authors had discussed their pulmonary vascular resistance data in more detail, since a drop in P_d would result from any decrease in left atrial pressure.

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