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CHOLINERGIC MODULATION OF SINGLE LATERAL GENICULATE NEURONS IN THE CAT*

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Summary—The effects of physostigmine, nicotine and scopolamine were studied on the activity of single lateral geniculate neurons in the acute cat. Most of the lateral geniculate neurons selected were P-cells. These increased their responses to ipsilateral optic tract and midbrain reticular formation stimulation.

Nicotine and physostigmine in doses of 25 μg/kg i.v. significantly increased the spontaneous firing rate of single geniculate neurons. Scopolamine in a dose of 0·5 mg/kg i.v. depressed their firing rates to control levels. Physostigmine enhanced their post-stimulus discharge rate to optic nerve stimulation. This enhancement was depressed by scopolamine. The effects of midbrain reticular formation stimulation were further enhanced by physostigmine and reduced by scopolamine in about 86% of lateral geniculate neurons studied. Generally, the effects of trains of pulses to the reticular formation (250 Hz/sec, 50 msec train duration, 0·05–0·1 msec pulses) were more marked than single stimuli.

It is concluded that a major cholinergic facilitatory system exists which influences lateral geniculate neurons. It is postulated that this involves the reticular formation. Evidence is presented for a predominant muscarinic cholinergic mechanism.

IT IS well known that the lateral geniculate nucleus contains catecholamines, 5-hydroxytryptamine (AMIN, CRAWFORD and GADDIN, 1954; VOGT, 1954; BOGDANSKI, WEISSBACH and UDENFRIEND, 1957; COBBIN, LEEDER and PALLORD, 1965; FUXE, 1965; SHUTE and LEWIS, 1966), acetylcholine, cholinesterase and choline acetyltransferase (BURGEN and CHIPMAN, 1951; FELDBERG and VOGT, 1948; HEBB and SILVER, 1959; DEFFENU, BERTACCINI and PEPEU, 1967; SHUTE and LEWIS, 1963, 1966). Electrophysiological and iontophoretic studies of lateral geniculate neurons indicate that monoamines usually depress these cells (CURTIS and DAVIS, 1962; DEFFENU *et al.*, 1967; PHILLIS, TEBECIS and YORK, 1967a). CURTIS and DAVIS (1963) and PHILLIS, TEBECIS and YORK (1967b) reported that about 50% of these neurons were excited by acetylcholine and only 4% depressed.

BISHOP, LEVICK and WILLIAMS (1964) and LEVICK and WILLIAMS (1964) reported on the interspike distribution of single lateral geniculate units. In addition, GERSTEIN and LIANG (1960), SATINSKY (1968) and CHOW, LINDSLEY and GOLLENDER (1968) have described the post-stimulus histogram of lateral geniculate neurons to afferent stimuli.

The purpose of the present study was to investigate the effects of certain cholinergic agonists and antagonists on single lateral geniculate P-cell discharge. Both spontaneous neuronal activity and that evoked by optic tract and reticular stimulation were analyzed

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using on-line digital computer techniques for determining the post-stimulus histograms of these cells.

METHODS

Twenty-two adult cats of either sex, weighing 2·5–4 kg, were used. Each was anesthetized with diethyl ether-air for all surgical procedures. A pair of steel bipolar electrodes was inserted stereotaxically into the right optic tract (A. 11·0, L. 7·0, H. −4·0) and the mesencephalic reticular formation (A. 2·0, L. 3·0, H. −1·0) with the aid of SNIDER and NIEMER's (1961) stereotaxic brain atlas. A pair of silver wire electrodes were placed in the visual cortex on the right side, 3 mm under the surface. By this means the visual cortex was stimulated with single shocks to evoke antidromic unit activity of lateral geniculate cells. Orthodromic responses to optic nerve stimulation were also obtained from the same cells.

After completion of the operative procedure the animal was given local anesthesia (0·5% lidocaine) at all wound edges and immobilized with i.v. decamethonium (0·5–1 mg/kg/hr). Artificial respiration was maintained and body temperature was kept at 36–37°C by means of an automatic heating pad (Gorman-Rupp Industries, Inc., Model K-1-3). Under these conditions, the mean$\pm$S.E. of the animal blood pH, pO_2 and pCO_2 was as follows: pH=7·37$\pm$0·01, pO_2=101·00$\pm$5·74 mm Hg and pCO_2=36·00$\pm$6·37 mm Hg (respiration volume, 250 ml, respiration rate, 22/min and sample number, 4). These values were almost the same as those of normal arterial blood. Arterial BP was recorded by means of a transducer from the right femoral artery.

Single square wave pulses (0·05 msec, 10 V) were applied to the right optic tract. The evoked responses in the ipsilateral visual cortex were recorded simultaneously with a Grass P-5 amplifier and displayed on a Tektronix dual beam oscilloscope. Single square wave pulses (0·1 msec, 5 V) were applied to the mesencephalic reticular formation 50 msec prior to optic tract stimulation to observe their facilitating effects (NAKAI and DOMINO, 1968, 1969). Recording of unitary discharges was begun 3–4 hr after termination of diethyl ether anesthesia. Unitary activity of lateral geniculate neurons was recorded with tungsten and steel microelectrodes. These were prepared as described by HUBEL (1957) and BOUDREAU, BIERER and KAUFMAN (1968). Electrode resistance was 1–10 MΩ. The microelectrodes were inserted stereotaxically into the right lateral geniculate (A. 7·5, L. 10·5, H. 3·0).

Evoked responses to the optic tract and antidromic stimulation were recorded as described by VASTOLA (1957), IWAMA, SAKAKURA and KASAMATSU (1965), and SAKAKURA and IWAMA (1967). The microelectrode was connected to a cathode follower, Grass P-5 amplifier and displayed on a Tektronix dual beam oscilloscope. A peak detector converted action potentials into pulses of constant amplitude and duration (TMC, Models 605 and 607). These were fed into a TMC CAT 400B and written out on a printer, Model 500A. On-line post-stimulus time histograms of single unit activity were thus obtained. At the end of each experiment, a current of 22·5 V d.c. was applied for 20 sec to the microelectrode and the brain was fixed with 12·5% formaldehyde for subsequent histologic examination. All experiments were done under dark room conditions. In some experiments both eyeballs were enucleated to rule out drug effects on the retina.

RESULTS

Typical evoked responses in the visual cortex were obtained by single electrical stimuli to the right optic tract (BISHOP and O'LEARY, 1938, 1940; BISHOP, 1953; BISHOP and MACLEOD, 1954; SUZUKI, TAIRA and MOTOKAWA, 1960; NAKAI and DOMINO, 1968, 1969). Stimulation

of the reticular formation just prior to optic tract stimulation also enhanced these responses (ANGEL, MAGNI and STRATA, 1965a,b, 1967a,b; CHI and FLYNN, 1968; LONG, 1959; NAKAI and DOMINO, 1968, 1969; OGAWA, 1963; SUZUKI and TAIRA, 1962; SUZUKI and ICHIJO, 1967).

Evoked potentials to optic tract stimulation in the visual cortex and lateral geniculate were observed in every experiment in order to obtain electrophysiological evidence that the electrodes were properly located before recording unitary activity.

Spontaneous firing rate of lateral geniculate neurons

The criteria for identifying a lateral geniculate unit were a spike response with a relatively short and fixed latency (less than 1·5 msec) and a response to diffuse illumination of the eye with an "on" or "off" discharge (BISHOP, BURKE and DAVIS, 1962; SUZUKI and ICHIJO, 1967; CHOW *et al.*, 1968). Eleven lateral geniculate neurons with latencies over 1·5 msec were omitted from this study. All lateral geniculate neurons responded to ipsilateral light stimulation. Most of them responded as "on", "on-off", or "off" types (ADRIAN and MATTHEWS, 1927a,b, 1928; HARTLINE, 1938; HUBEL and WIESEL, 1962; McILWAIN and CREUTZFELDT, 1967; ERULKAR and FILLENZ, 1958; KAHN, MAGNI and PILLAI, 1967; CHOW *et al.*, 1968). The mean spontaneous firing rate$\pm$S.E. of 63 lateral geniculate neurons under dark conditions was 22·35$\pm$1·90 sec (Fig. 1). This frequency is almost the same as that reported by BISHOP *et al.* (1964), SUZUKI and ICHIJO (1967), LEVICK and WILLIAMS (1964) and CHOW *et al.* (1968).

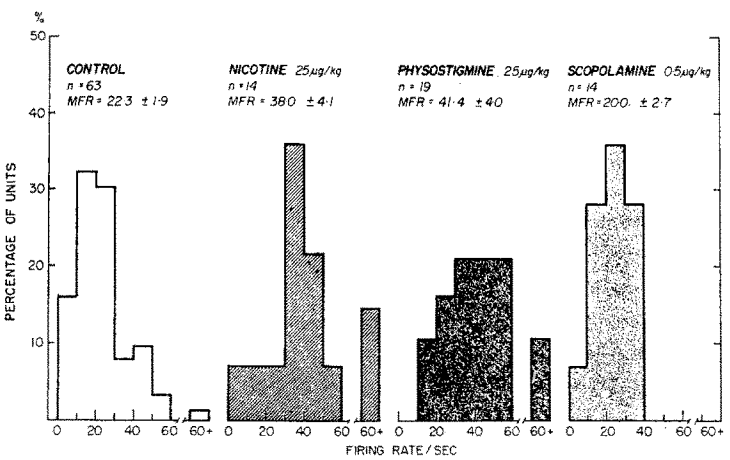

FIG. 1. Frequency distribution of spontaneous unit discharge of lateral geniculate neurons following various cholinergic agonists and antagonists. On the x-axis is shown the frequency/sec and on the y-axis the percentage of P-cells (n=63) before and after various drugs as noted. The data for nicotine was obtained 2 min after, that for physostigmine 5 min after, and that for scopolamine 5 min after i.v. injection. Note that nicotine and physostigmine increased the spontaneous firing rate and scopolamine reduced it toward control levels. MFR, mean firing rate$\pm$S.E.

Unit responses to single optic tract stimulation

Post-stimulus time histograms were recorded for 37·5 and 500 msec. The data were subdivided into 12·5 msec intervals and analyzed statistically using the Student's *t*-test.

Analysis time 37·5 *msec.* Thirty-four lateral geniculate neurons responded to optic nerve tract stimulation as follows: 28 units (82·6%) increased, 3 units (8·7%) decreased, and 3 units (8·7%) did not change their firing rate to the single shocks to the optic tract. A latency of 0·75–1 msec to single optic tract stimulation was observed most frequently as shown in Figs. 2 and 3.

Analysis time 500 *msec.* Eighteen lateral geniculate neurons which responded to optic nerve tract stimulation were classified as follows: 4 lateral geniculate neurons (22·5%) decreased and 14 (77·5%) increased their firing rates to optic tract stimulation.

Unit responses to single shocks to the reticular formation

Analysis time 37·5 *msec.* Thirty-four lateral geniculate neurons which responded to single reticular stimulation were classified as follows: 22 units (64·5%) increased, 3 units (8·7%) decreased, and 9 units (26·8%) did not change their firing rate. A latency of about

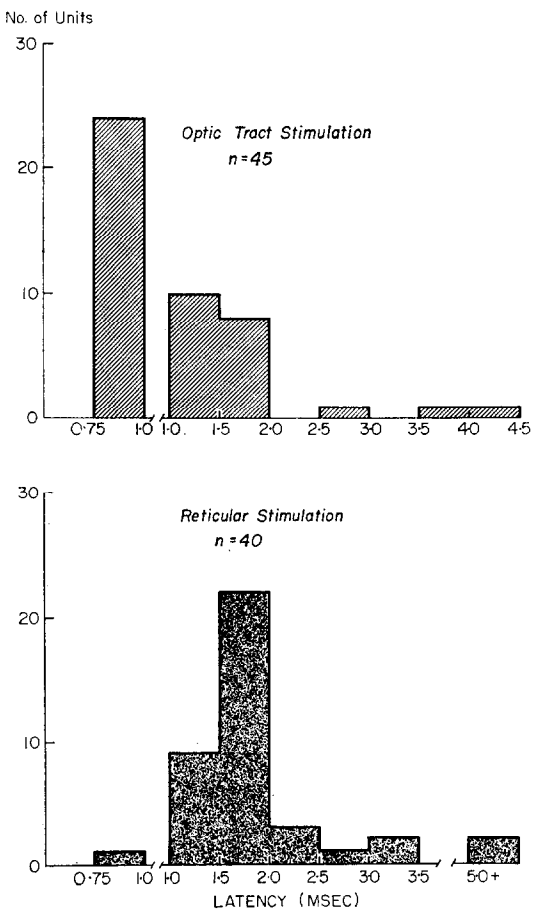

FIG. 2. Latency of lateral geniculate discharge to optic tract and reticular stimulation. The distribution of cell discharges are plotted as a function of latency after stimulation. Note that, as expected, optic tract stimulation resulted in shorter discharge latencies than reticular formation stimulation. The shortest latency to discharge for optic tract stimuli was 0·75 msec and usually at least 1 or more msec for reticular stimulation.

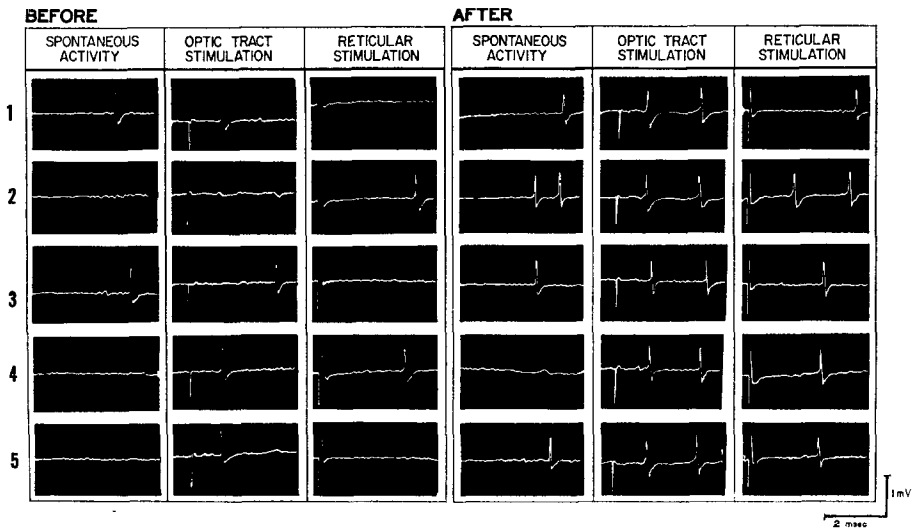

FIG. 3. Effects of physostigmine on spontaneous and elicited single unit activity in the lateral geniculate. A lateral geniculate neuron (P-cell) was recorded before drug under no stimulation in the dark and following single square wave pulses to the ipsilateral optic tract (0·05 msec, 5 V) and midbrain reticular formation (0·1 msec, 5 V). Time and voltage calibration as shown. Note that after 25 μg/kg of physostigmine the unit was much more responsive.

1·75–2 msec from the beginning of stimulation to the onset of effects was obtained most frequently (Fig. 2).

Analysis time 500 *msec.* Eighteen lateral geniculate neurons which responded to reticular formation stimulation were classified as follows: 14 units (77·5%) increased, 3 units (17·0%) decreased, and 1 unit (5·5%) did not change their firing rate. The latency from the beginning of reticular stimulation to the onset of effect was about 2 msec and lasted much longer (Fig. 2).

Effects of nicotine

Modification of mean spontaneous firing rates. Unit responses were recorded 2 min after the i.v. administration of 25 μg/kg of nicotine. After nicotine the mean arterial BP rose rapidly to about 60–88 mm Hg above control levels and lasted for about 60–80 sec. Nicotine caused 14 units to increase their mean spontaneous firing rate ± S.E. to 38·00 ± 4·18/sec. This value was significantly higher than for the control group (22·3 ± 1·9. $P < 0·001$).

Modification of unit responses to optic tract stimulation. Fourteen lateral geniculate neurons which responded to optic tract stimulation were studied. Nicotine in doses of 25 μg/kg i.v. caused 9 neurons (64·3%) to enhance their response rates to single optic tract stimuli. The majority of neurons excited by optic tract stimulation responded within 3 msec. After 2–3 msec of an excitatory phase there was an inhibitory phase of 3–4 msec duration (Fig. 4). Five neurons (35·7%) excited by optic tract stimulation were not enhanced by nicotine.

Modification of unitary responses to single reticular stimuli. Following nicotine (25 μg/kg i.v.), 5 lateral geniculate neurons (35·7%) showed enhanced responses as compared to control but those neurons were not depressed by scopolamine in doses of 0·5 mg/kg i.v.

Nine neurons (64·3%) excited by reticular formation stimulation were not enhanced by nicotine in doses of 25 μg/kg i.v. (Fig. 4).

Effects of bilateral eye enucleation. Four cats were subjected to bilateral eyeball enucleation. Under diethyl ether-air anesthesia both optic nerves were exposed and subsequently cut. Control responses and experimental procedures were the same as above prior to and after optic nerve transection. The spontaneous firing rate was tremendously increased following enucleation. Responses to optic tract stimuli were markedly enhanced as well (Fig. 4). The post-stimulation discharge pattern was periodic every 1·5–1·8 msec and continued for about 10 msec. The responses to reticular formation stimulation were slightly enhanced 1·5 msec after stimulation and inhibited about 2–3 msec after the enhancement (Fig. 4). After enucleation the maximal firing rates were not consistently altered by i.v. nicotine but were reduced by scopolamine (Fig. 5).

Effects of physostigmine

Modification of mean spontaneous firing rate. Facilitation of unit responses was usually observed 5 min after administration of 25 μg/kg i.v. of physostigmine. Nineteen lateral geniculate neurons were recorded. After physostigmine the mean spontaneous firing rate±S.E. was 41·4±4·0/sec compared to the control level of 22·3±1·9/sec. This increase was statistically significant ($P < 0{\cdot}001$). Following physostigmine no consistent changes in mean arterial BP were observed.

Modification of unit responses to single optic tract stimuli. Fourteen units which were excited by optic tract stimulation showed enhanced discharge following 25 μg/kg i.v. physostigmine. However, their response latency did not change as compared to controls (Fig. 3). Neurons facilitated by physostigmine showed exaggerated periodic bursts at intervals of 2·5–5 msec which were also seen in the controls (Fig. 6). The enhanced responsiveness induced by physostigmine was antagonized by scopolamine.

Modification of unit responses to single stimuli to the reticular formation. The discharge rate of 14 neurons was enhanced by the administration of 25 μg/kg i.v. physostigmine. In addition to single shocks, trains of stimuli (pulses 0·1 msec, 250 Hz/sec, train duration 50 msec) were even more effective in facilitating single lateral geniculate units. The effects lasted about 100–120 msec but their response latency did not change. Physostigmine further enhanced their discharge rate.

Effects of scopolamine

Effects on mean spontaneous firing rate. The mean spontaneous firing rate of 14 lateral geniculate neurons was recorded 5 min after 0·5 mg/kg scopolamine. The mean spontaneous firing rate±S.E. was 20·0±2·7/sec. There was a tendency for a shift to the lower frequencies but the mean decrease was very slight (Fig. 1). However, burst discharges were not observed following scopolamine.

Modification of unit responses to single optic tract stimuli. Fourteen neurons were recorded. Following scopolamine (0·5 mg/kg i.v.), there was no increase to optic tract stimulation. Five (35·7%) neurons had depressed firing rates and 9 neurons (64·3%) did not change their firing rate to optic nerve tract stimulation (Table 1). These effects of scopolamine continued for at least 1 hr or more.

Modification of unit responses to reticular stimuli. Nine neurons showed depressed firing rates and 5 did not change their firing rate to reticular formation stimulation following 0·5 mg/kg i.v. of scopolamine.

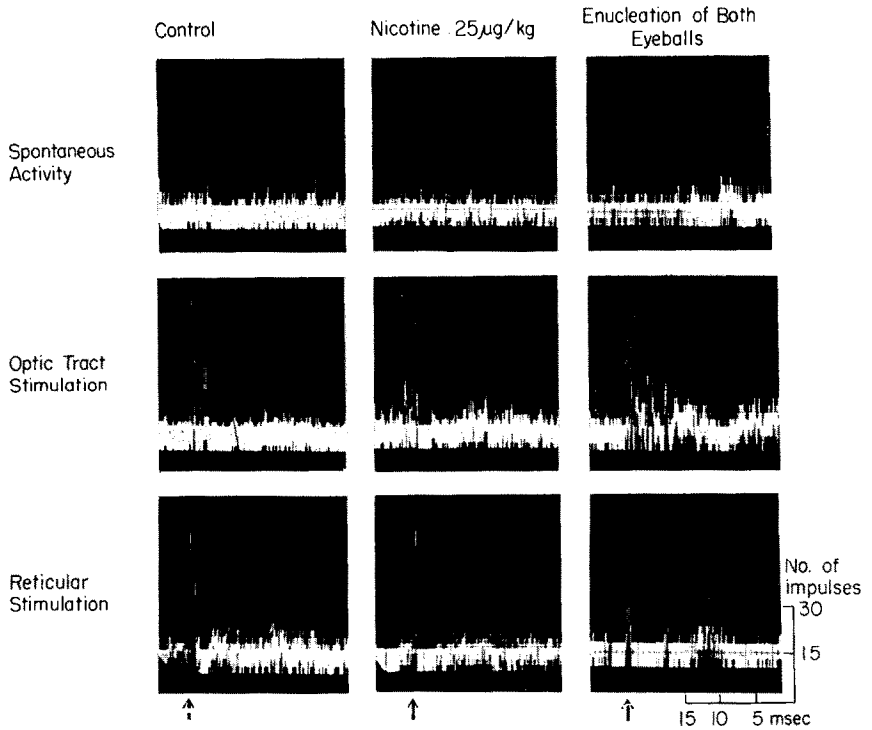

FIG. 4. Post-stimulus time histogram of a lateral geniculate neuron after nicotine and bilateral enucleation. The figure illustrates displays from a CAT 400 computer. A mean of 30 sweeps was obtained. Each section = 0·78 msec. The number of impulses and the time interval are shown in the calibration bars. The stimulus artifact is shown at the arrows below each histogram except for the upper row which records spontaneous activity. Note that nicotine increased the frequency of firing to optic tract and reticular stimulation. Bilateral enucleation caused a very marked increase in neuronal discharge, especially to optic tract stimulation. In each case recordings were made under dark conditions.

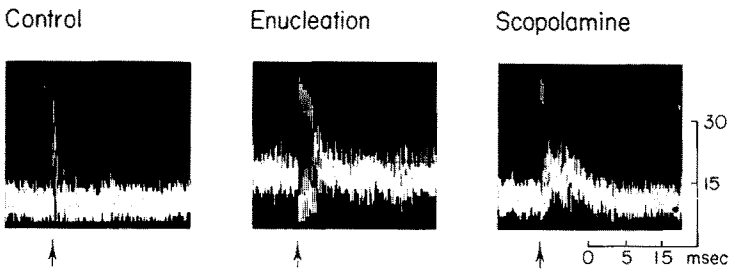

FIG. 5. Post-stimulus time histogram of the response of a lateral geniculate neuron to single shock optic tract stimuli. The time histograms are similar to those described in Fig. 4. Note that bilateral enucleation caused a marked increase in spontaneous and evoked neuronal discharge. This is reduced but somewhat prolonged following 0·5 mg/kg of scopolamine. Calibration as noted.

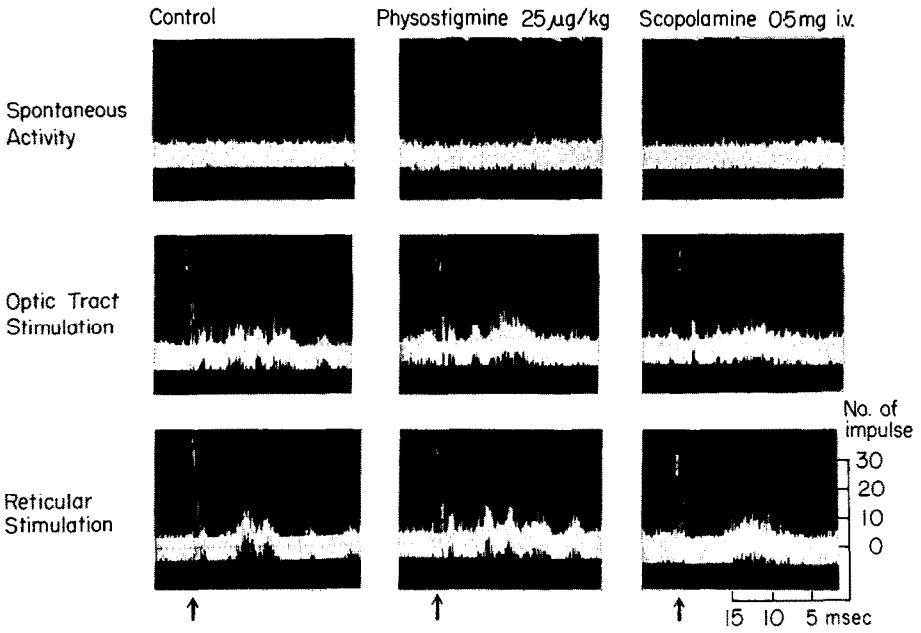

FIG. 6. Post-stimulus time histogram of a lateral geniculate neuron before and after physostigmine and scopolamine. The time histograms are similar to those described in Fig. 4. Note that 5 min after physostigmine there was an increase in spontaneous discharge and the early components were enhanced after optic tract and reticular stimulation with a redistribution of period bursts. Ten minutes after physostigmine the administration of scopolamine restored the histogram toward control. Calibration as noted.

TABLE 1. THE SAME UNIT RESPONSES TO OPTIC TRACT AND RETICULAR FORMATION STIMULATION BEFORE AND AFTER ADMINISTRATION OF VARIOUS DRUGS

Site of stimulation	Response patterns	2 min after nicotine 25 μg/kg i.v.	5 min after physostigmine 25 μg/kg i.v.	5 min after scopolamine 0·5 mg/kg i.v.	No. of units
Optic tract	Excited	Enhanced	Enhanced	No effect	9
	Excited	No effect	Enhanced	Depressed	5
Reticular formation	Excited	Enhanced	Enhanced	No effect	5
	Excited	No effect	Enhanced	Depressed	9

Unit responses to optic tract and reticular formation stimulation before and after administration of nicotine, physostigmine and scopolamine in sequence. The experimental schedule was as follows: (a) Identification of lateral geniculate units as P-cells, (b) recording control responses to optic tract and reticular stimulation, (c) repeating procedure "b" 2 min after administration of 25 μg/kg i.v. nicotine, (d) a 20-min interval for recovery, (e) repeating procedure "b" 5 min after administration of 25 μg/kg i.v. physostigmine, (f) another recording period 10 min later, and (g) repeating procedure "b" 5 min after administration of 0·5 mg/kg i.v. scopolamine.

Optic tract stimulation. Fourteen neurons showed enhanced discharge to optic tract stimulation following physostigmine. Most of these were unaffected by the administration of nicotine but were depressed by scopolamine. Another 5 neurons showed enhanced discharge following nicotine. These neurons did not change their responses following scopolamine.

Reticular formation stimulation. Fourteen neurons showed enhanced responses after physostigmine but 9 of these did not show any change following nicotine. These 9 were also depressed following scopolamine (Fig. 7). Five other neurons which did not change their firing rates following scopolamine were enhanced by nicotine. These data suggest a cholinergic modulation on the lateral geniculate neuron to reticular formation stimulation.

DISCUSSION

HUBEL (1960), TAIRA and OKUDA (1962) and LEVICK and WILLIAMS (1964) observed that the discharge patterns of lateral geniculate neurons were regulated by the level of activity of the reticular formation during activation, non-rapid-eye-movement sleep or general anesthesia. By using bilaterally enucleated cats under unrestrained conditions, SAKAKURA and IWAMA (1967) also observed that the discharge patterns of lateral geniculate neurons were regulated by the level of reticular formation activation. SUZUKI and TAIRA (1962) reported that the discharge patterns of "on" or "off" geniculate neurons to light stimulation were modified by reticular activity, but optic nerve fiber units were not.

In the present study many lateral geniculate neurons were excited following physostigmine and showed increased responses to reticular stimulation. Furthermore, the enhanced responsiveness of these cells induced by physostigmine was abolished by scopolamine suggesting they were of the muscarinic type.

Other lateral geniculate neurons were also excited by nicotine as well as physostigmine, and showed an increased response to optic tract stimulation. Units elicited by optic tract stimulation were not depressed by scopolamine. However, in these neurons, the facilitatory effect of reticular formation stimulation was depressed completely by scopolamine.

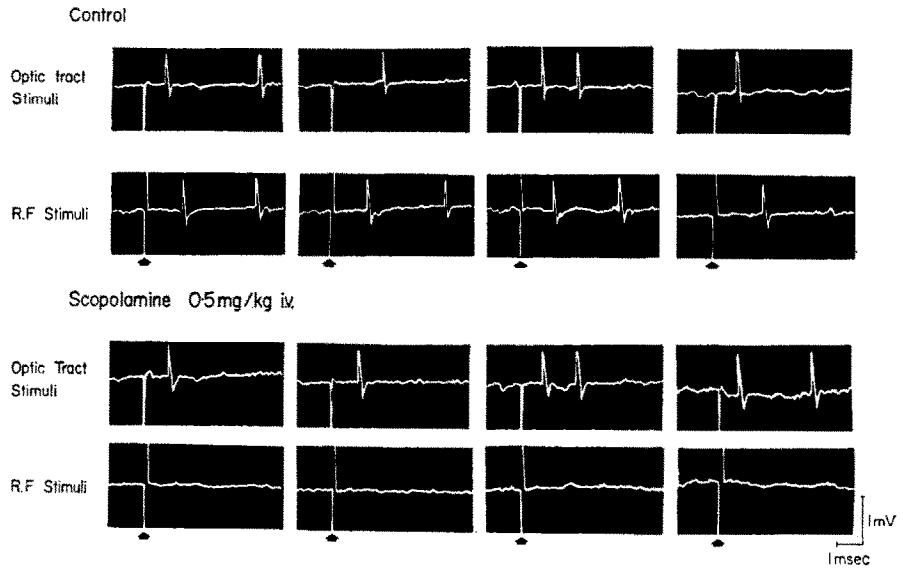

FIG. 7. Effects of scopolamine on single unit discharge of a lateral geniculate neuron to optic tract and reticular stimulation. In the upper two sets of records the response of a neuron to single shocks to the optic tract and reticular formation are shown in sequence. Note that after 0·5 mg/kg i.v. scopolamine the responses to optic tract stimulation were essentially unchanged, but markedly reduced to reticular stimulation. Calibration as noted.

The facilitatory effect of reticular formation stimulation on lateral geniculate neurons has been observed by SUZUKI and TAIRA (1962) and OGAWA (1963). In the present study, this facilitatory effect was strongly enhanced by physostigmine and blocked by scopolamine, but was not changed by nicotine. ADRIAN and MATTHEWS (1927a,b, 1928) reported that the frequency of unitary discharges on optic nerve fibers of the conger eel were altered by the intensity of light stimulation. This was confirmed by HARTLINE (1938). HUBEL and WIESEL (1962), ERULKAR and FILLENZ (1958) and SUZUKI and KATO (1966) reported that there was some binocular interaction on the single neurons of the visual cortex. A small portion of the cells were color-coded and some of the neurons could discriminate the moving target (HUBEL and WIESEL, 1968). Since all visual inputs from the retina to the cerebral cortex must pass through the lateral geniculate nucleus and since the connection between optic nerve terminals and lateral geniculate neurons is not one-to-one (HUBEL and WIESEL, 1961), it seems logical that the function of the lateral geniculate neurons should be complicated and that the chemical transmitters or modulators may differ from each other.

An excitatory action of acetylcholine applied by local iontophoretic injection on lateral geniculate neurons was reported by CURTIS and DAVIS (1963) and PHILLIS, TEBECIS and YORK (1967b). The typical response of acetylcholine applied iontophoretically on geniculate neurons is very slow to develop, frequently taking up to 60 sec. The characteristics of this excitant action differ from those observed in the excitation of Renshaw cells by acetylcholine (MCCANE, PHILLIS and WESTERMANN, 1966). PHILLIS *et al.* (1967b) concluded that acetylcholine was not the major excitatory synaptic transmitter released at optic nerve terminals by orthodromic volleys. The present data certainly support this conclusion. Intracarotid injection of 50–100 μg physostigmine was shown to enhance the amplitude of the post-synaptic responses to optic nerve stimulation (DAVID, MURAYAMA, MACHNE and UNNA,

1963). The present data show that physostigmine enhanced unit responses to optic tract stimulation. Although it is obvious that acetylcholine cannot be the excitatory synaptic transmitter released at optic nerve terminals by orthodromic volleys, it still may act as a facilitatory modulator especially from the reticular formation. PHILLIS *et al.* (1967a) suggested that inhibitory effects of reticular stimulation were mediated by a monoaminergic projection system and the facilitatory effects of reticular stimulation were mediated by a cholinergic one. The present data support the hypothesis of a cholinergic modulatory system which is mostly facilitatory. Furthermore, it would seem that about 2/3 of the lateral geniculate neurons show a muscarinic response and another 1/3 a nicotinic cholinergic response under dark conditions. It is important to remember that tonic inhibitory effects from the retina control lateral geniculate neurons under dark conditions. After retinal blockade (BISHOP *et al.*, 1964; SUZUKI, 1967; ARDUINI and HIRAO, 1960) or enucleation of both eyeballs (ERULKAR and FILLENZ, 1958; NAKAI and DOMINO, 1968) the evoked response in the visual cortex and lateral geniculate is tremendously enhanced.

SAKAKURA and IWAMA (1967) reported that the spontaneous firing rate of lateral geniculate neurons in the chronic cat is very low ($3{\cdot}7 \pm 2{\cdot}7$/sec) in non-rapid-eye-movement sleep. During arousal this increases to $9{\cdot}9 \pm 4{\cdot}9$/sec. High intraocular pressure in both eyeballs depresses the firing discharge rate of lateral geniculate neurons (SUZUKI and ICHIJO, 1967) but post-synaptic potentials evoked by optic tract stimulation in lateral geniculate bodies are increased. OGDEN and BRAWN (1964) suggested that the efferent fibers from the lateral geniculate to the retinal amacrine cells caused inhibitory effects on the ganglion cells.

In the present study, enucleation of both eyeballs during recording of the same units showed that the firing discharge rate and optic stimulation response were tremendously increased but reticular stimulation caused only a slight increase. These effects suggest that there was some feedback or presynaptic inhibition (SUZUKI and KATO, 1966, 1967) between the lateral geniculate and the retina. We have not ruled out an action of physostigmine, nicotine or scopolamine on such a system. However, although consistent nicotine effects were not observed after enucleation, scopolamine clearly reduced the frequency of optic evoked units indicating an action beyond the retina within the brain. Finally, it should be emphasized that recording single units from the lateral geniculate after i.v. administration of various drugs does not in any way prove that the drugs are acting at the lateral geniculate. For example, drugs may alter the threshold of response to electrical stimulation of the reticular formation, etc. particularly at sites relatively distant from the electrode tip. Other neuropharmacological techniques must be used such as iontophoretic drug application to localize the precise site of drug effect. This approach is currently being pursued and will be the subject of a later communication.

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