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Effects of pontine reticular formation lesions on optokinetic head nystagmus in rats*,**

D.W. Sirkin[1], Y. Zedek, and P. Teitelbaum

Program in Neural and Behavioral Biology and Department of Psychology, University of Illinois at Urbana-Champaign, 603 E. Daniel St., Champaign, IL 61820, USA

Summary. Electrolytic lesions were produced in the pontine reticular formation (PRF) of adult hooded rats. Unilateral lesions abolished quick phases of optokinetic head nystagmus to the side of the lesion. Some lesions also had temporary effects on slow phases of optokinetic head nystagmus. Effects of bilateral lesions were similar, except that they affected head movements in both directions. A class of "fast" head movements abolished by PRF lesions thus emerges that is analogous to the class of rapid eye movements abolished by similar lesions in other species, a finding that can be related to the coupling which has been observed between "fast" head and eye movements.

Key words: Head movements – Optokinetic nystagmus – Pontine reticular formation – Nucleus reticularis pontis caudalis

Introduction

It has been known for some time that the medial pontine reticular formation (PRF) is important for rapid eye movements (Lorente de Nó 1933; Teng et al. 1958). The deficits in eye movements produced by PRF lesions have been studied most extensively in the monkey, where it has been shown that a class of "rapid" or "fast" horizontal eye movements are abolished. The class encompasses voluntary saccades, including those elicited by visual stimuli, and quick phases of both vestibular and optokinetic nystagmus (e.g. Teng et al. 1958; Cohen et al. 1968; Henn et al. 1982). In addition, electrophysiological and anatomical studies in rabbit (Duensing and Schaefer 1957), cat (Yoshida et al. 1982 and references cited therein), and monkey (reviewed in Henn et al. 1982) have established the pontine and pontomedullary reticular formation as a premotor area for fast eye movements.

However, it has also long been known that stimulation of the PRF causes head and body turning as well as eye movements, and that lesions of the PRF produce postural and locomotor disturbances (e.g. Ingram et al. 1932; Bürgi and Monnier 1943). Furthermore, the PRF is known to be a source of input to the spinal cord (e.g. Tohyama et al. 1979, Sirkin et al. 1980a), and even to contain neurons synapsing directly on spinal motoneurons (Peterson 1979). It is interesting that some of the PRF neurons projecting to the cord have an excitatory input to abducens neurons (Grantyn et al. 1980). Unit recordings in unrestrained animals have shown relationships to head movements (e.g. Duensing and Schaefer 1960; Lestienne et al. 1982; Siegel and Tomaszewski 1983). Vidal et al. (1983) found two units at the posterior end of the PRF in cat that had a better relation to neck muscle electromyographic activity than to eye position.

On the basis of experiments with PRF lesion rats, Sirkin et al. (1980b) suggested that the PRF is a premotor center coding "fast" head movements as well as fast eye movements. PRF lesions in the rat abolished orienting head movements (also reported to be abolished by PRF lesions in cat – Jones 1979), spontaneous head turns in the open field, and quick phases of vestibular head nystagmus. They also abolished amphetamine- and apomorphine-induced head turns (Sirkin and Teitelbaum 1983). The experiments we now report were performed to decide if the PRF-damaged rat's head movement deficits could be

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1 Present address: 611 W. Iowa St., Urbana, IL 61801, USA

Offprint requests to: D.W. Sirkin (address see footnote)

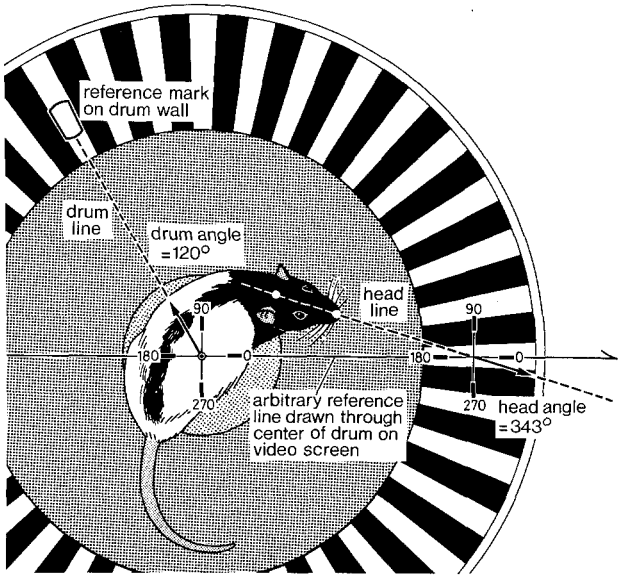

Fig. 1. Diagram indicating how drum and head angular position in space were measured on still frames of video records of responses to optokinetic stimulation. See text for details

generalized to a deficit in a class of "fast" head movements by analogy to what has been done for eye movement deficits in the PRF-damaged monkey (see above). The main findings have been briefly presented previously (Sirkin et al. 1982).

Material and methods

In adult Long-Evans black and white hooded rats, stereotaxically placed anodal electrolytic lesions were made in the pontine reticular formation (9.3–9.7 mm posterior to bregma, 0.8 mm lateral, 8.0 mm ventral to dura, with bregma and lambda at same height) as described previously (Sirkin et al. 1980b). Behavioral tests were performed on intact rats (n = 9), unilateral PRF lesion rats (n = 7), and bilateral PRF lesion rats (n = 6).

Optokinetic stimulation

A 39 cm diameter black and white striped drum (vertical stripes, 5.5°) could be rotated at roughly constant velocities in either direction by a small electric motor. 60–90°/s drum velocities were most frequently used (in pilot experiments velocities in this range were found to be efficient in eliciting head nystagmus in rats). The rat was placed on a small platform (10 cm diameter, 13.8 cm height) in the middle of the drum. The rat's movements in the drum were recorded on video tape with a video camera positioned directly above the drum.

Graphical records of selected segments of the video record were constructed by hand from measurements made on the video screen; the angular position in space of the rat's head, as well as the position of a reference mark on the rotating drum wall were followed sequentially through still frames. Figure 1 illustrates the system used to measure angles for graphing. The measurements were always made as illustrated, regardless of the directions of motion of the stimulus pattern (drum) and the head. These directions are therefore not indicated in the diagram. The arbitrary reference line drawn on the video screen remained in place from frame to frame; it may be thought of as being fixed to the stationary platform on which the rat is standing. The point of intersection of the "head line" (drawn by connecting the images of two dots painted on the nose and occiput of the rat) and the reference line was taken as the origin for measuring the head angle (angular position). This point of intersection could be in front of the rat's nose, as in the diagram, or in back of the rat's head, as would be the case, for example, were the rat in the diagram to look towards the reference mark. In practice, a stationary y-axis was also drawn through the center of the drum perpendicular to the reference line (x-axis). To measure the head angle when the head line was parallel or almost parallel to the reference line, the intersection of the head line and the y-axis was taken as the origin. It should be noted that the rat was completely unrestrained (except for its movements being restricted by the small dimensions of the platform), and neither the position of the head nor the position of the reference mark on the drum wall had any particular correspondence to the reference line at the onset of pattern motion. Thus the "zero-position" defined by the reference line is really completely arbitrary and has no relation to the experimental situation. It is therefore not indicated in Figs. 3–5. Video records were first monitored at normal speed and in slow motion. Then they were monitored again frame-by-frame (33 msec intervals) to determine the appropriate sampling interval for graphing. The sampling intervals for drum and head positions (angles) ranged from 333 ms for steady drum or head movements down to 100 ms for small head movements with frequent direction changes.

For constant velocity drum rotations, the drum position traces (Figs. 3–5) have a slight, regular wave in them. This was an artifact of our monitoring system: the video monitor screen distorted the image at the periphery of the screen so that the round drum appeared ovoid. This distortion was insignificant near the center of the screen, so our measurements of head position were not significantly affected by it.

Histology

At the end of the behavioral experiments each lesion rat was given an overdose of anesthesia and perfused through the heart with formol-saline. For histological analysis of the lesion sites, alternate frozen sections of the brain were stained with cresyl violet and with the Weil stain. A typical lesion is illustrated in Fig. 2.

Results

Intact rats

It has been previously noted (e.g. Smith and Bridgman 1943; Vestal and King 1968; Hayes and Ireland 1972) that rodents respond to an optokinetic stimulus with both head and eye nystagmus, and occasionally with turns of the whole body. Our intact rats showed head nystagmus episodes of variable length interspersed with periods when head nystagmus was not observed. They generally made optokinetic head movements (either nystagmus or continuous following) at least 30% of the time during a recording session (typically about 10 min long). Good

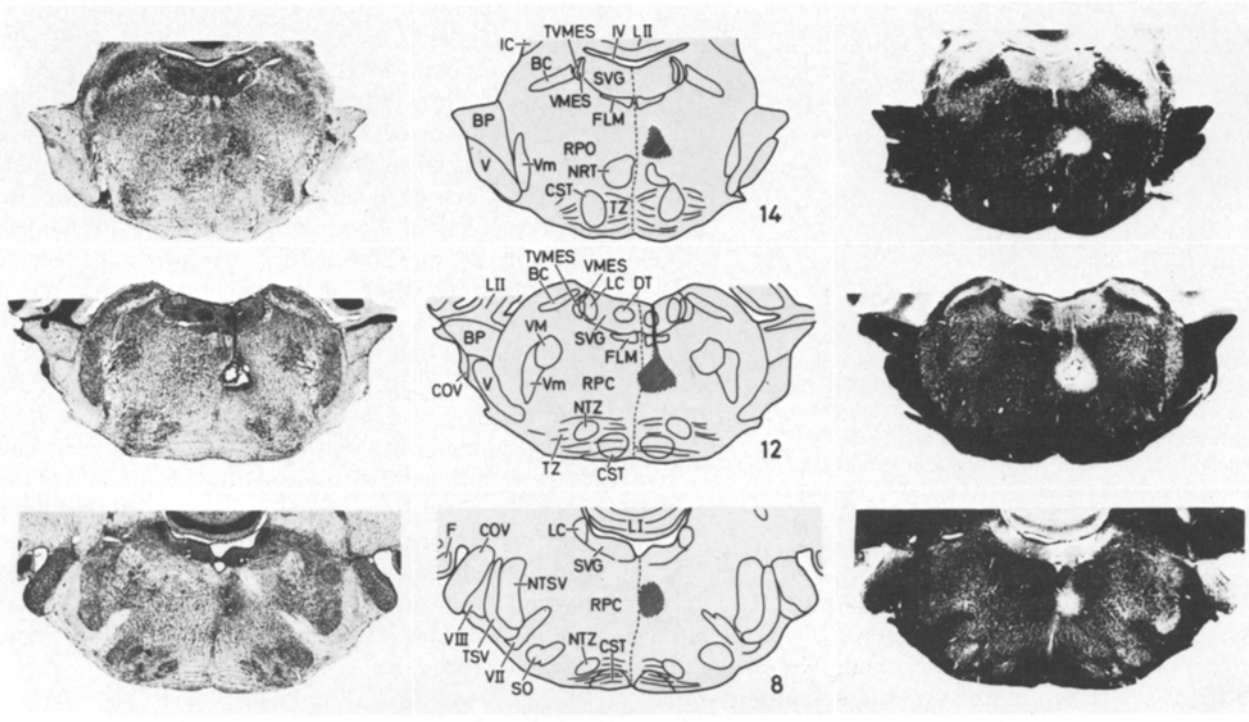

Fig. 2. Photomicrographs of cresyl-violet-stained sections, section diagrams, and photomicrographs of Weil-stained sections (left to right) at the anterior end, middle, and posterior end (top to bottom) of the unilateral PRF lesion in rat PRF 27A. Note section numbers next to the diagrams. Sections separated by 200 μm were numbered in succession. (Thus the total distance between the anterior and posterior sections shown here is 1.2 mm.) Abbreviations: BC = brachium conjunctivum; BP = brachium pontis; COV = ventral cochlear nucleus; CST = corticospinal tract; DT = dorsal tegmental nucleus (Gudden); F = flocculus; FLM = medial longitudinal fascicle; IC = inferior colliculus; IV = fourth ventricle; LC = locus coeruleus; LI, LII = cerebellar lobules I and II; NRT = nucleus reticularis tegmenti pontis; NTSV = nucleus of the spinal tract of the trigeminal nerve; NTZ = nucleus of the trapezoid body; RPO = nucleus reticularis pontis oralis; RPC = nucleus reticularis pontis caudalis; SO = superior olive; SVG = subventricular grey; TSV = spinal tract of the trigeminal nerve; TVMES = mesencephalic tract of the trigeminal nerve; TZ = trapezoid body; V = trigeminal nerve; VII = facial nerve; VIII = vestibulocochlear nerve; Vm = motor root of the trigeminal nerve; VM = motor nucleus of the trigeminal nerve; VMES = mesencephalic nucleus of the trigeminal nerve

responses were frequently observed immediately after changing the direction of drum rotation. This facilitatory effect of direction change has been noted previously in guinea pigs and turtles (Hayes and Ireland 1972). During periods when head nystagmus could not be observed, an intact rat would sometimes face the rotating drum wall but remain immobile, in which case the experimenter could often observe eye nystagmus by peering into the drum and looking at the rat closely.

All but one of the 9 intact rats had episodes of distinct head nystagmus. The exceptional animal exhibited very slight and infrequent head nystagmus movements, but during periods when the head was still, clear ocular nystagmus could be observed.

A record of typical head nystagmus from an intact rat is shown in Fig. 3. The slow phases of head nystagmus (movements to the right) have a velocity as high as some of the quick phases because of the high drum velocity chosen (72°/s).

Effects of lesions on quick phases of optokinetic head nystagmus

Ipsiversive quick phases of optokinetic head nystagmus were abolished in all 7 rats with unilateral PRF lesions. This statement is based upon many hours of direct observation and review of the video records. The responses of a rat with a right PRF lesion to optokinetic stimulation 99 days after surgery are shown in Fig. 4. In Fig. 4b the animal can be observed to have circled to the left during drum rotation to the left; i.e. it exhibited a continuous slow phase response without any quick phases of optokinetic head nystagmus to the right.

Rats with bilateral lesions (n = 6) showed no quick phases of optokinetic head nystagmus in either direction. In the optokinetic drum they exhibited continuous slow phase movements (circling) in both directions. These circling responses may last longer than 5 min during constant drum rotation. We have

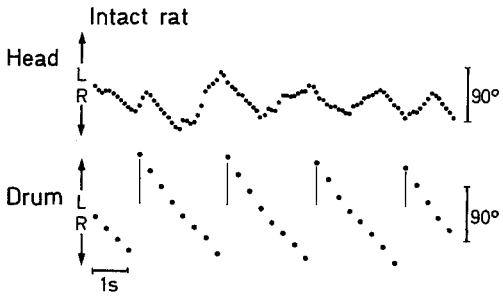

Fig. 3. Records of optokinetic head nystagmus in an intact rat obtained from video tape recordings (graphs of head angular postion in space and of angular position of a reference mark attached to the rotating optokinetic drum wall). Note the vertical lines in the drum position graph. They indicate where the graph was broken and replotted with 180° = 0° or 360° = 0° in order to make a compact record of continuous rotation. The rat is showing head nystagmus during constant velocity drum rotation to the right (clockwise)

observed a loss of quick phases of optokinetic head nystagmus in damaged rats up to 204 days after surgery. Only in one rat with unilateral damage did we observe a return of ipsiversive quick phases when we tested it 230 days after surgery. The lesion in this rat was atypically placed: it was ventral and caudal to the site of the lesion shown in Fig. 2.

Effects on slow phases

An additional and unexpected finding was that PRF lesions temporarily affected slow phases of optokinetic head nystagmus, although, in agreement with previous findings (Sirkin et al. 1980b), no deficits in slow phases in responses to passive body rotation in the light were noted.

At 2 or 3 days after surgery, of 9 rats tested, 6 had clear deficits in slow phases of optokinetic head nystagmus; i.e. slow phases could not be elicited at all, or else had very low gain (head displacements of only a few degrees after several complete revolutions of the drum). In rats with unilateral lesions these deficits were in ipsiversive slow phases, except in one case that had a lesion lateral and caudal to that shown in Fig. 2. In this case some ipsiversive slow phases were observed, but no contraversive slow phases. It is unlikely that the lesion rats were making ocular nystagmus responses and thus obviating the need for head movement responses to the optokinetic stimulus: the lesions presumably produced a long-lasting abolition of quick phases of optokinetic ocular nystagmus, as we verified by direct observations in two bilateral lesion rats.

The effects on slow phases of head nystagmus, unlike the effects on quick phases, were subject to a marked recovery. In most cases, the recovery was complete in 4–18 days. The recovery of ipsiversive slow phases in rat PRF 27A is illustrated in Fig. 5. In Fig. 5a, from a videorecording made 3 days after surgery, it showed first a continuous contraversive following response, indicating an absence of ipsiversive quick phases of optokinetic head nystagmus. In the second half of the record, after the drum changed direction, the rat showed only a very slight ipsiversive slow phase (starting at arrow in head movement trace). This was the largest response to ipsiversive drum rotation that the rat made during the recording session. In Fig. 5b, from a recording made 11 days after surgery, it can be seen that ipsiversive slow phases, along with contraversive quick phases, had returned during drum rotation towards the side of the lesion (the right side), while ipsiversive quick phases were still absent. The long ipsiversive slow phase seen after the second arrow in the head movement trace may indicate a slight impairment in contraversive quick phases resulting from PRF damage across the midline (Fig. 2).

Discussion

We have found that PRF lesions in the rat abolish quick phases of optokinetic head nystagmus. Thus a syndrome of effects on head movements in the rat emerges that is analogous to the well-studied syndrome of oculomotor deficits in the monkey (Teng et al. 1958; Cohen et al. 1968; Lang et al. 1982). A class of "fast" head movements abolished by PRF lesions can be defined. It includes quick phases of both vestibular and optokinetic nystagmus, spontaneous turns in the open field, and orienting movements to visual stimuli (present results and Sirkin et al. 1980b).

With regard to vestibular head nystagmus, PRF lesions in the rat selectively abolish quick phases (Sirkin et al. 1980b). However, with regard to optokinetic head nystagmus, the present study revealed that PRF lesions caused temporary deficits in slow phases, in addition to abolishing quick phases. Deficits in slow phases of optokinetic ocular nystagmus have occasionally been reported following PRF lesions in the monkey (Cohen et al. 1968; Goebel et al. 1971; Lang et al. 1982). The impairment in slow phases might be due to partial damage to the visual pathway to the vestibular nuclei via the nucleus reticularis tegmenti pontis (N.r.t.) that probably is part of the functional link carrying the optokinetic signal from the retina to the extraocular muscles (Azzena et al. 1974; Cazin et al. 1980; Precht and Strata 1980). [Sirkin and J.-T. Cheng (unpub-

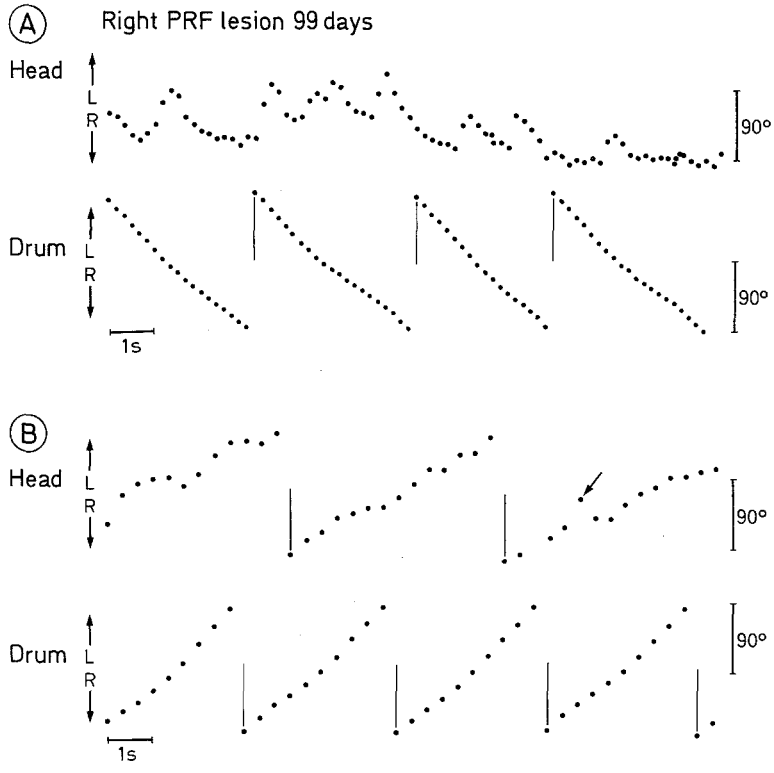

Fig. 4A and B. Record of optokinetic response in rat PRF 80 99 days after a right pontine reticular formation (PRF) lesion. **A** Head nystagmus with slow phases to the right and quick phases to the left during rotation of drum to the right. **B** Circling to the left (continuous slow phase movement) during rotation of drum to the left. Arrow indicates point corresponding to frame where rat appeared to start to slip off platform in drum

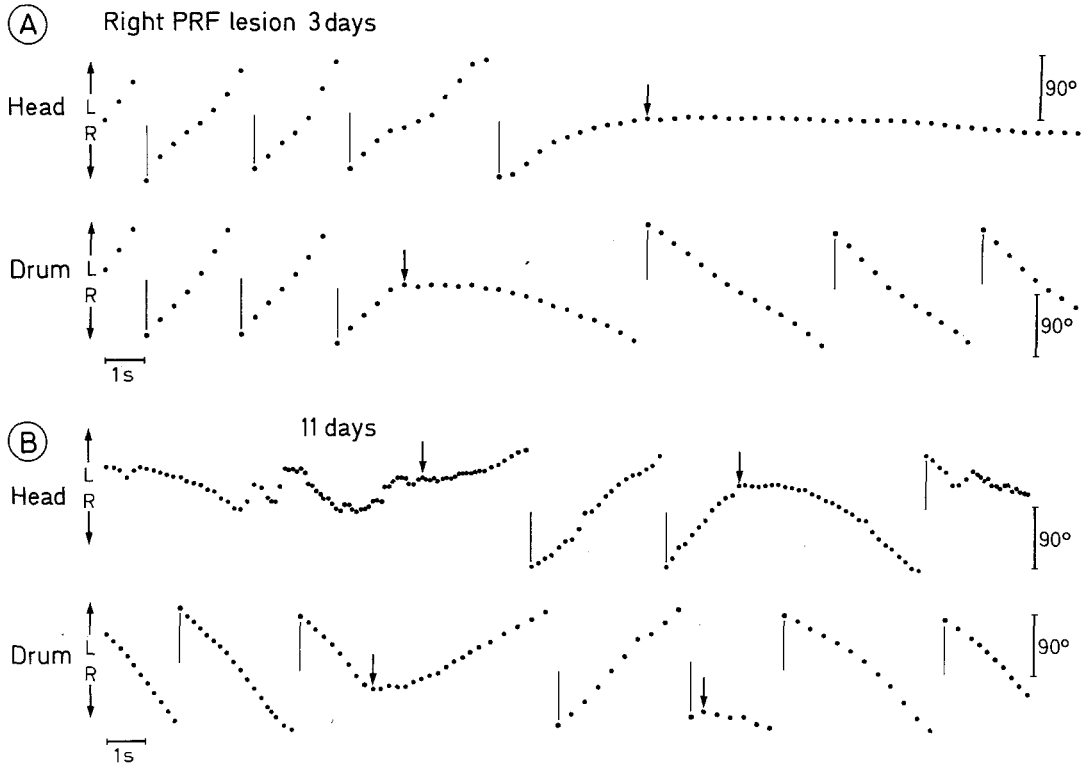

Fig. 5A and B. Recovery of ipsiversive slow phases of optokinetic head nystagmus in rat PRF 27A with a right PRF lesion. **A** 3 days post-op: absence of quick phases of optokinetic head nystagmus to the right (continuous circling to the left during drum rotation to the left) and also absence of slow phases to the right (practically no head movement to the right during drum rotation to the right). **B** 11 days post-op: return of slow phases to right, revealing intact quick phases to the left, but quick phases to the right are still not seen. Arrows mark direction changes of drum and of the slow phase of head nystagmus

lished preliminary observation) found that a rat with bilateral lesions in the region of the N.r.t. showed no optokinetic head nystagmus.] In the present study, we were unable to observe a consistent relation between lesion location and effects on slow phases of optokinetic head nystagmus. None of the lesions involved the N.r.t.

Simultaneous eye movement and neck electromyographic recording have indicated a linkage in the eye and head movement control systems (Vidal et al. 1982), and studies of eye-head coordination have reported coupling of "fast" eye and head movements in many species (e.g., Bizzi et al. 1971; Collewijn 1977; Fuller 1981; Kubo et al. 1981; Dieringer et al. 1983). The neural substrate for this behavioral linkage which appears to be present also in the rat, though perhaps relatively weakly (J.H. Fuller, submitted), might involve the PRF. This is suggested by the deficits in eye and head movements after PRF lesions in the rat as described here and in Sirkin et al. (1980b).

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