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.

[12] D. P. Wallach, Biochem. Pharmac. *5*, 166 (1960).
[13] R. P. Bobbin and P. S. Guth, Fed. Proc. *28*, 2885 (1969).
[14] R. P. Bobbin, G. Gonzales and P. S. Guth, Nature *223*, 70 (1969).
[15] G. A. R. Johnson and V. J. Balcar, J. Neurochem. *22*, 609 (1974).

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

[1] R. Jung and R. Hassler, in *Handbook of Physiology*, Sect. 1, *Neurophysiology* (Eds. J. Field, H. W. Magoun and V. E. Hall; Am. Physiol. Soc., Washington 1960), vol. 2, p. 863.
[2] I. Kadobayashi and G. Ukida, Expl. Neurol. *33*, 518 (1971).
[3] I. Kadobayashi, Expl. Neurol. *37*, 463 (1972).
[4] I. Kadobayashi, Pflügers Arch. ges. Physiol. *332*, 10 (1972).
[5] I. Kadobayashi, Y. Amano, H. Yamane and Y. Miyamoto, Folia psychiat. neurol. jap. *26*, 95 (1972).
[6] I. Kadobayashi and M. Nakamura, Experientia *30*, 260 (1974).
[7] H. H. Jasper and C. Ajmone-Marsan, *A Stereotaxic Atlas of the Diencephalon of the Cat* (National Research Council of Canada, Ottawa 1954).

geniculate neurons (109) were affected by conditioning stimulation of the substantia nigra. In type 1 neurons, responses of 23 units to flash were enhanced (Figure 1) but those of 13 were inhibited by nigral stimulation, while no change was observed in 15. In type 2 neurons, firing of 11 units in response to flash was enhanced but that of 23 was inhibited by nigral stimulation (Figure 2). The remaining 14 were not affected by such stimulation. In type 3 neurons, firing of 19 was enhanced but that of 20 was inhibited by nigral stimulation, whereas that of the remaining 19 was unaffected. In each type, similar proportions of neurons were enhanced or inhibited by stimulation of the substantia nigra regardless of whether the nucleus stimulated was ipsilateral or contralateral to the recording site. Nigral stimulation alone evoked no response in 102 units tested.

Discussion. This study demonstrates that responses of the lateral geniculate neurons to light are modified by nigral stimulation. Modification of visual signals at the lateral geniculate level by stimulation of the reticular formation[8–10], lenticular nucleus[2] and caudate nucleus[3] has been reported. Anatomically[1,11–13], the substantia nigra receives afferent fibres from the lenticular nucleus, caudate nucleus and subthalamus, and from the frontal, parietal and temporal cortices. Efferent fibres from the substantia nigra terminate in the neostriatum (caudate nucleus and putamen), pallidum, midbrain reticular formation, superior colliculus and parietal cortex. Recent histochemical investigations[14,15] have revealed dopaminergic pathways from the substantia nigra to the neostriatum and to the cortex.

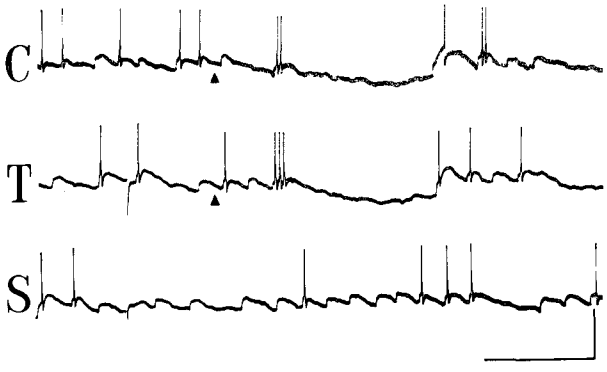

Fig. 1. Enhancement of response of a type 1 neuron to flash by nigral stimulation. C) Response to flash alone. T) Enhancement of the response by conditioning stimulation of the contralateral substantia nigra 75 msec before flash. S) No response to nigral stimulation alone. Triangle indicates flash stimulus. Positive upwards. Calibration: 10 mV; 100 msec.

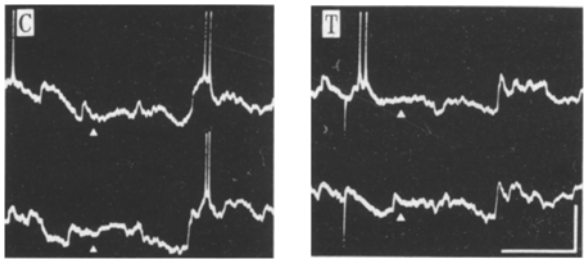

Fig. 2. Inhibition of firing in response to flash in a type 2 neuron by nigral stimulation. C) Responses to repeated flashes. T) Inhibition of firing by conditioning stimulation of the contralateral substantia nigra 75 msec before each flash. Both are continuous records. Calibration: 10 mV; 100 msec.

Though PHILLIS et al.[16] reported inhibitory action of dopamine on the lateral geniculate neurons, no direct fibres from the substantia nigra to the lateral geniculate body were reported. Histochemical experiments[17] demonstrated only noradrenaline and serotonin terminals in the lateral geniculate body. In this study, too, nigral stimulation alone evoked no response in the lateral geniculate body. So nigral modification of the reponse to light in the lateral geniculate body may be mediated mainly via the reticular formation.

Nigral stimulation more often brought about enhancement of the response to light in type 1 neurons excited primarily by flash, but more frequently inhibition in type 2 neurons which showed a primary neuronal silence after flash. This resembles the finding obtained by stimulation of the lenticular[2] and caudate nuclei[3]. FUSTER[18] also reported similar phenomena that reticular stimulation often caused enhancement of firing in visual cortical cells activated by light but it usually had the contrary effect upon light-inhibited cells. It has been reported that the lenticular and caudate nuclei receive afferent fibres from the centromedian nucleus of the thalamus[1], which belongs to the reticular ascending system[19]. Reciprocal fibre connections exist between substantia nigra and striatum (neostriatum and pallidum). The pallidum and substantia nigra send efferent fibres to the midbrain reticular formation and nucleus ventralis anterior of the thalamus. From physiological studies, FRIGYESI and MACHEK[20] claimed that dual projection systems link the caudate nucleus to the dorsal thalamus and that nigrothalamic connections exist via collaterals of nigrocaudate axons.

Thus, the reticular system sends outputs to the nigrostriatal system, and receives feedback from that at the midbrain level and thalamic level. So activity of the reticular system might be modulated by feedback through the nigro-striatal system. Thus considered, it can be easily understood that stimulation of the nigro-striatal system modifies visual signals[2–5] as well as auditory and somatosensory ones[6].

[8] H. SUZUKI and N. TAIRA, Jap. Physiol. *11*, 641 (1961).
[9] T. OGAWA, Science *139*, 343 (1963).
[10] W. SINGER and U. DRÄGER, Brain Res. *41*, 214 (1972).
[11] M. B. CARPENTER and R. E. MCMASTERS, Am. J. Anat. *114*, 293 (1964).
[12] F. A. METTLER, in *Handbook of Clinical Neurology* (Eds. P. J. VINKEN and G. W. BRUYN; North-Holland Publisher, Amsterdam 1968), vol. 6, p. 1.
[13] S. MASUDA, Adv. neurol. Sci., Tokyo *12*, 15 (1968).
[14] N.-E. ANDÉN, A. DAHLSTRÖM, K. FUXE, K. LARSSON, L. OLSON and U. UNGERSTEDT, Acta physiol. scand. *67*, 313 (1966).
[15] O. LINDVALL, A. BJÖRKLUND, R. Y. MOORE and U. STENEVI, Brain Res. *81*, 325 (1974).
[16] J. W. PHILLIS, A. K. TEBÈCIS and D. H. YORK, J. Physiol., Lond. *190*, 563 (1967).
[17] K. FUXE, Acta physiol. scand. *64*, Suppl. 247, 37 (1965).
[18] J. M. FUSTER, Science *133*, 2011 (1961).
[19] T. E. STARZL, C. W. TAYLOR and H. W. MAGOUN, J. Neurophysiol. *14*, 479 (1951).
[20] T. L. FRIGYESI and J. MACHEK, Brain Res. *27*, 59 (1971).