Exp Brain Res (1988) 69: 635–644

Experimental Brain Research

Physiological and anatomical identification of the nucleus of the optic tract and dorsal terminal nucleus of the accessory optic tract in monkeys

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Summary. Physiological and anatomical criteria were used to clearly establish the existence of a pretectal relay of visual information to the ipsilateral inferior olive in the macaque monkey. After injection of horseradish peroxidase into the inferior olivary nucleus, retrogradely labelled neurons were found in the nucleus of the optic tract (NOT) and the dorsal terminal nucleus of the accessory optic tract (DTN). The labelled cells were distributed in a sparse band arching below the margin of the brachium of the superior colliculus between the dorsal and lateral borders of the brainstem at the caudal edge of the pulvinar. Various types of cells could be distinguished. More superficially the cells were extremely spindle shaped, cells deeper within the midbrain had more compact somata. NOT-DTN neurons in the same region were also found to respond with short latencies to electrical stimulation of both the inferior olive and the optic chiasm. All neurons in the NOT-DTN which were antidromically activated from the inferior olive were also found to have direction specific binocular visual responses. Such neurons were excited by ipsiversive motion and suppressed by contraversive motion, regardless of whether large area random dot stimuli moved across the visual field or small single dots moved across the fovea. Direct retinal input to these neurons was via slowly conducting fibers (3–9 m/s) from the monkey's optic tract conduction velocity spectrum. As shown previously for non-primates, NOT-DTN cells may also in the monkey carry a signal representing the velocity error between stimulus and retina (retinal slip), and relay this signal into the circuitry mediating the optokinetic reflex.

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Key words: Nucleus of the optic tract – Dorsal terminal nucleus – Inferior olive – Visual responses – Macaque monkey

Introduction

The mammalian nucleus of the optic tract (NOT) and dorsal terminal nucleus of the accessory optic tract (DTN) consist of a scattered group of neurons located along the ventral margin of the brachium of the superior colliculus (BSC) (Figs. 2 and 3). Lesion and stimulation studies in vertebrates as diverse as amphibians (Fite and Montgomery 1982; Lazar et al. 1983; Manteuffel et al. 1983; Cochran et al. 1984), reptiles, birds (Fite et al. 1979; Gioanni et al. 1983), rats (Cazin et al. 1980), rabbits (Collewijn 1975a), cats (Precht and Strata 1980; Hoffmann 1986), and monkeys (Kato et al. 1986; Schiff et al. 1987) have shown that the NOT and the related nuclei of the accessory optic tract are necessary structures for the optokinetic reflex (OKR) or for visual modification of the vestibulo-ocular reflex (VOR) (Ito et al. 1977). The major known projection of NOT and DTN cells is to the inferior olive (Hoffmann et al. 1976; Maekawa and Takeda 1979; Terasawa et al. 1979; Walberg et al. 1981; Sekiya and Kawamura 1985) which relays visual information to the cerebellum as a climbing fiber input (Maekawa and Simpson 1973).

Since previous studies using cats have shown that neurons in NOT and DTN have identical visual response properties (Hoffmann and Schoppmann 1981; Hoffmann 1983; see also Grasse and Cynader 1984, 1986) and anatomical connections (Ballas et al. 1981; Ballas and Hoffmann 1985) these supposedly separate nuclei may really constitute a functional entirety. Previous anatomical and physiological studies have shown that both the NOT and DTN receive their major visual input directly from the

contralateral retina in non-primates (Scalia 1972; Collewijn and Holstege 1984; Ballas et al. 1981; Farmer and Rodieck 1982) but have also indicated that direct retinal input of the same nuclei is proportionally smaller in monkeys (Giolli 1963; Hendrickson et al. 1979; Benevento 1975; Itaya and van Hoesen 1983; Perry and Cowey 1984; Hutchins and Weber 1985; Weber 1985; Cooper and Magnin 1986). Recent lesion and stimulation studies indicate, however, that the NOT is still important for the OKR even in monkeys (Kato et al. 1986; Schiff et al. 1987). Therefore as a step toward determining their physiological functioning, we attempted to both physiologically and anatomically identify the NOT and DTN and their connections in the macaque monkey. Preliminary reports have been published elsewhere (Hoffmann 1985; Hoffmann and Distler 1986).

Methods

Experimental animals

Three Macaca fascicularis (3–4 kg) and four Macaca mulatta (3–8 kg) were used in these and related experiments. The animals were initially anaesthetized with 20 mg/kg ketamine administered i.m. An intravenous catheter was then introduced into a forearm vein and the monkeys were intubated before being deeply anaesthetized with a subsequent dose of ketamine i.v. Thereafter the animals were placed in a stereotaxic apparatus for surgery and electrode placement, and artificially ventilated with nitrous oxide and oxygen (3 : 1) to greatly reduce the need for subsequent doses of ketamine. At the end of surgery the animals were paralyzed with synthetic toxiferine (Alloferin®) and maintained on a continuous infusion of 6 ml/h saline containing 0.5 ml/kg/h Alloferin and 1 mg/kg/h pentobarbital throughout the 36–72 h recording sessions.

Surgery and electrode placement

To allow access to the optic chiasm (OX), NOT, DTN, and inferior olive (IO) a sagittal incision was made from anterior 20 to posterior 25, and the skin and muscle were retracted.

Inferior olive. Two small holes were opened 1–2 mm on either side of the midline at the most posterior extent of the parietal bone (about 25–30 mm posterior) and a pair of bipolar stimulating electrodes were lowered, at an angle of 45° forward, towards the dorsal cap at the end of the inferior olive. The electrode position had been calibrated to reach the stereotaxic values posterior 2, lateral 1.5, 5 below earbars in Macaca fascicularis (Szabo and Cowan 1984), and posterior 3, lateral 1.5, 6–10 below earbars in Macaca mulatta (Snyder and Lee 1961; Smith et al. 1972). The correct depth of the IO electrode was judged by recording the characteristic climbing fiber and complex spike field potential with an electrode lowered into the cerebellum (Eccles et al. 1967). When angled 45° forward the stimulating electrodes usually had to be moved about 30–35 mm from the surface of the brain to the effective stimulation site within the inferior olive.

Optic chiasm. A second pair of bipolar stimulating electrodes were lowered through holes symmetrically placed 2 mm on either side of the midline at approximately anterior 18. The location of the optic chiasm was first verified by recording strong and brisk visual responses with a tungsten microelectrode.

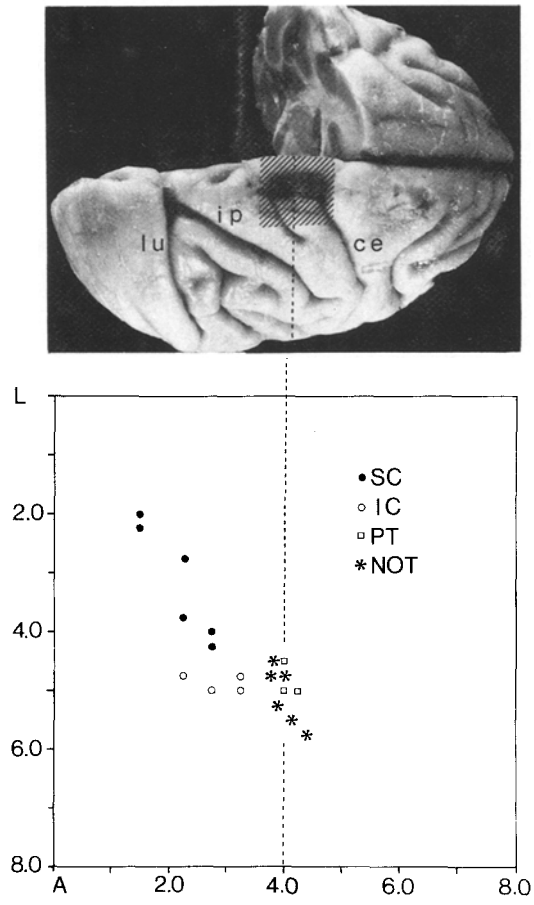

Fig. 1. Scheme illustrating the strategy to localize the nucleus of the optic tract (NOT) and dorsal terminal nucleus of the accessory optic tract (DTN) in Macaca fascicularis. A top view of the monkey's brain is given to outline the area through which vertical penetrations were aimed at the NOT and DTN (shaded square). The following cortical sulci were used as landmarks. lu: lunate sulcus, ip: intraparietal sulcus, ce: central sulcus. Below the photograph of the brain an enlargement of the shaded area is given. It extends from zero to 8 mm anterior (A) along the X-axis and from 8 mm lateral (L) to zero along the Y-axis. In Macaca mulatta this area is 2 mm more posterior. The dotted line at A4 (A2 in Macaca mulatta) marks the position on the brain surface where the electroce had to penetrate to reach the NOT. This was typically very close to a big blood vessel covering the central sulcus. Penetrations which hit the superior colliculus (SC) are marked by filled circles, the inferior colliculus (IC) by open circles, the pretectum (PT) by squares, and the NOT or DTN by stars

Superior colliculus, NOT and DTN. Two rectangular bone openings centered at anterior 2 and lateral 4 were made on either side of the midline to allow access to the superior colliculus (SC), NOT and DTN (Benevento 1975). A tungsten-in-glass recording electrode was first lowered at various places to identify and localize the SC, identifiably by clear and brisk visual responses, small receptive fields, and the characteristic retinotopic organization (Cynader

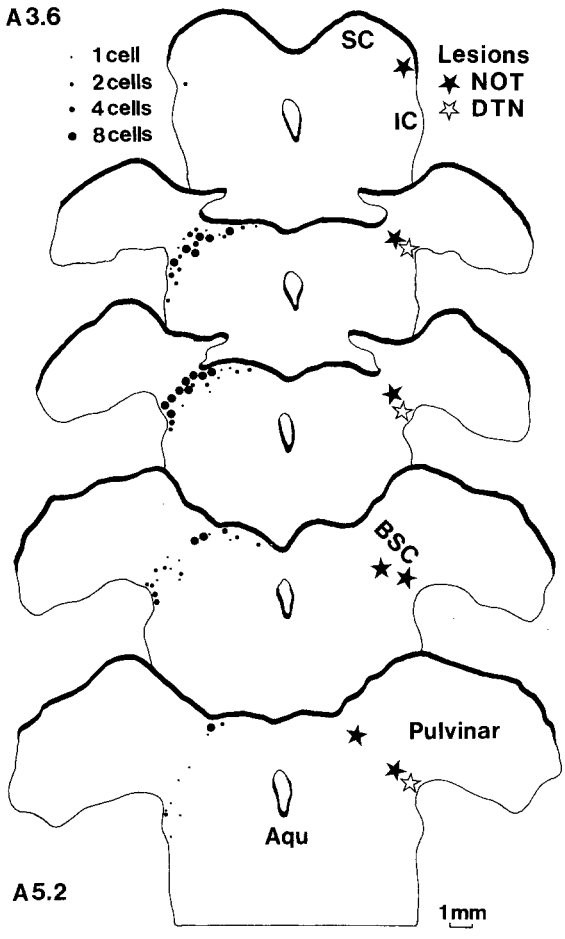

Fig. 2. Serial reconstruction of a macaque monkey's rostral midbrain showing on the left the location of retrogradely labelled cells after horseradish peroxidase injections into the inferior olive and on the right the locations of microlesions in the nucleus of the optic tract and dorsal terminal nucleus. Five 400 μm thick slabs are arranged from top to bottom from anterior 3.6 to anterior 5.2. Each slab summarizes the data from 3 animals and five 80 μm sections per animal. Abbreviations: NOT: nucleus of the optic tract, DTN: dorsal terminal nucleus of the accessory optic tract, SC: superior colliculus, IC: inferior colliculus, BSC: brachium of the superior colliculus, Aqu: aqueduct. Size of filled circles is equivalent to number of retrogradely labelled NOT or DTN cells. Each black and open asterisk marks a microlesion at the recording site of an NOT or DTN cell, respectively

and Berman 1972). Once the SC was localized the recording electrode was used to optimize the location of the OX stimulating electrodes by monitoring the field potential recorded in the SC.

Visual stimulation and data analysis. Visual stimuli were random dot patterns (dot size 1°, area 50 × 40° horizontal and vertical) as well as dots and slits of light of varying sizes. Stimuli were projected via a double mirror system onto a tangent screen 171 cm in front of the animal. Two sine waves voltages 90° phase shifted were applied to the galvanometers carrying the mirrors to produce stimulus movement along a circular path on the screen (Schoppmann and Hoffmann 1976). Triangular signals of different amplitude but of equal phase and frequency could also be selected to move the stimuli along straight paths in different directions. Spike trains were conventionally amplified and passed through a window discriminator circuit. Standard pulses were fed into the lab-interface of a PDP11/34 computer for on-line computation of average response histograms (bin width 1 ms–1 s) displayed in cartesian or polar coordinates. Response strength was calculated as either spikes per second (absolute) or as percent of maximal response (relative).

Histology. In most experiments the physiological study was combined with an anatomical investigation. After the inferior olive had been localized with the stimulating electrodes they were withdrawn and the needle of a Hamilton microliter syringe was lowered to allow injection of 1 μl of 30% horseradish peroxidase (HRP) in distilled water. Afterwards the stimulating electrodes were put back in place. After the end of the recording session, microlesions were placed at the recording sites of NOT- and DTN-units by passing 5 μA (electrode tip positive) for 5–10 s. At the end of experiments the animals were sacrificed with an overdose of pentobarbital and perfused through the heart with 1.25% glutaraldehyde and 2% paraformaldehyde in phosphate buffer (pH 7.4). Alternate sections were reacted for tetramethylbenzidine-HRP histochemistry (Mesulam 1978, as modified by Horn and Hoffmann 1987) and Nissl staining for confirmation of recording sites in the NOT and DTN.

Results

Based upon the results of previous studies of the NOT and DTN in cats (Hoffmann and Schoppmann 1981; Grasse and Cynader 1984; Ballas and Hoffmann 1985), three criteria were used to classify putative NOT cells in monkeys. These were, 1) the recording location immediately anterior and lateral to where collicular cells with receptive fields near the vertical zero meridian were found, 2) the strong direction selective response to movement of a large random dot pattern, and 3) the antidromically evoked response from the inferior olive (IO). The orthodromic response to optic chiasm (OX) stimulation proved to be a too unreliable response to be useful as a classifying criterion.

Identification of NOT cells

1. Location. The midbrain was approached from above using vertical penetrations aligned with the sagittal and frontal stereotaxic planes (Fig. 1). The first step in locating NOT and DTN cells was to identify the representation of the fovea in the SC. From here the recording electrode was moved in 0.5 mm steps laterally and forward until the fiber layer of the brachium of the SC was encountered. With more anterior penetrations, the most medial and caudal aspects of the pulvinar was encountered first, and only after penetrating its cell layers did the electrode approach the fibers of the BSC. In this region a systematic search for neurons fulfilling the

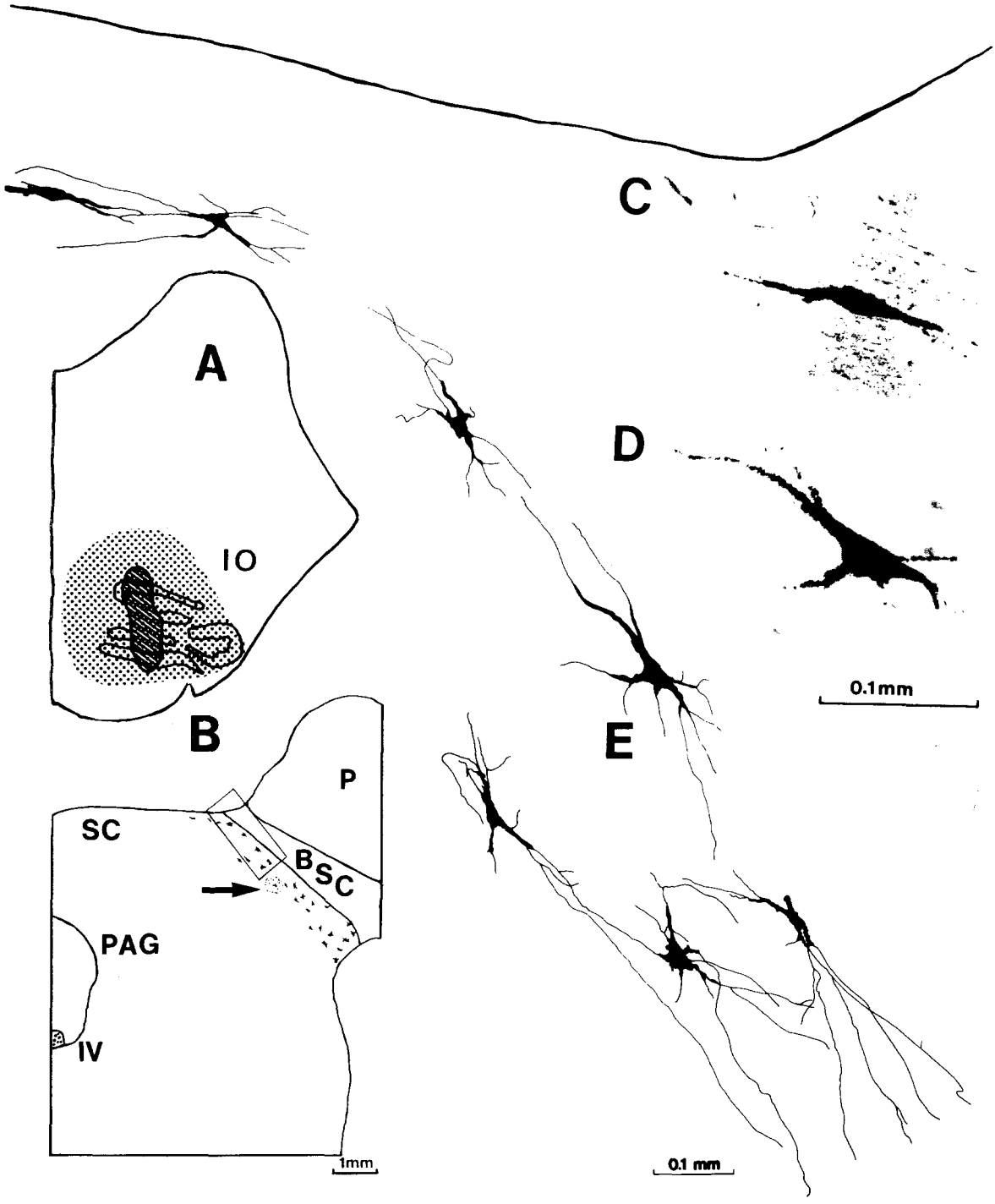

Fig. 3A–E. Synopsis of cells within the nucleus of the optic tract (NOT) and dorsal terminal nucleus (DTN) projecting to the inferior olive in macaque monkeys. **A** Drawing of a section through the lower brainstem at the level of the inferior olive (I.O.) showing the injection site (stripes and dots) and the spread of the tracer horseradish peroxidase (dots). The penetration is rostral to the dorsal cap so that axons from the NOT were probably damaged and could have taken up the tracer. **B** Summary scheme of 10 superimposed 40 μm frontal sections through a monkey's pretectum. Black arrow points to a micro lesion in the NOT at the recording site of a neuron exhibiting direction selective visual responses and an antidromic spike to electrical stimulation at the inferior olive. The lesion was found to be located in the middle of a band of cells retrogradely labelled by an injection of horseradish peroxidase into the inferior olive. **C–E** Photomicrographs and camera lucida drawings of retrogradely labelled NOT-cells. For further description of cell types see text. Abbreviations: SC superior colliculus, PAG periaqueductal grey, IV nucleus nervus trochlearis, P pulvinar, BSC brachium of the superior colliculus

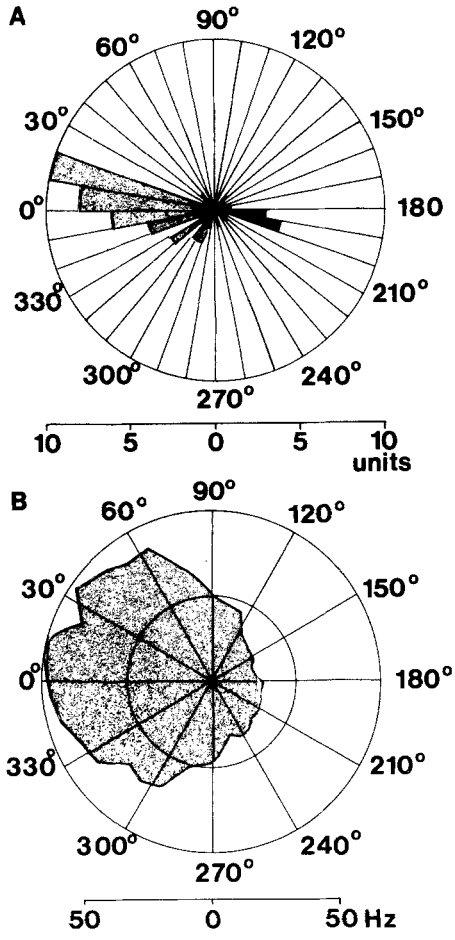

Fig. 4A, B. Preferred directions of visual stimulus motion (**A**) and directional tuning curve (**B**) of neurons recorded in the nucleus of the optic tract (NOT) and dorsal terminal nucleus (DTN) of macaque monkeys. **A** The preferred directions of 39 neurons from 7 animals are plotted in 10° wide sectors of a polar histogram. 27 neurons from the left NOT preferring movements to the left are presented by shaded sectors, 12 neurons from the right NOT preferring movements to the right by black sectors. Most neurons prefer movements along the horizon. **B** Continuous mapping of direction specificity was carried out by moving an extensive random dot pattern along a circular path and accumulting average response histograms (see methods). The average responses measured for individual cells in spikes/s were then averaged for all 7 cells investigated in the left NOT of one animal and displayed in polar coordinates. The central circle represents spontaneous activity (30 spikes/s), the outer circle maximal activation (67 spikes/s). The activity is clearly reduced below spontaneous activity when the stimulus moves in the direction opposite to the preferred one

above three criteria was started. While searching for NOT and DTN neurons a large-area random dot pattern was moved horizontally across the tangent screen. This facilitated the localization of NOT neurons because a clearly direction specifically modulated neuronal background activity could be heard when these neurons were approached. When the electrode was lowered in the left NOT neuronal activity increased sharply with leftward movement whereas on the right side the activity increased with rightward movement of the stimulus pattern. Single NOT units were isolated and identified with the help of antidromic activation from the inferior olive.

Figure 2 shows a summary diagram of all recovered microlesions marking the recording sites of NOT and DTN neurons fulfilling at least two of our criteria as well as the distribution of retrogradely labelled cells in the NOT after HRP injections into the inferior olive. The cells retrogradely labelled after IO injections (Fig. 3A) were distributed in a sparse band arching below the margin of the BSC between the dorsal and lateral borders of the brainstem at the caudal edge of the pulvinar (Figs. 2 and 3E). A variety of NOT cells were observed, some with distinctly different morphological appearance. More superficially the cells were extremely spindle shaped with an elongated soma fusing with dendrites of diameter equal to that of the soma (Fig. 3C). Cells deeper within the midbrain had more compact somata with several dendrites branching in different directions from the soma (Fig. 3D). Camera lucida drawings of several cells are presented in Fig. 3E. Such detail was achieved by using a combination of dark field illumination and polarized light and by reconstructing neurons across several sections of 40–80 μm thickness.

2. Direction selectivity. In 31 penetrations through the monkeys pretectum 125 putative NOT neurons were studied. The 31 neurons on the right side all preferred stimulus movements to the right in the visual field. All 94 units recorded on the left side preferred stimulus movements to the left. Thus all NOT and DTN cells preferred ipsiversive stimulus movement. The directional tuning curves obtained in 39 neurons with large area random dot stimuli moving along a circular path were broad (half width: 120°) and the preferred directions often deviated somewhat ± 30° from the horizon. The preferred directions of individual neurons are shown in Fig. 4A and the pooled responses of all neurons recorded in the left NOT of one animal are represented in the polar histogram of Fig. 4B. Movement in the direction opposite to the preferred one almost always led to the weakest response. In addition to the clear response to large area random dot stimuli NOT and DTN neurons were also strongly activated by single small spots and narrow slits of light (1° visual angle). When these stimuli crossed the fovea they elicited responses in the same direction and as strong as whole field stimulation. All cells tested were binocular, and the preferred direction in visual space was always identical through either eye.

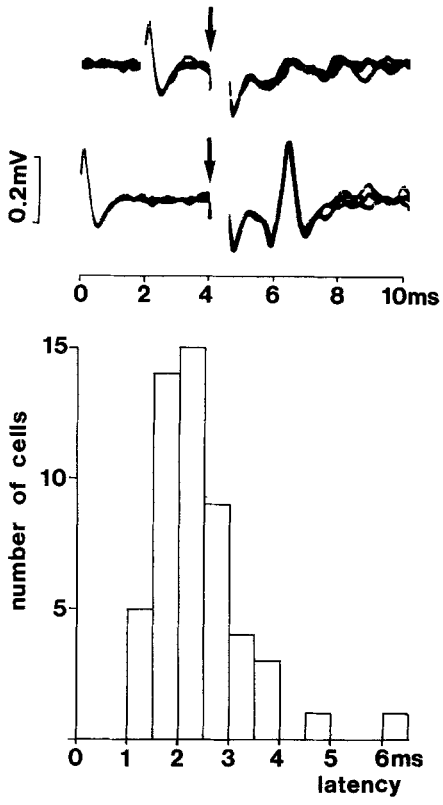

Fig. 5. Latency frequency distribution of antidromic responses elicited from inferior olive in 52 cells of the nucleus of the optic tract and dorsal terminal nucleus. The antidromic nature of the action potential was verified by a collision test as shown on top. Spontaneous spikes were used to trigger the electrical pulse with an adjustable delay. Pulse onset is marked by the black arrow. In the upper trace spontaneous spikes precede the electrical pulses by less than the latency of the antidromic response. The antidromic action potentials collide with the spontaneous spikes and are obliterated. In the lower trace spontaneous spikes precede the electrical pulse by more than the latency of the antidromic response and the antidromic action potentials occur with a fixed latency of 2 ms. Time is presented on the abscissa in ms. Amplitude of action potentials in mV or number of cells are presented on the ordinate

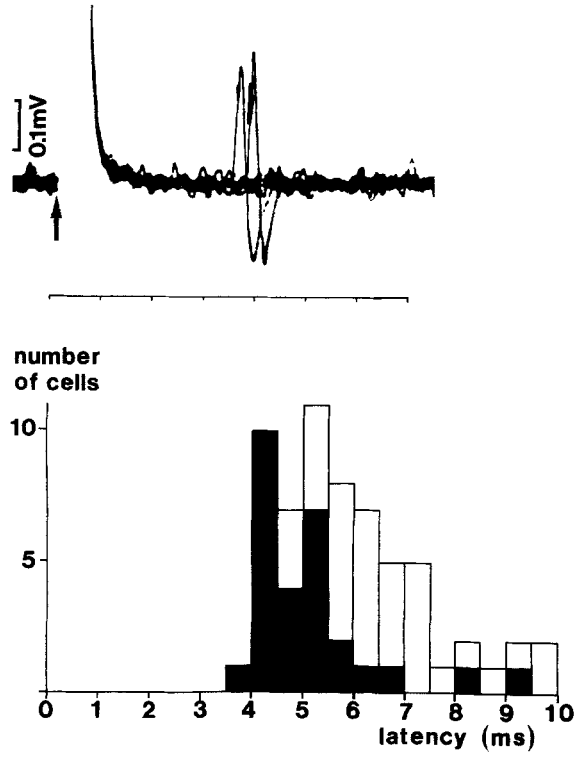

Fig. 6. Latency frequency distribution of orthodromically evoked action potentials in cells of the nucleus of the optic tract (NOT) and dorsal terminal nucleus (DTN) by electrical stimulation of the optic chiasm (OX) in macaque monkeys. Time is presented on the abscissa in ms, spike amplitude in mV and number of cells is given on the ordinate. On top an example of NOT and DTN cell responses to OX stimulation is given. 5 superimposed oscilloscope traces are presented. Onset of electrical stimulation is marked by the black arrow. Only 2 spikes at latencies of 3.5 ms and 3.7 ms are elicited. Black bars in the histogram (bottom) represent the shortest latency measured in each cell. Open bars represent the latencies of second and third spikes sometimes elicited by one electrical shock

3. Antidromically evoked responses from the inferior olive. The results of electrical stimulation of the inferior olive are shown in Fig. 5. The antidromic character of the action potential elicited in NOT and DTN cells by electrical stimulation of the inferior olive was verified by three criteria: 1) the fixed spike latency that varied by less than ± 0.1 ms; 2) the constant occurrence of the spike at stimulation frequencies as high as 200/s; and 3) a collision test to show that an orthodromic spike obliterated the antidromic spike whenever the former preceded the latter by less than twice the latency between stimulation of the inferior olive and the antidromic response (collision test, see Fig. 5 top). All 52 cells antidromically activated by inferior olive stimulation met the other criteria for putative NOT cells, suggesting that only pretectal neurons preferring ipsiversive stimulus movement project to the inferior olive. 26 cells recorded in the same location could not be activated antidromically but also preferred ipsiversive movement. Although it was not possible to complete all the tests on every cell there was a remarkable correlation between ipsiversive directional preference and the occurrence of an antidromic action potential in the NOT cells. The latency spectrum of antidromic activation had a clear peak at 2 ms (Fig. 5, bottom). In the region of the NOT and in the SC no cells with other response properties were found to be antidromically driven.

4. Orthodromically evoked responses from the optic chiasm. In order to test for a direct retinal input to the NOT and DTN in monkeys, electrical shocks

were applied to the optic chiasm (OX). Only about half of the cells meeting the other criteria for NOT cells could be effectively influenced by OX-stimulation. A typical example and the frequency distribution of the response latencies are depicted in Fig. 6. In order to quantify the efficacy of OX-stimulation we applied 10 shocks with maximal stimulus strength and counted the number of spikes elicited. On average only about 3–5 spikes were generated by 10 shocks (Fig. 6, top). This result, taken together with the lack of response to OX-stimulation in more than half of the NOT and DTN cells, indicates a weak and irregular synaptic drive from retinal axons. The latency of a given cell was quite stable but the whole population showed latencies in the range from 3–7 ms (Fig. 6, bottom). Assuming a conduction distance from OX to NOT and DTN of about 20–22 mm and one synaptic delay of 0.5 ms the conduction velocity of retinal axons involved in this pathway is 3–9 m/s.

Discussion

This study clearly establishes the existence of a pretectal relay of visual information to the ipsilateral inferior olive in the monkey and indicates that NOT and DTN neurons in the macaque have properties qualitatively similar to those previously reported for these cells in other mammals (for recent reviews see Simpson 1984; Hoffmann 1986).

1. Locaction

The location and distribution of the physiological recording sites and the cells retrogradely labelled after olivary HRP injections in the monkey is nearly identical to their distribution in the cat (Walberg et al. 1981; Ballas and Hoffmann 1985; Sekiya and Kawamura 1985). The only noticeable difference in this regard is that substantially fewer cells were retrogradely labelled in the monkey as compared to the cat. In the recording experiments, however, NOT and DTN cells were much more easily and frequently found in the monkey than the cat. A possible explanation of this discrepancy is that a smaller proportion of these cells project to the IO in the monkey. A parallel finding in the electrophysiological studies was that a substantial proportion of NOT and DTN cells in the monkey were not antidromically activated by IO stimulation, whereas nearly 100% of such cells in the cat were activated (Hoffmann 1983). It is unlikely that these results were due to errors in placement of the HRP injections or stimulation electrodes since excellently filled cells were obtained and groupings of antidromically activated and non-activated cells were identified in the same animal using the same stimulation site for the bipolar electrodes. Such pairs of electrodes activate a large area of tissue and our reconstructions verified their location within the IO. These results support previous claims by Magnin et al. (1983), Cazin et al. (1984) and Maekawa et al. (1984) that some of the NOT neurons project to brainstem sites other than the IO.

2. Cell properties

The monkey NOT and DTN cells are driven by ipsiversive movement of large stimuli, similar to these cells in other mammals (Collewijn 1975b; Cazin et al. 1980; Hoffmann and Schoppmann 1981; Grasse and Cynader 1984). A clear difference in the monkey, however, is the responsiveness of NOT and DTN cells to very small stimuli as well as to large patterns. This property was also reported by Westheimer and Blair (1974) in their study of visual responses in the region near the medial terminal nucleus of the monkey accessory optic tract. The distribution of preferred directions for cells in the NOT appears similar in the monkey and rabbit (Maekawa et al. 1984) including the few cells which were driven by contraversive movement and which were not antidromically activated by IO stimulation.

The observation that 100% of monkey NOT and DTN cells are binocularly driven is distinctly different from all other mammals. In the cat only 40% of NOT cells and 90% of DTN cells were found to be binocular (Hoffmann and Schoppmann 1981; Grasse and Cynader 1984). Since only a small retinal projection to the ipsilateral NOT and DTN is anatomically demonstratable in monkeys (Lin and Giolli 1979; Hutchins and Weber 1985) and the cells remain binocular after callosal section (personal observation) the balanced input from the ipsilateral and contralateral retina presumably employs mostly ipsilateral geniculocortical relays.

3. Antidromic latencies from IO

The latency for antidromic activation of NOT and DTN cells after IO stimulation of approximately 2 ms is similar to the shortest of the latencies observed in the cat (Hoffmann 1983) and rabbit (Maekawa et al. 1984). No latency difference between DTN and NOT neurons was observed.

4. Orthodromic latencies from OX

The latency of the orthodromic response in the NOT and DTN after OX stimulation is also similar in monkeys and in cats. The latencies of 2–8 ms and

3–7 ms in cats and monkeys, respectively, for estimated conduction distances of 15 mm and 21 mm, result in calculated conduction velocities (assuming one synaptic delay of 0.5 ms) of 3–9 m/s in monkeys and 2–10 m/s in cats (cats data from Hoffmann and Schoppmann 1981; Grasse and Cynader 1984). Although somewhat similar in cat and monkey, the retina-NOT conduction velocity appears to be much faster in rabbits (10–30 m/s, Collewijn 1975b; Maekawa et al. 1984). Despite the similar activation latency, the retinal input to the NOT in the monkey appeared to have a proportionally lower weighting than retinal input in the cat. OX shocks in the cat had an almost 100% probability of activating their physiologically identified target cells in the NOT. In the monkey this probability was on the order of 30%. All these properties reflect an increased cortical input to the NOT in monkeys (paper in preparation) but with preservation of direct retinal input as well.

Direction selective ganglion cells with slowly conducting axons belonging to the slowest group in the optic tract have not yet been found in the monkey retina. Such slowly conducting axons are shown in the present study to project into the NOT, DTN and to the SC. Their incidence as a proportion of total ganglion cells would make this type of unit extremely difficult to record in monkeys (Perry and Cowey 1984). The observation of a residual asymmetric monocular OKR immediately after bilateral occipital lobectomy in monkeys (Zee et al. 1986) clearly suggests that a direction selective signal may be carried by the slowly conducting fibers projecting from the retina to the contralateral NOT and DTN as has been suggested for rabbits (Oyster et al. 1972) and cats (Hoffmann and Stone 1985). Monkey retinal ganglion cells with slowly conducting axons and special receptive field properties have been found (Schiller and Malpeli 1977; de Monasterio 1978) and it may be argued that such slowly conducting axons form a substantial proportion of the monkey's optic nerve (Sanchez et al. 1986), analogous to the cat (Bishop et al. 1969; Hoffmann 1973). Therefore, these special or rarely encountered ganglion cells may be much more numerous in the monkey retina than previously reported. The very pronounced late field potential recorded in the SC of the monkey after electrical stimulation of the optic chiasm in this study could be mediated by such slowly conducting fibers.

5. Significance of the NOT in primates

The output of NOT and DTN cells provides an important link in the pathway subserving the OKR. It is particularly striking that there is a clear segregation of preferred directions for NOT and DTN neurons on each side of the brain and that all such cells are binocular. These findings are consistent with the nearly complete symmetry of monocularly tested OKR in normal adult monkeys (Pasik and Pasik 1964; Koerner and Schiller 1972) and with the direction specific deficit after unilateral NOT-lesion (Kato et al. 1986). A lesion of the left NOT in monkeys leads to a deficit of OKR with leftward optokinetic stimulation and vice versa just as reported for other vertebrates (see Introduction). Similar cases have not yet been reported in humans since it is unusual to have vascular or traumatic lesions restricted to the appropriate region. In addition to its importance for the OKR it also seems clear that the visual modification of the monkey's VOR relies on the NOT-inferior olive pathway (Lisberger et al. 1984; Miyashita 1986).

Optokinetic responses in humans can be elicited by selective retinal stimulation, even by single dots, and the greatest effect is achieved with presentation of moving stimuli to the central retina (Cheng and Outerbridge 1975; Dubois and Collewijn 1979). This corresponds to the higher sensitivity of NOT and DTN neurons when single small objects were moved across the fovea. A possible contribution of these neurons to smooth pursuit can of course only be tested in alert monkeys and experiments in this direction will be our next goal.

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Received April 23, 1987 / Accepted July 31, 1987