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Pathways Mediating Optokinetic Responses of Vestibular Nucleus Neurons in the Rat

L. Cazin*, W. Precht, and J. Lannou**

Neurobiologische Abteilung, Max Planck Institut für Hirnforschung, Deutschordenstrasse 46, D-6000 Frankfurt, Federal Republic of Germany

Abstract. 1. The effects of various brain lesions on the responses of vestibular nuclear neurons (Vn) of the horizontal semicircular canal system to optokinetic stimulations were studied to elucidate the optokinetic path from the retina to the vestibular nuclei. A previous study performed in intact rats served as a control [2].

2. It was shown that the pretectal region including the n. of the optic tract is the first central relay in the optokinetic path; it receives its functionally effective input from the contralateral eye. Unilateral lesions of this area rendered all Vn responses unidirectional when tested with binocular stimulation. Lesions of other visual centers such as the superior colliculi or visual cortices had no influence on the optokinetic response properties of Vn.

3. The area of the n. reticularis tegmenti pontis (NRTP) proved to be an important link between pretectum and vestibular nuclei: Unilateral lesions produced effects similar to those described for pretectal lesions. Pretectal axons to NRTP descend lateral to the MLF and tectospinal tract.

4. It was demonstrated that the vestibular commissure plays the crucial role in mediating the mirror image optokinetic effects to Vn on the opposite side and assures the bidirectionality of the responses to binocular stimulation.

5. Cerebellectomy did not significantly affect the Vn responses to the optokinetic stimuli presented in this study.

6. Electrical stimulation of the pretectum excited type II and inhibited type I Vn ipsilaterally and had the opposite effect on Vn located on the opposite side. NRTP stimulation excited type II and inhibited type I ipsilaterally; latency analysis of these effects suggested that the pretectal stimuli excited ipsilateral NRTP neurons which, in turn, excited ipsilateral type II Vn. Ipsilateral type I inhibition as well as the concurrent contralateral type II inhibition and type I excitation are produced by the inhibitory action of type II on type I and the commissural system.

7. Systemic application of picrotoxin abolished all optokinetic responses of Vn except the type II activation. This finding further supports the hypothesis described above.

8. Unilateral pretectal or NRTP lesions abolished OKN to surround motion in the direction of the lesion.

Key words: Optokinetic system – Vestibular nuclei – Pretectum – Eye movement.

Introduction

In a preceding paper we described the response characteristics of rat vestibular nucleus neurons (Vn) of the horizontal semicircular canal system to optokinetic stimulation [2]. It was shown that in the rat, as in other species (for ref. see [2]), the great majority of Vn respond to rotation of large-field pattern in a direction-selective fashion in the absence of any vestibular stimulation. In spite of the interspecies similarities in response pattern the rat exibits a number of distinct differences when responses were analyzed more quantitatively. The most dramatic difference was an almost complete absence of a response in rat Vn to nasotemporal stimulation with monocular stimulus presentation. Similarly, optokinetic nystagmus (OKN) was absent in this direction. In particular, this finding makes the study of the yet unknown optokinetic pathway to Vn somewhat easier in the rat than in other species in which both nasotemporal and temporonasal

*,** Supported by a fellowship from the Max Planck Society
Present address: Université de Rouen, Lab. Neurophysiologie, 10 Boulevard de Broglie, 76 Mont-Saint-Aignan, France

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responsiveness are noted [8, 14]. Such species differences may be related to the ratio between crossed and uncrossed optic projections to the pretectum [1, 5, 16], differences in the functional organization of retinal ganglion cells and/or central optokinetic pathways and the presence or absence of a fovea [18].

The present experiments were, therefore, undertaken in the rat to trace the optokinetic pathways to the vestibular nuclei. It is known that this species is afoveate and has predominantly, if not exclusively, crossed optic projection to the pretectum [16]. To this end, lesions were placed in various relay nuclei and tracts that may serve as candidates for mediating optokinetic effects. After the lesions have been made Vn responses to optokinetic stimuli were studied and they were compared to those previously established in control animals [2]. In addition, electrical stimulation of relay nuclei was applied to further establish the course of the optokinetic path. To correlate deficiencies in Vn responses with optokinetically induced eye movements (OKN) horizontal eye movements (EOG) were recorded in several of the lesioned animals. The present data will be compared to those established with similar techniques in the cat [14] which has both crossed and uncrossed projections [1]. Portions of this work have appeared in abstract form [13].

Materials and Methods

Recording and stimulation procedures as well as data analysis techniques have been described in detail in the preceding paper [2]. Here we shall only briefly summarize the essential points and describe additional procedures used in the present study.

Adult brown rats (DA-HAN) were used throughout this study. Electrolytic lesions (pretectum, midbrain reticular formation, sup. colliculus, medial longitudinal fasciculus, n. reticularis tegmenti pontis), suction lesions (visual cortex, cerebellar) and section lesions with a fine knife (vestibular commissure) were performed under ether anesthesia and animals were prepared for single unit and/or electrooculogram (EOG) recordings in the same session.

With each type of lesion experiments were started between 2 h and 2 days after cessation of ether anesthesia. Since there was no significant difference between the response characteristics measured acutely and those recorded after 2 days all data were pooled and treated as one population. In case of unilateral lesions the state of the animal during the recording session was judged from the comparison of the amplitudes of the unit responses to optokinetic stimuli of 1 deg/s to the intact side with the mean response curve described earlier [2]. When the sensitivity of the responses clearly diverged from the normal range of control responses the experiments were terminated. With the exception of the bilateral pretectal lesion all other bilateral lesions performed in this study yielded optokinetic responses that were similar to those obtained in control animals [2] indicating that the animals were in good condition.

In case of the former we had to rely on the sensitivity of the animal to arousing stimuli (e.g. sound or touch) which were often seen in reticular units recorded just ventral to the vestibular nuclei. Vestibular responses of Vn proved rather unreliable indicators of general condition since they were the last responses to disappear when the condition of the animal became worse.

In order to obtain optimal recording stability for complete quantitative analysis of single Vn, we found it necessary to relax (with Flaxedil) and artificially respire animals during the recording sessions. It should be emphasized that in this relaxed state the eyes do not move, so that the velocity of the visual surround stimulus is equal to retinal slip velocity. In most cases surround velocity measured 1°/s. This value was chosen because most units showed a response maximum at this velocity [2].

In 14 animals stimulating electrodes consisting of stainless steel wires insulated except for the tip, were inserted into the pretectum and n. reticularis tegmenti pontis (NRTP) for monopolar stimulation. Stereotaxic coordinates were taken from the atlas by Pellegrino and Cushmann [11]. Stimulus currents ranged from 30–200 μA. Peristimulus histograms of Vn firing were generated with the aid of a Nicolet computer, and sample records of actual spikes were taken with a kymograph camera.

In 4 additional animals an isotonic sodium chloride solution containing picrotoxin (2 mg/kg) was injected intravenously while recording Vn activity in response to optokinetic stimuli.

All lesions were reconstructed from cresyl violet stained serial sections. Recording sites in the vestibular nuclei were identified as described earlier [2].

Results

The optokinetic responses of a total of 233 Vn which selectively responded to horizontal angular acceleration in the dark (pure vestibular stimuli) were studied in 30 rats lesioned in various parts of the brain (see below). As in the preceding paper [2] Vn were recorded in the vestibular nuclei (medial and superior nuclei) on either side of the lesions and were classified according to their vestibular responses as type I or type II neurons. A given Vn response to optokinetic stimulation was considered qualitatively normal when it showed: 1) the well-known bidirectionality (symmetrical or asymmetrical) to ipsi- and contralaterally directed stimuli with binocular viewing and 2) the unidirectional responses in monocular condition [2]. To assess the integrity of the responses at the quantitative level we studied the response magnitudes of most units with optokinetic stimulus velocities of 1°/s (left/right). This velocity has been shown to yield the maximal frequency increases ($+\Delta f$) and decreases ($-\Delta f$) in rat Vn in our control study [2]. In the following, those lesions which resulted in the most dramatic changes in Vn activity will be described first followed by the description of the weakly or non-effective lesions.

Lesions Strongly Affecting Optokinetic Responses

a) Pretectal Lesions. There is strong experimental evidence suggesting that the pretectum is a crucial link in the afferent path of the horizontal optokinetic reflex arc in rabbit [3] and cat [14]. Among the various pretectal nuclei the nucleus of the optic tract (NOT) is, most likely, the first relay nucleus since its neurons in

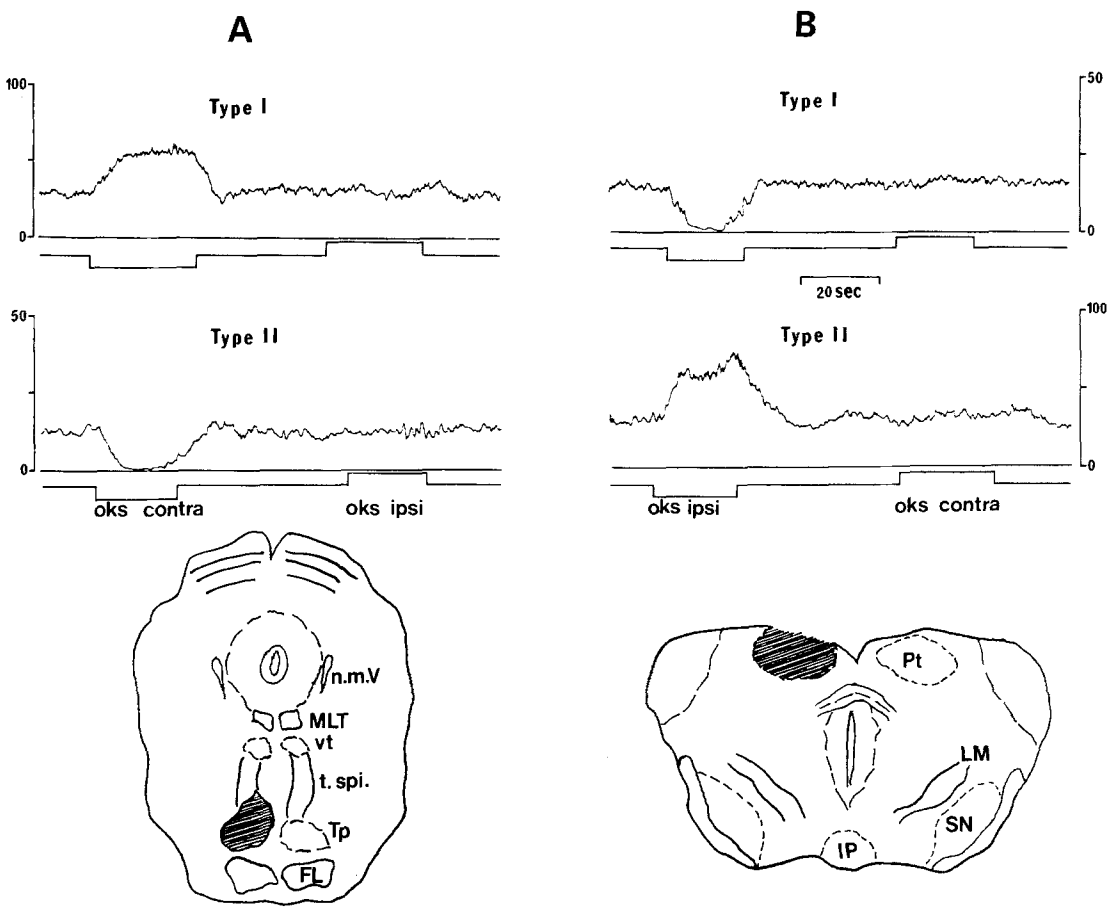

Fig. 1 A and B. Effects of lesions in the left Nucleus reticularis tegmenti pontis (**A**) (*Tp*) or in the left pretectal area (**B**) on optokinetic responses of type I and II vestibular neurons. The projection drawing below each set of recordings give the extent of the lesions (hatched area) at their maximal extensions. Note that on the side ipsilateral (contralateral) to the lesions, the responses to ipsilateral (contralateral) OKS (1°/s constant velocity) are completely abolished. *n.m.V* nucleus mesencephalicus V; *MLT* medical longitudinal tractus; *vt* nucleus ventralis tegmenti; *t.spi.* tractus tecto-spinalis; *FL* fasciculus longitudinalis; *LM* lemniscus medialis; *IP* nucleus interpeduncularis; *SN* substantia nigra

rabbit and cat have response characteristics similar to those recorded in Vn and compatible with OKN and receive direct projections from the retina [4, 7]. Furthermore, electrical stimulation of the NOT generates nystagmus while lesions abolish OKN [3, 4, 14]. To test the importance of the pretectum in the rat for optokinetic responses of Vn we placed unilateral (5 animals) and bilateral (2 animals) lesions in the area of the NOT and recorded Vn activity thereafter.

Figure 1B shows a projection drawing of the extent of one lesion in the left pretectum and the effect on type I and type II Vn responses in the right vestibular nucleus during optokinetic stimuli (ipsi- and contralateral) with both eyes open. With this lesion optokinetic responses of both type I and type II Vn became unidirectional, i.e. both types did not respond to contralateral stimulation. Similarly, responses from the nucleus ipsilateral to the lesion were unidirectional but of opposite polarity (Table 1). In contrast, when the eye ipsilateral to the pretectal lesion was covered no responses were seen in ipsi- and contralateral Vn. This suggests that only the contralateral retinotectal projection was important. Absence of any responses was also obtained in animals with bilateral pretectal lesions.

It should be noted that inspite of the disturbance of Vn response directionality, the Δf values of type I and type II neurons (Table 1A) are not significantly different to those recorded in control animals when comparing the binocular or monocular conditions (Table 1, in [2]).

b) Midbrain Reticular Lesions. A total of 23 units was recorded in 2 rats that had unilateral lesions in the midbrain reticular formation just ventral to the pretectum. As shown in Table 1 B the results obtained with this type of lesions are identical to those obtained with

Table 1 A—C. Effects of various lesions on Vn type I and type II responses to optokinetic stimuli (OKS stimulus velocity = 1 deg/s) in paralyzed animals with both eyes opened. **A** Unilateral (left) pretectal lesions (5 rats), **B** unilateral midbrain reticular lesions (2 rats); **C** unilateral (left) lesion of the n. reticularis tegmenti pontis (4 rats). Of the 39 units, 5 showed a very weak response to ipsi-(lesioned side) and contralateral OKS (intact side). Δf = mean frequency increase ($+\Delta f$) or decrease ($-\Delta f$) of Vn discharge in imp/s

A	Lesioned side		Intact side	
	Type I ($n = 12$)	Type II ($n = 15$)	Type I ($n = 5$)	Type II ($n = 11$)
OKS contralateral	Excitation $+\Delta f = 16 \pm 6.78$	Inhibition $-\Delta f = 9.93 \pm 4.24$	No excitation	No inhibition
OKS ipsilateral	No inhibition	No excitation	Inhibition $-\Delta f = 11 \pm 4.05$	Excitation $+\Delta f = 15.05 \pm 7.33$

B	Lesioned side		Intact side	
	Type I ($n = 6$)	Type II ($n = 6$)	Type I ($n = 4$)	Type II ($n = 7$)
OKS contralateral	Excitation $+\Delta f = 15.33 \pm 7.65$	Inhibition $-\Delta f = 8.42 \pm 2.63$	No excitation	No inhibition
OKS ipsilateral	No inhibition	No excitation	Inhibition $-\Delta f = 10.88 \pm 3.71$	Excitation $+\Delta f = 11.14 \pm 5.41$

C	Lesioned side		Intact side	
	Type I ($n = 13$)	Type II ($n = 18$)	Type I ($n = 6$)	Type II ($n = 2$)
OKS contralateral	Excitation $+\Delta f = 11.04 - 3.13$	Inhibition $-\Delta f = 11 \pm 5.42$	No excitation	No inhibition
OKS ipsilateral	No inhibition	No excitation	Inhibition $-\Delta f = 10.83 \pm 6.55$	Excitation $+\Delta f = 9 \pm 1.41$

the dorsal pretectal lesions. The similarity even holds at the quantitative level as a comparison of Δf values in Table 1 A and B shows ($P < 0.05$).

c) Lesions in the n. Reticularis Tegmenti Pontis (NRTP). So far, our lesion studies have shown that in the rat the NOT region as well as structures ventral to it are essential for generating the proper optokinetic responses in Vn. It appears that pretectal neurons which receive inputs from the contralateral eye project to, or travel through, deeper areas in the midbrain. We now ask: what is the next link in the optokinetic path before is reaches Vn? It was found that lesions involving the region of the NRTP affected Vn responses the same way pretectal and deep midbrain lesions did (Table 1 C). This finding suggests that the optokinetic path either synapses in or passes through this nucleus.

A typical lesion of the left NRTP is shown in Fig. 1 A, and the responses recorded from type I and type II neurons located in the left vestibular nuclei to ipsi- and contralateral optokinetic stimuli are illustrated. It will be noted that these effects are very similar to those described for pretectal lesions (compare Table 1 A and C). Interestingly, lesions placed at the same anterior-posterior level but more dorsally and involving the tectospinal tracts (2 animals), ventral tegmental nucleus (2 animals) or medial longitudinal fascicle (3 animals) had no appreciable effects on Vn responses to optokinetic stimuli.

Whereas the Δf values of the pretectal and midbrain lesioned animals were not significantly different from each other and from control values, Δf values were different in NRTP lesioned animals (Table 1 A – C, D): the $+\Delta f$ values were significantly ($P < 0.05$) smaller than those of controls and close to the $-\Delta f$ values. The latter, however, were not significantly different from those noted in control animals (Table 1, in [2]).

d) Lesion of the Vestibular Commissure. In the preceding paper we have shown that with both eyes open type I and type II neurons responded with a decrease/increase to ipsilaterally directed stimulus motion and showed an increase/decrease on reverse stimulation (see Table 1, in [2]). This response bidirectionality was abolished when one eye was closed, i.e., type I and type II units located ipsilateral to the closed eye

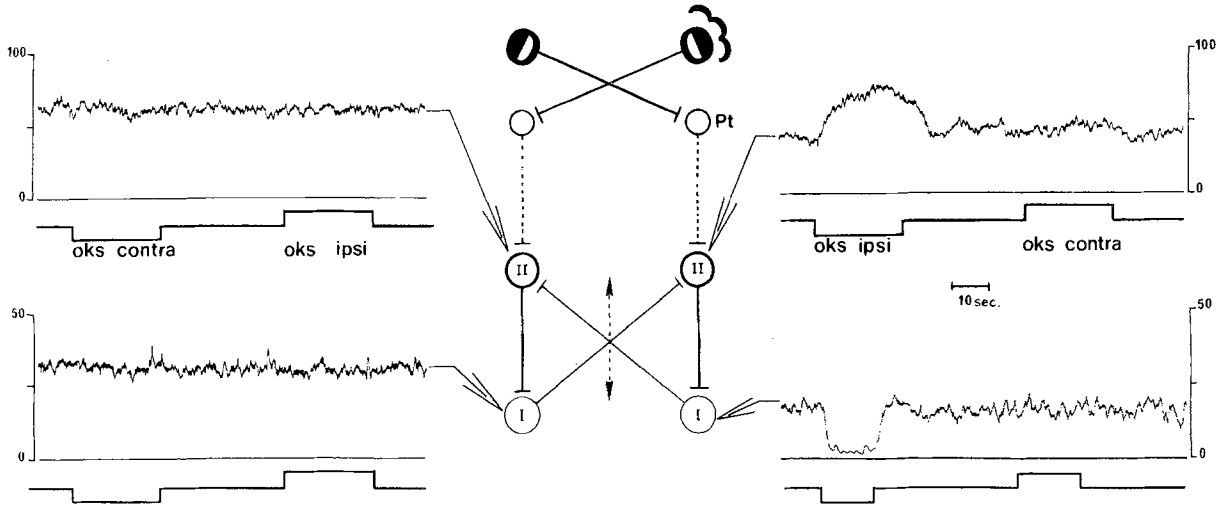

Fig. 2. Effects of midline section of the vestibular commissure on monocular optokinetic responses of type I and II vestibular neurons. Note the lack of response to OKS (1°/s) on the side contralateral to the covered eye. On the ipsilateral side, responses are unidirectional and only elicited by OKS ipsilateral to the recording side. The schematic between the recordings gives the basic wiring of the commissural connections. Note that type II neurons are inhibitory and type I excitatory in nature in this simplified diagram (for details, see text)

Table 2. Effects of sectioning the vestibular commissure on the responses of Vn to optokinetic stimuli (OKS velocity = 1°/s) in one or two eye opened condition. Numbers give mean $\pm \Delta f$ values obtained in 38 units in 6 rats. Of these, only 3 units showed weak responses to OKS contra, presumably due to incomplete sectioning of the commissure

D	Both eyes opened		Ipsilateral eye covered		Contralateral eye covered	
	Type I ($n = 21$)	Type II ($n = 17$)	Type I ($n = 13$)	Type II ($n = 6$)	Type I ($n = 13$)	Type II ($n = 6$)
OKS contralateral	No excitation	No inhibition	No excitation	No inhibition	No excitation	No inhibition
OKS ipsilateral	Inhibition $-\Delta f = 10.59 \pm 6.56$	Excitation $+\Delta f = 13.32 \pm 9.91$	Inhibition $-\Delta f = 12 \pm 5.59$	Excitation $+\Delta f = 9 \pm 5.40$	No inhibition	No excitation

decreased/increased their firing on ipsilateral and showed no responses on contralateral optokinetic stimuli; on the contralateral side units showed the reverse pattern (Table 1, in [2]). In the following we demonstrate that in the rat both bidirectionality of Vn responses in binocular conditions and the unidirectional responses of Vn recorded in monocular conditions on the side contralateral to the covered eye are generated solely by vestibular commissural transfer.

Figure 2 and Table 2 illustrate the experimental results obtained after sectioning the vestibular commissure. With both eyes opened Vn responded essentially as they did in monocular condition with an intact commissure. The same pattern was noted when the commissure was cut and the ipsilateral eye was covered (Table 2, Fig. 2). However, no responses were observed in type I and type II Vn in lesioned animals in which the contralateral eye was covered (Table 2, Fig. 2). It should be noted that the $+\Delta f$ values of type II measured in commissurotomized animals are slightly lower (Table 2) than those in intact animals ([2], Table 1).

e) Effects of Picrotoxin on Vn Responses. On the basis of previous studies [10, 17] it may readily be assumed that type II neurons are inhibitory interneurons acting on type I on the same side (see schematic in Fig. 2). Given the results shown in Table 2 and Fig. 2 and the previous work on the commissural system it may be assumed that inhibition of type I neurons observed during ipsilateral stimulation is caused by active inhibition through type II neurons which are excited by the descending pretectal pathway. Type I excitation during contralateral stimulation, however, would be

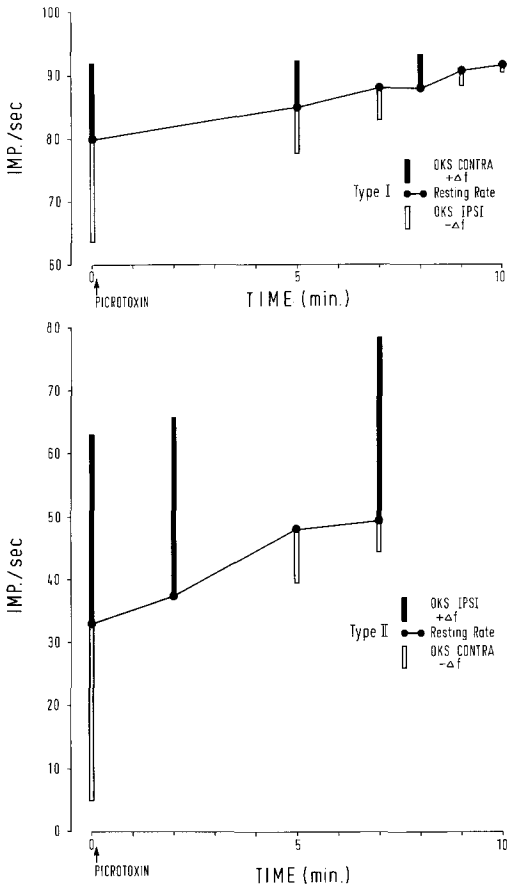

Fig. 3. Effect of i.v. picrotoxin (2.0 mg/kg i.p.) on optokinetic responses of type I and II vestibular neurons. Note that the resting rate of both types increases with time after injection. The magnitude of frequency increase (full bars) and decrease (open bars) decreases with time after systemic injection. Picrotoxin affects only the frequency decrease of type II and not its frequency increase

generated by disinhibition from this type II inhibition. Type II inhibition on contralateral stimulation would likewise depend upon the commissural path and be generated by disfacilitation due to inhibition of type I on the other side. It has also been shown that GABA is a likely inhibitory transmitter in the commissural system [15].

To test the above assumptions and to further elucidate the role of the inhibitory commissural mechanism in the generation of optokinetic Vn responses we studied these neurons after i.v. injection of picrotoxin which is known to block GABA mediated inhibition, i.e. also the commissural inhibition [9, 15]. Figure 3 (upper part) shows that under picrotoxin two effects are noted in type I neurons: 1) an increase of their resting rate and 2) a loss of their responses to ipsi- and contralateral optokintic stimuli. On the other hand, type II neurons (Fig. 3, lower part) lose only their

Table 3A–C. Effects of unilateral superior colliculus lesions (**A**) visual cortex removal (**B**) and total cerebellectomy (**C**) on Vn responses to optokinetic stimuli (OKS velocity = 1 deg/s). Numbers indicate mean $\pm \Delta f$ in imp/s $\pm$ standard deviation

A	Type I ($n = 9$)	Type II ($n = 8$)
OKS contralateral	Excitation $+\Delta f = 15.53 \pm 13.26$	Inhibition $-\Delta f = 9.50 \pm 7.04$
OKS ipsilateral	Inhibition $-\Delta f = 12.60 \pm 8.96$	Excitation $+\Delta f = 18.08 \pm 8.51$

B	Type I ($n = 9$)	Type II ($n = 14$)
OKS contralateral	Excitation $+\Delta f = 11.56 \pm 3.32$	Inhibition $-\Delta f = 14.08 \pm 9.23$
OKS ipsilateral	Inhibition $-\Delta f = 10 \pm 5.13$	Excitation $+\Delta f = 18.96 \pm 9.74$

C	Type I ($n = 13$)	Type II ($n = 12$)
OKS contralateral	Excitation $+\Delta f = 16.91 \pm 7.43$	Inhibition $+\Delta f = 13 \pm 9.51$
OKS ipsilateral	Inhibition $-\Delta f = 17.81 \pm 9.88$	Excitation $-\Delta f = 19.38 \pm 16.43$

inhibitory response whereas excitation is unaltered. The increase in resting rate of type II Vn may be caused by both release from cerebellar inhibition (blockage of GABA mediated Purkinje cell inhibitions of Vn) and a general excitatory effect of picrotoxin on Vn. Combining these observations and the effects produced by midline commissural lesions it appears that, except for the type II excitation, all other responses of Vn depend upon the commissural inhibitory system.

Lesions not Affecting the Vn Responses

It has already been mentioned that lesions of tectospinal tract or the MLF had no effect on the optokinetic responses of Vn. In support of the results with tectospinal lesions is the absence of effects following large unilateral lesions in the superior colliculus (2 rats). Table 3A shows that both the qualitative and quantitative response characteristics in these animals are not different ($P < 0.05$) from normal when measured with the standard stimuli. Similar negative results were obtained from 3 rats in which the visual cortex was removed by suction (Table 3B).

Finally, Vn were studied in 3 cerebellectomized (including the flocculi) rats to elucidate a possible cerebellar role in the generation of optokinetic re-

sponses. As can be seen in Table 3C Vn responses are very much like those reported for intact animals (Table 1, in [2]).

Electrophysiology of the Optokinetic Path

In the above analysis two of the major relay stations in the optokinetic path have been identified as the pretectal area and the area of the NRTP. It seems interesting, therefore, to study the responses of identified type I and type II neurons to electrical stimulation of these regions. Since stimulation of relatively small areas in the CNS always includes the problem of current spread to neighbouring structures, great care was taken not to use current intensities much above threshold. The thresholds of the effects described below were ca. 30–40 μA and even with stimulus intensities of 200 μA the qualitative ipsi- and contralateral effects on type I and type II were consistent with those obtained at threshold.

The results of this work are summarized in Fig. 4. Stimulation of the ipsilateral pretectum affected most type II neurons (26 units) and the effect was always excitatory (Fig. 4A, D, F) whereas contralateral stimulation inhibited the resting rate of type II (Fig. 4B). Excitation was stimulus linked in many cases and showed latencies between 3–8 ms (mean = 5.21 ± 1.90; $n = 17$, Fig. 4L). In 9 units, the diffuse, long latency excitation could only be seen by averaging many traces (Fig. 4D) and comparing them to controls (Fig. 4C). Alternatively, the diffuse effect was documented by increasing the stimulus rate (50/s) and recording the cell activity on running film (50 mm/s).

Type I neurons (12 units) were inhibited by ipsilateral (Fig. 4H, I) and excited by contralateral (Fig. 4K) pretectal stimuli. Contrary to type II excitation, type I inhibition was predominantly diffuse and required higher stimulus repetition rates (Fig. 5I–K). In several cases, however, the effects were clearly stimulus linked (Fig. 4H) and latencies, which measured about 5–7 ms could be determined.

Stimulation of the ipsilateral NRTP had the same effect on both type I and type II neurons as the pretectum except that the latencies were shorter after NRTP stimulation (Fig. 4E–G). Thus, type II excitation occurred after a mean latency of 3.05 ± 1.42 ms ($n = 10$) which is significantly shorter than that obtained with pretectal stimulation (Fig. 4L, open columns). The type I inhibition measured ca. 3 ms but was often of the diffuse type.

In short, the effects obtained with electrical stimulation of pretectal and NRTP areas are consistent in their polarities with those noted during natural optokinetic stimuli.

Optokinetic Nystagmus (OKN) After Lesions in the Pretectum and NRTP

In our previous study on albino rats [12] the absence of OKN was accompanied by a complete lack of modulation of Vn by optokinetic stimuli. We were, therefore, interested in the OKN behavior in our pretectal and NRTP lesioned animals which also showed a severe disturbance of Vn responses to one side.

As demonstrated in Fig. 5 both unilateral pretectal (5 animals) and NRTP lesions (7 animals) completely abolished OKN when the stimulus pattern was moved towards the side of the lesion. This is in perfect agreement with our single unit data. Thus, under this condition type II excitation and type I inhibition are missing on the side ipsilateral to the lesion (Table 1A, C).

Discussion

The present experiments show that the pretectum and not the tectum is the first central relay station in the optokinetic pathway from the retina to those Vn related to the horizontal canal system. This finding is in good agreement with previous studies in rabbit [4] and cat [7] showing that neurons in the pretectum, specifically in the nucleus of the optic tract (NOT), receive retinal afferents [1, 16] and have response characteristics similar to those recorded in Vn of the rat and of various other species. Although our pretectal lesions always included the NOT we cannot exclude the interruption of fibers to other pretectal nuclei or concomitant lesions of nearby nuclei even in case of small lesions (Fig. 5). Single unit work in the pretectum of the rat is needed before a final answer as to the exact location of units sensitive to horizontal optokinetic stimuli can be given.

The fact that the results obtained with monocular stimulation in normal rats [2] where qualitatively and quantitatively identical to those obtained with binocular stimulation in animals having unilateral pretectal lesions further indicates that 1) the retinopretectal projection is contralateral only, at least in a functional sense, 2) that there is no significant bilateral interaction between the pretecta, and 3) that also in the lesioned condition the effective stimulation is essentially restricted to the temporonasal direction. The missing contribution of the ipsilateral eye is most clearly demonstrated by the complete lack of Vn responses to optokinetic stimuli when one pretectum was lesioned and the eye ipsilateral to that lesion was covered (Table 1A). It should be noted that contrary to the rat, Vn in the cat with unilateral pretectal lesions showed still a high percentage (ca. 30%) of normal responses and only about 30% of units responded unidirec-

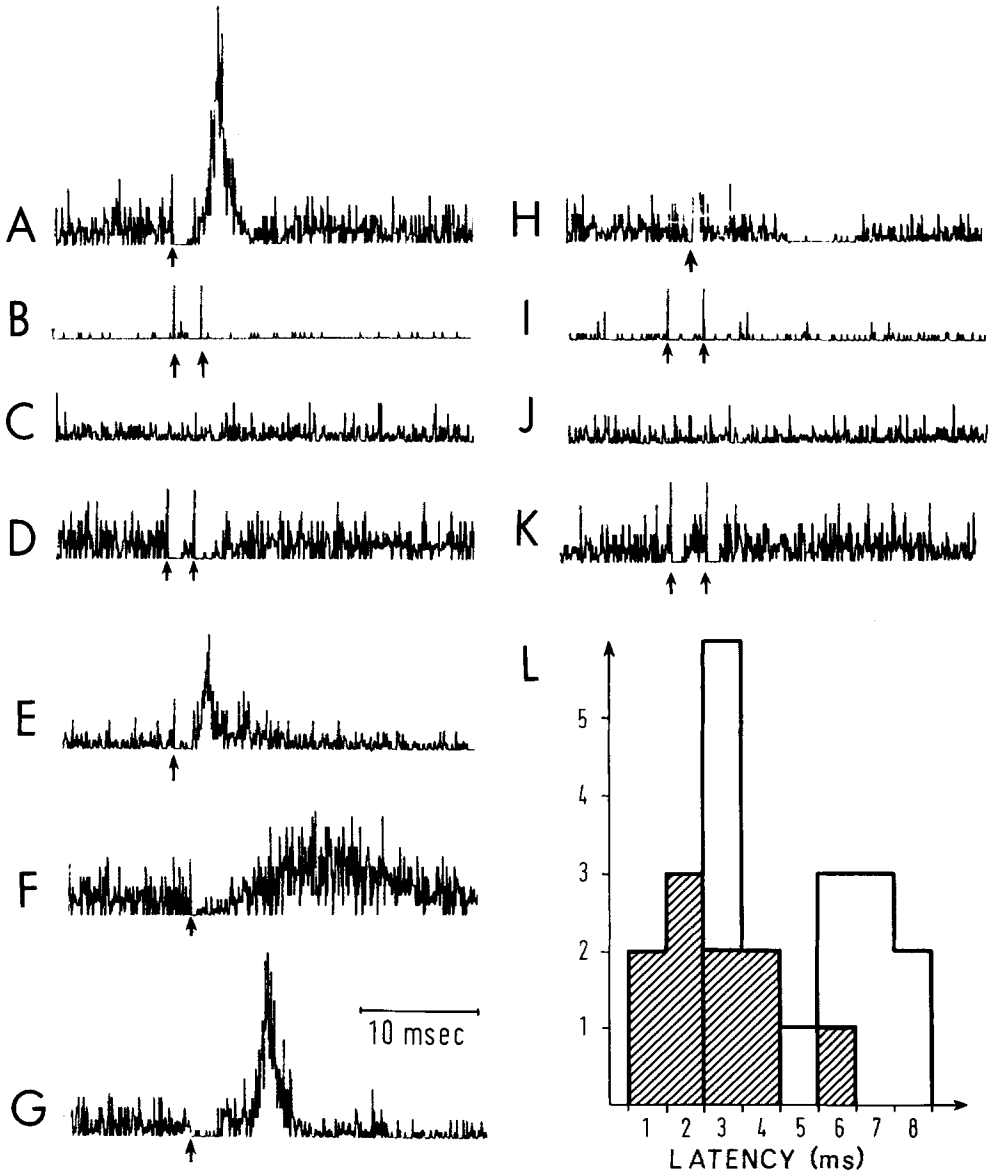

Fig. 4A—L. Effects of electrical stimulation of the pretectum and NRTP on Vn. **A** Peristimulus histogram during ipsilateral pretectal stimuli (3/s; 2,000 sweeps; 50 μA) on type II neuron. **B—D** Effects of contra (**B**) and ipsilateral (**D**) pretectal stimuli (5/s; 2,000 sweeps; 60 μA) on the same type II neuron; control (2,000 sweeps) in **C**. Note the diffuse excitation and inhibition in **D** and **B**, respectively. **E** Short latency activation of type II neuron by ipsilateral NRTP stimulation (5/s, 2,000 sweeps; 60 μA). **F, G** Activation of same type II neuron by ipsilateral pretectal (**F**) and NRTP (**G**) stimulation. Note slight difference in latency of onset and peaks between stimulation sites. **H** Effect of pretectal stimulation on ipsilateral type I (5/s; 1,000 sweeps; 60 μA). **I—K** Effects of ipsi- (**I**) and contralateral (**K**) pretectal stimuli on same type I neuron (5/s; 100 sweeps); **J** is control (100 sweeps). **L** Frequency distribution of type II excitations following pretectal and NRTP stimulations

tionally. There was also a seizable number of Vn not responding to optokinetic stimuli (30%) under this condition [14]. These findings also stress some important differences in the optokinetic system between these two species the most prominent one being the bidirectionality of Vn and OKN responses to monocular stimuli seen in the intact cat [8, 14]. It has been shown that in the cat the visual cortex is necessary for bidirectionality, i.e. it generates nasotemporal optokinetic responses [21].

As to the further course of the optokinetic path our studies indicate that pretectal axons do not seem to project via the tectospinal tract or the MLF but rather traverse somewhat more laterally the midbrain reticular formation (note effects of deeper midbrain lesions summarized in Table 1 B) and reach the NRTP ipsilaterally. The NRTP lesion studies, of course, do not allow the conclusion that pretectal fibres actually terminate in the nucleus. However, there is recent anatomical evidence in the rat showing that the NOT

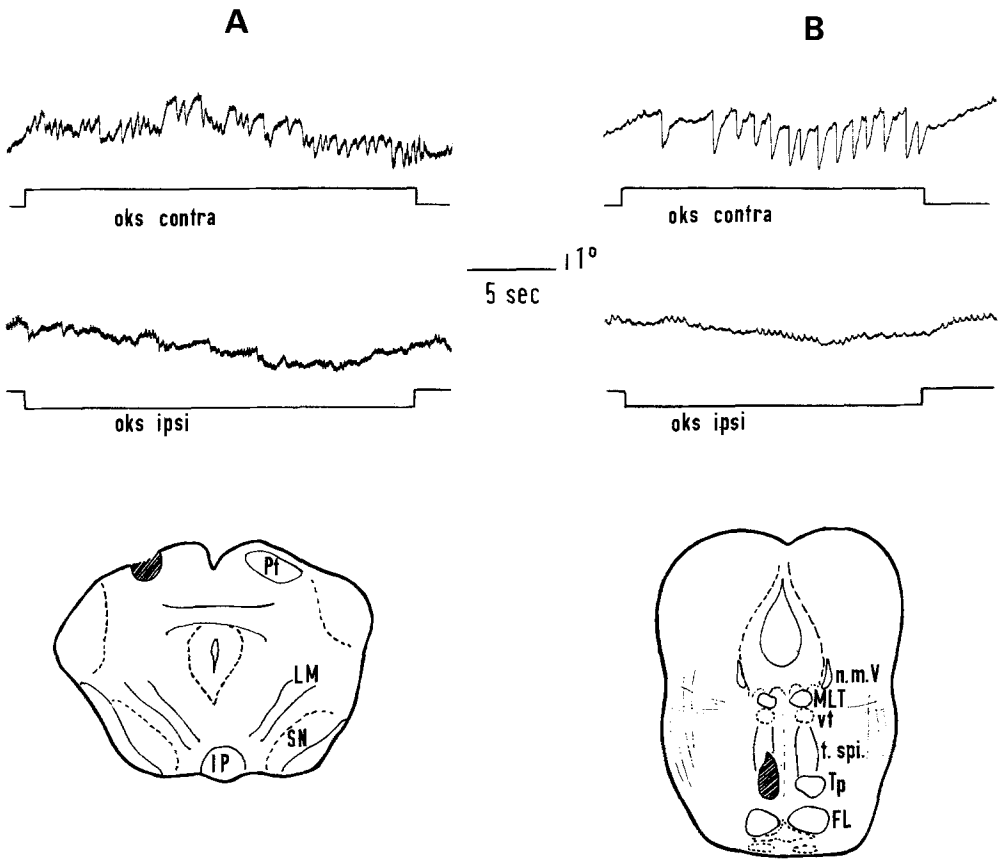

Fig. 5A and B. Effects of pretectal and NRTP lesions on OKN. In **A** (pretectal) and **B** (NRTP) EOG recordings and projection drawing of the lesions are shown. OKN was evoked by surround motion with a velocity of 5°/s. Both eyes were open. Note absence of OKN when the pattern moved in the direction of lesion. Calibrations: time: 5 s, amplitude of eye movement 1°

projects to the ipsilateral NRTP [18]. The relatively large (more than the delay due to conduction time) difference in latency for type II activation after pretectal and NRTP stimulation also tends to suggest that pretectal fibers synapse on NRTP neurons. The effects of NRTP lesion on Vn responses to optokinetic stimuli were qualitatively the same as those obtained with lesions of the pretectum and midbrain reticular formation. There were, however, some quantitative differences in the response magnitude ($+\Delta f$ values) of Vn in NRTP lesioned animals when compared to rats with pretectal or reticular lesions. At present, the reason for this differences is not clear; it may indicate interaction between the bilateral NRTPs.

How does the signal get from the NRTP to the vestibular nuclei? A direct path is possible since there is anatomical evidence for NRTP projection to the vestibular nuclei [6]. Our results obtained with electrical stimulation of the NRTP may suggest but do not prove such a connection (see below). In addition to this direct route, polysynaptic pathways through the reticular formation have to be considered. Regarding a possible route through the cerebellum it can be stated that it is certainly not essential since cerebellar ablation did not significantly alter the qualitative and quantitative nature (at least at a stimulus velocity of 1 deg/s) of the Vn responses (Table 3C). This finding is similar to that obtained in cat [8]. There exist projections from the NRTP to the inferior olive [19] which may have been severed by the NRTP lesion as well. It is possible that axon collaterals from the inferior olive to the Vn carry some optokinetic signal. However, olivary lesions in the cat [14] did not significantly alter the Vn responses to optokinetic stimuli a finding which makes the above pathway an unlikely candidate in the rat as well.

The intriguing finding that all Vn studied in rat show a bidirectionality (increase in one and decrease in the opposite direction) on ipsi- and contralateral optokinetic stimulation in binocular conditions and only unidirectional responses with monocular stimuli (Table 1, in [2]) requires crossing of activity and reversal in sign of the response at some level along the pathway. We found that on cutting the vestibular commissure interconnecting the bilateral vestibular nuclei Vn responses became unidirectional in the

binocular condition (Table 2). The clearest demonstration of the importance of the commissural transfer may be obtained when the eye contralateral to the Vn recorded from was covered in commissurotomized animals. In this case no modulation was observed in either type I or type II units. This finding clearly indicates that no effective transfer occurs rostral to the vestibular nuclei, e.g. between the pretecta. It also implies that in the rat the bidirectionality of the Vn response to optokinetic stimulation is achieved by the vestibular commissure which assures that the sensitivity to temporonasal surround motion of each eye is transmitted to Vn on both sides.

One may now ask: how does the optokinetic pathway from NRTP to the vestibular nuclei approach the different types of Vn on both sides? Since for any given stimulus type I and type II units are always affected in the opposite sense there may exist either two paths, one excitatory to type II and one inhibitory to type I units, or one excitatory path from the ipsilateral NRTP to type II Vn which are inhibitory in nature [10, 17] and, in turn, inhibit type I Vn on the same side. Since some type I Vn are commissural neurons exciting type II on the opposite side [17] their frequency decrease will result in disfacilitation of type II on the opposite side and since type II on that side, in turn, inhibit type I the latter will be disinhibited concurrently. Some evidence that might support the latter assumptions was obtained by the results based on electrical stimulation of NOT and NRTP. On the ipsilateral side all type II and type I Vn were excited and inhibited, respectively, from either stimulation site but the latencies for excitation were always shorter than those for inhibition (by about 1–2 ms) and the inhibition was more difficult to obtain with single shock stimulation. Also, the earliest latency for excitation of type II (1.1 ms) from the NRTP is compatible with a monosynaptic connection. It should be emphasized, however, that only two Vn showed such short latencies whereas the remainder had longer latencies for spike activations. Intracellular studies as well as anatomical work in the rat are needed to prove the existence of a monosynaptic projection. From the functional point of view it is not so crucial, however, if type II neurons are activated mono- or oligosynaptically from the NRTP.

Contralateral stimulation had the opposite effect, i.e. type I excitation and type II inhibition; both effects were mostly of the long latency, diffuse type suggesting that they were mediated through the polysynaptic chain of the vestibular commissure.

Furthermore, the response modifications of Vn obtained under picrotoxin which is known to affect or block the commissural inhibition [15] lend support to the hypothesis that the direct effect of the optokinetic path on Vn is excitation of type II Vn ipsilaterally and that all other responses are the result of the excitation of the inhibitory neuron and its role in the commissural path (Fig. 3).

As in Vn of other species [20] the optokinetic responses of rat Vn seem to closely parallel the slow phase of the OKN: Whenever Vn are not or only partially modulated by a given optokinetic stimulus such as in albino rats [13] or in unilateral pretectal or NRTP lesions (Table 1), OKN is also missing to both or one direction, respectively (Fig. 5). This parallelism between Vn responses and the motor response (OKN), however, does not hold in all conditions, i.e. there may also be dissociation of the two signals [8, 14, 20] suggesting that sites other than the vestibular nuclei are also important for proper OKN performance. This data implies that the Vn response is neither a pure sensory nor pure motor signal but may represent an internally reconstructed estimate of true visual surround velocity.

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