1.6 mg/kg of body wt. Control groups were injected only physiological solution. The oxygen consumption was measured individually in a gas analyzer, based on the closed circular airing system adapted to the small animals[11]. The measurements were started at 30 min before the injection of noradrenaline and continued after the injection over the period of the duration of the effect. All the measurements were realized at 30 °C, starting at 07.00 h or 20.00 h. Thyroidectomy was performed under ether anesthesia and oxygen consumption measurement was carried out on the 7th day following the operation.

Results and discussion. The results are expressed in calories per $m^2/24$ h and presented in Figure 1. As is evident, the initial values of the heat production, prior to the injection of noradrenaline or of physiological solution, were somewhat higher in the evening than in the morning experiments. These findings are similar to those reported by Popović et al.[4]. In the normal control rats, a significant increase in heat production was observed 25 min after the injection of noradrenaline in both the morning and the evening experiments, being 21% and 40% respectively. Maximum increase was reached at about 40 min after the injection of noradrenaline. The difference between the maximal calorigenic effect registered in the morning experiment and that obtained in the evening experiment, in the first period of the duration of the effect of noradrenaline (Figure 2), was statistically significant ($p < 0.01$).

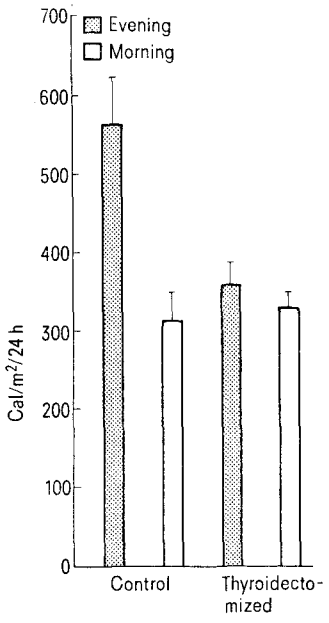

Fig. 2. Differences between the maximal level of the heat production under the influence of noradrenaline and the initial values obtained prior to the injection in the morning and in the evening experiments in normal control and thyroidectomized rats (Mean ± SEM of 10 animals).

The evidence that the same amount of noradrenaline produced markedly higher calorigenic effect if applied in the evening than in the morning suggests the existence of the diurnal fluctuation of the sensitivity to this hormone in the rat. As the circadian rhythm of thyroidal iodine release was found[12], and the disappearance of the circadian rhythm of oxygen consumption after the thyroidectomy was registered[4], we suspected that the thyroid might be involved in the control of the diurnal fluctuation of the sensitivity to the applied noradrenaline in the rat. To investigate this possibility, a preliminary study was undertaken to examine the effect of noradrenaline in the thyroidectomized rats. As shown in Figure 1, in thyroidectomized animals the initial values of heat production prior to the injection of noradrenaline was significantly lower than in the controls ($p < 0.01$). Noradrenaline still produced a significant increase in heat production in both groups, i.e. in animals examined in the morning as well as in those examined in the evening ($p < 0.01$). It should be pointed out that the level of the heat production under the influence of the same dose of noradrenaline (1.6 mg/kg of body weight) was significantly lower in thyroidectomized animals than in the controls ($p < 0.01$). In addition to this no difference in the calorigenic effect of the injected noradrenaline was found between groups examined in the morning and in the evening. Therefore, diurnal fluctuation in the calorigenic effect of the applied noradrenaline seems to be dependent on the thyroid.

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Destruction of Afferent Nerve Terminals in the Inner Ear of Frog by Aminooxyacetic Acid

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Summary. The drug aminooxyacetic acid, which inhibits GABA-transaminase, destroys the afferent nerve endings in the inner ear of the frog. The efferent nerve endings and the sensory cells are not affected.

Sensory cells in the *acustico-lateralis* system of vertebrates are innervated by afferent and efferent nerve fibres[1,2] (Figure 1). The synaptic connections between the sensory cells and the nerve fibres on structural and functional grounds appear to be chemically mediated[3,4]. The synaptic transmitter at the efferent contacts is probably cholinergic[5,6] but the transmitter is unknown at the afferent synapse, although catecholamine-like compounds[7–9], glutamate[10], and γ-aminobutyric acid[11] (GABA) are possible candidates.

Injection of drugs that interfere with catecholamine metabolism have previously been shown to affect the

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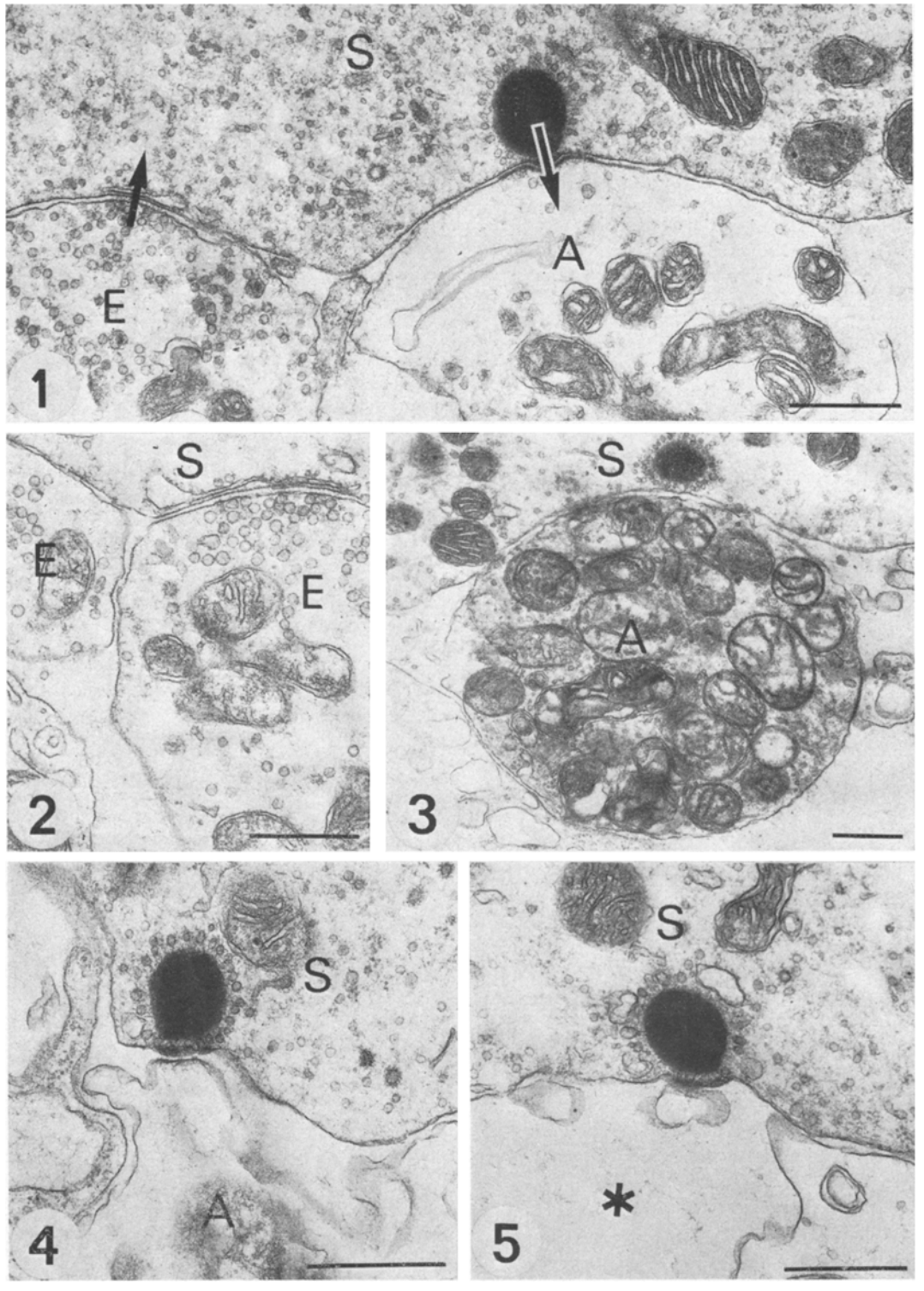

Fig. 1. Synaptic regions of a control sensory cell (S). Both afferent (A) and efferent (E) nerve endings are shown. The afferent presynaptic region of the sensory cell is characterised by the presence of a large electron-dense 'synaptic bar' surrounded by synaptic vesicles. The arrows indicate the presumed direction of transmission at the two synapses.

Fig. 2. An efferent synapse from an AOAA treated frog. Appearance is little different from Figure 1.

Fig. 3. An afferent synaptic region from an AOAA treated frog. The sensory cell (S) is unaffected, whereas in the afferent nerve ending (A) the mitochondria are considerably distorted and swollen.

Fig. 4. AOAA treated frog. The sensory cell (S) shows little effect, but the afferent fibre (A) is damaged and pulling away from the sensory cell.

Fig. 5. AOAA treated frog. The sensory cell (S) is relatively unaffected, but the afferent nerve fibre has almost completely disappeared. The asterisk indicates the region which should be occupied by the afferent fibre. Scale = 0.5 μm and applies to all figures.

fine structure of the presynaptic organelles in the sensory cells[7–9], but not the fine structure of either the efferent or afferent nerve terminals.

The report that GABA could be synthesized by the inner-ear and lateral-line prompted us to study the effect of aminooxyacetic acid (AOAA) upon the fine structure of these sense organs. This drug, which inhibits GABA-transaminase, prevents the breakdown of GABA[12], and might be expected to affect the fine structure of the sensory cells if they were engaged in GABA metabolism.

Intraperitoneal injections of AOAA (8 × 5 mg/kg over 48 h) into adult *Rana temporaria* do not appear to affect the sensory cell fine structure (Figures 1 and 3) or that of the efferent nerve terminals (Figures 1 and 2). The drug does, however, produce dramatic changes in the afferent nerve fibres. These effects vary in magnitude from swelling of the mitochondria (Figure 3) through shrinkage of the nerve terminal (Figure 4) to complete breakdown of the terminals in synaptic contact with the sensory cells (Figure 5). Thus AOAA appears to produce a selective destruction of the afferent nerve endings in the inner ear.

The electrophysiological action of AOAA at least in mammals is to decrease the amplitude of the auditory nerve compound action potential[13,14]. It also increases the threshold of the Preyer pinna reflex in response to sound in guinea-pigs[14]. However, it was concluded that the effects of AOAA are not mediated by its actions on GABA metabolism[14]. This is tenable because recent work[15] has shown that AOAA, in addition to inhibiting GABA transaminase also prevents in general the uptake of amino acids by cells.

Whatever the physiological effects of this drug, there remains the question of its site of action. Our structural findings suggest that it acts upon the afferent nerve fibres rather than the sensory cells.

The virtual absence of any structural effects of AOAA upon the sensory cells also suggests that they are probably not involved with the metabolism of GABA, and furthermore, tends to exclude this compound and possibly other amino acids from being the sensory cell neurotransmitter in the inner ear.

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Modification of Visual Signals by Nigral Stimulation

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Summary. Responses of the lateral geniculate neurons to light were modified by stimulation of the substantia nigra. Nigral stimulation often caused enhancement of firing in neurons responding primarily to flash, but it usually had the contrary effect on units inhibited by light.

The substantia nigra has been regarded as part of the extrapyramidal motor system[1], and its participation in sensory activities remains obscure. In our previous studies[2–5], modification of visual inputs, both at the lateral geniculate level and at the visual cortical level by stimulation of the lenticular (the lenticular nucleus = globus pallidus and putamen) and caudate nuclei, was demonstrated. More recently, enhancement of visual, auditory, and somatosensory evoked responses in the primary receiving areas by stimulation of the substantia nigra was found[6]. The purpose of the present investigation was to study effects of electrical stimulation of the substantia nigra on responses of the lateral geniculate body neurons to light.

Methods. Experiments were performed on 9 cats immobilized with gallamine triethiodide, and on 9 cats lightly anesthetized with hexobarbital. Immobilized cats were artificially ventilated. All wound edges and pressure points were anesthetized locally with procaine, and pupils were dilated with atropine. Light flashes were presented by a xenon flash lamp facing the eyes at a distance of 30 cm. Glass micropipettes (10–40 $M\Omega$ resistance) filled with 1.5 M potassium citrate solution or 1.0 M potassium acetate solution saturated with methyl blue or fast green FCF were used for recording of unit activity of the lateral geniculate body. Unit potentials were amplified, monitored by an amplifying system and photographed by a continuously-recording camera. Bipolar stimulating electrodes were inserted in the substantia nigra[7] (A 5.0, L 4.5, H − 4.5), which was stimulated with a single square wave pulse (4.5–5.0 V, 0.1–0.15 msec duration). Intervals between conditioning shock to the substantia nigra and light flash were 9–19, 30–40, or 60–75 msec, which were found to be effective in the preceding study[6]. The position of all stimulating electrodes was histologically verified.

Results. 157 neurons of the lateral geniculate body were studied. 56 were impaled intracellularly and the others were recorded extracellularly. According to their primary reaction to flash, these lateral geniculate neurons could be classified into 3 groups[2,3]. 51 showed a primary excitation after flash (type 1), 48 were primarily inhibited by flash and were followed by firing (type 2). The others were interneurons, irregularly responding cells, and scarcely responding neurons (type 3). Most of the lateral

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