Peak Firing Rates of Rat Anterodorsal Thalamic Head Direction Cells Are Higher During Faster Passive Rotations

Michaël B. Zugaro* Alain Berthoz and
Sidney I. Wiener

*CNRS-Collège de France, Laboratoire de Physiologie de la
Perception et de l'Action, Paris, France*

ABSTRACT: Head direction cells discharge selectively when the head of the animal is oriented in a specific direction. The goal of this study was to determine how sensory signals arising from passive rotations (e.g., triggered by vestibular stimulation and dynamic visual inputs) influence the responses of anterodorsal thalamic head direction cells in the absence of voluntary movement cues (e.g., motor command, efference copy, and associated kinesthetic signals). Three unrestrained rats consumed water from a reservoir at the center of a circular platform while passively subjected to sinusoidal rotatory oscillations at fast ($153 \pm 27°/s$, sd) and slow ($38 \pm 15°/s$) peak velocities. In 14 anterodorsal thalamic head direction cells, the preferred directions, angular response ranges and baseline firing rates remained stable, but the peak firing rates were, on average, 36% higher during the fast rotations (Wilcoxon matched-pairs test, $p < 0.001$; variation range: +11%~+100%). No cell changed its peak firing rate by less than 10%, while three cells (21%) increased their peak firing rates by more than 50%. The velocity-dependent increase in peak firing rates was similar for left and right rotations, and the skewness of the directional response curves were not significantly different between left and right turns (Wilcoxon matched-pairs tests, n = 14, ns). These results show that sensory signals concerning self-movements modulate the responses of the head direction cells in the absence of active locomotion. *Hippocampus 2002;12:481–486.* © 2002 Wiley-Liss, Inc.

KEY WORDS: spatial orientation; heading; passive rotations; idiothetic; angular velocity

INTRODUCTION

Head direction (HD) neurons discharge selectively when a monkey, rat or mouse orients its head in a specific, "preferred" direction, independently of location or ongoing behavior (Ranck, 1984; Taube, 1998; Robertson et al., 1999; Khabbaz et al., 2000). Although salient visual cues exert a dominant influence in updating the preferred directions of HD cells (Taube, 1995;

Goodridge and Taube, 1995; Zugaro et al., 2001a), several lines of evidence indicate that sensory signals evoked during displacements also contribute to updating the HD signal. When rats are passively rotated in darkness at accelerations exceeding the vestibular system threshold, the preferred directions remain stable relative to the environment, but the preferred directions shift when accelerations are below threshold (Blair and Sharp, 1996). Vestibular lesions suppress directionally selective responses in rat anterodorsal nucleus of the thalamus (AD) neurons (Stackman and Taube, 1997). In intact animals, when the visual cues and the animal are displaced independently in order to provide conflicting cues, a small but significant influence of self-movement signals can be detected (Zugaro et al., 2000).

Discharge rates of HD cells in the AD are reportedly slightly higher during faster head turns (Taube, 1995; Blair and Sharp, 1995; Blair et al., 1997; Stackman and Taube, 1997; Blair et al., 1998). However, because these results were obtained in freely behaving animals, it is not known whether this effect is mediated by sensory signals (e.g., triggered by vestibular stimulation and dynamic visual inputs), or by motor-related signals (e.g., motor efferent copy or corollary discharge). Furthermore, the literature remains controversial regarding this velocity dependence (compare the latter references with Taube and Muller, 1998), perhaps because none of the experiments to date was explicitly designed to address this issue. In all previous studies, the rats performed a random foraging task and data analyses extracted brief discontinuous episodes from the recording sessions according to instantaneous head velocities. This is problematic because the ensemble of self-movement signals may not have been comparable across such episodes.

In the present study, we studied the influence of sensory signals of self-movement on the discharge rates of AD HD cells in the absence of active locomotor signals. For this, cells were recorded as immobile unrestrained rats were passively rotated in clockwise/counterclockwise oscillations at two different velocities in successive sessions. The rats were not restrained because tight restraint suppresses the discharges of AD HD cells (Taube, 1995).

Hence the rats were trained to remain immobile and drink water from a central reservoir on a round elevated platform that was rotated (Zugaro et al., 2001b). The regular pace of the passive rotations provided smooth head rotations through the preferred directions. This ensured that self-movement signals were similar during successive turns, in contrast with the erratic movements rats tend to make while performing the foraging task (cf. Fig. 1B in Zugaro et al., 2001b).

MATERIALS AND METHODS

Electrode Implantation

Three male Long-Evans rats (200–250 g; CERJ, Le Genest-St-Isle, France) were implanted with bundles of eight Formvar-coated nichrome wire electrodes (diameter 25 μm, impedance 200–800 kΩ). Each bundle was inserted in a 30-gauge stainless steel cannula, and mounted on an advanceable connector assembly (Wiener, 1993). Before surgery, the animals were tranquilized with xylazine (0.1 ml IM) and then deeply anesthetized with pentobarbital (40 mg/kg IP). The electrodes were implanted above the AD (AP −1.6 mm, ML ±1.2 mm relative to the bregma, 3.8 mm ventral to brain surface), and the descender assembly was permanently fixed with dental acrylic and tiny skull screws (for details, see Zugaro et al., 2000). Electrode placements were verified histologically.

Data Acquisition

During the recording sessions, electrode signals passed through FETs, were differentially amplified (10,000×) and filtered (300 Hz to 5 kHz, notch at 50 Hz). A computer automatically collected the data at a rate between 20 and 30 kHz for post hoc discrimination (DataWave, Longmont, USA). Two small lamps (10 cm separation) mounted above the headstage were sampled by a video camera at 60 Hz. The rostral lamp was identified offline on the basis of movement patterns, first automatically by a custom program written by M.B.Z., and then by manual corrections of remaining errors. To determine the response properties of the HD cells, head angles and angular velocities were computed according to the methods presented in detail in Zugaro et al., (2001b). Briefly, head angles were computed from smoothed position samples and directional response curves were fit with a pseudo-Gaussian formula

$$f(\theta) = A + B \cdot e^{K \cos(\theta - \theta_0)} \tag{1}$$

where f(θ) is the firing rate, θ_0 is the preferred direction, $B \cdot e^{K}$ is the peak firing rate, $230°/\sqrt{K}$ the angular range, and A is the baseline firing rate. To avoid discontinuities between 0 and 360°, angular head velocities were computed as

$$\dot{\Theta}(t) = X(t) \wedge X'(t) \tag{2}$$

This formula describes the instantaneous angular velocity of a unit-length vector X(t) as its vectorial product with its derivative vector.
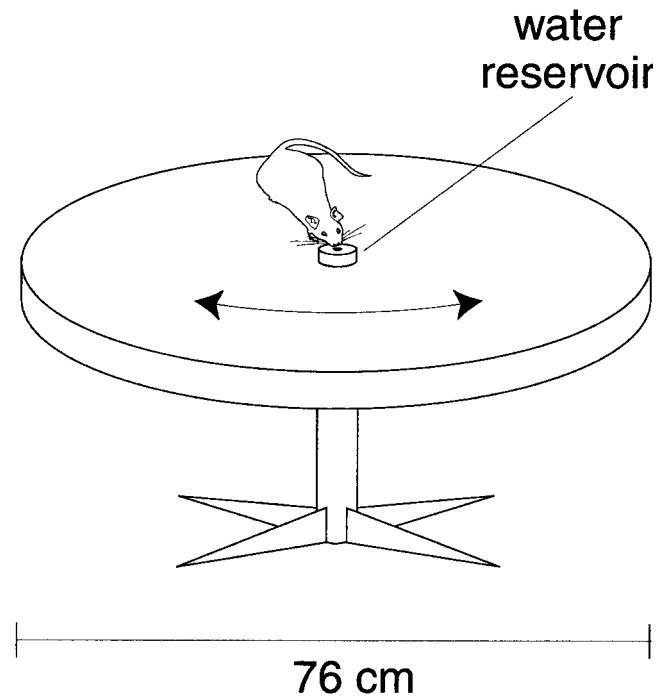

FIGURE 1. Experimental setup. The small elevated platform could be rotated around a central axis. A potentiometer sampled the azimuthal angle of the arena.

Thus, the vector series defined by the positions of the two lamps across time was smoothed (Gaussian filtering) and normalized as X(t_i). Approximation of X′(t_i) was obtained by filtering X(t_i) with a Gaussian-derivative function. Angular head velocity was then computed as the vectorial product of X(t_i) with X′(t_i).

Behavioral Task

The 3-m × 3-m square recording chamber was enclosed by black curtains suspended from the ceiling along three of the walls. On the fourth side, computers and electronic devices were visible and provided stable landmark cues. The rats were placed on an elevated circular platform (76-cm diameter; Fig. 1). The HD cells were recorded in three conditions. During a control phase (active displacements), the rat moved freely within the arena for at least 5 min, foraging for small food pellets (5-mg chocolate sprinkles) that were thrown onto the platform at pseudorandom locations (Muller et al., 1987). The experimenter kept moving about the room while distributing the food pellets in order not to provide a stable spatial reference. The next two phases of the experiment consisted of fast and slow passive rotations (Fig. 2). To rotate the rats passively without applying physical restraint, they were trained to remain immobile while receiving droplets of water (≈30 μl) distributed at brief intervals (0.5–1.5 s) from the water reservoir at the center of the arena (Fig. 1). For training, mildly water-deprived rats were first placed on the platform with water already present in the reservoir. These rats rapidly learned to drink from the reservoir and were shaped behaviorally to remain immobile as water droplets were distributed at

gradually longer intervals. An experimenter stood behind the rat and manually rotated the platform with clockwise/counter-clockwise oscillations (approximating sinusoidal profiles) centered on the preferred direction of the cell. A potentiometer sampled platform angular rotations at 100 Hz. This session continued for 5 min, or until the rat was satiated. To motivate the rats to perform the task, water rations were restricted to 10–15 ml/day. Body weight was maintained at ≥85% of normal values. Rats were completely rehydrated before each weekend. All protocols were in accord with institutional, national (Ministère de l'Agriculture et de la Pêche, with approval No. 7186) and international (NIH) standards.

RESULTS

Behavior

Figure 2 shows the time course of changes in the head direction of the rat as well as the platform orientation during the slow (A) and fast (B) rotations. This demonstrates that the rats remained rather immobile during the passive rotations. The average peak velocity over sessions was $153 \pm 27°/s$ (SD; range: 110–200°/s) during fast rotations, and $38 \pm 15°/s$ (range: 20–70°/s) during slow rotations. This corresponded to sinusoidal oscillations at 0.20 ± 0.04 Hz, with an average magnitude of $209 \pm 72°$, and at 0.08 ± 0.02 Hz, with a magnitude of $190 \pm 55°$, respectively. Throughout both passive rotations conditions, data were recorded as the rats were stationary and drinking the water droplets from the reservoir.

Cell Responses

Peak firing rates are modulated by angular velocity during passive rotations

Fourteen AD HD cells were recorded from 3 rats in 20 recording sessions. Six cells were recorded in more than one session (one cell in five sessions, and five cells in two sessions), yielding a total of 23 recordings; in six sessions, more than one cell were recorded simultaneously. Identification of the same neuron in repeated recordings was based on identification of the same waveform and on directional responses from a given electrode. In the following analyses, repeated measures obtained from the same cell were replaced by their mean.

Figure 3 shows the angular response curves of a typical HD cell with a greater peak firing rate during fast (140°/s, continuous curve) than during slow (30°/s, dashed curve) passive rotations. The peak firing rates computed from the analytically fit curves (dotted curves) were 81 impulses per second and 53 impulses per second, respectively. This corresponds to a 53% increase during fast rotations for this neuron.

For each HD cell, the peak firing rate was compared between slow and fast passive rotation conditions (Fig. 4). Overall, the peak firing rates of the HD cells were significantly higher during faster than during slower rotations (Wilcoxon matched-pairs test, $P < 0.001$, N = 14). No cell changed its peak firing rate by less than 10%, while 6 cells
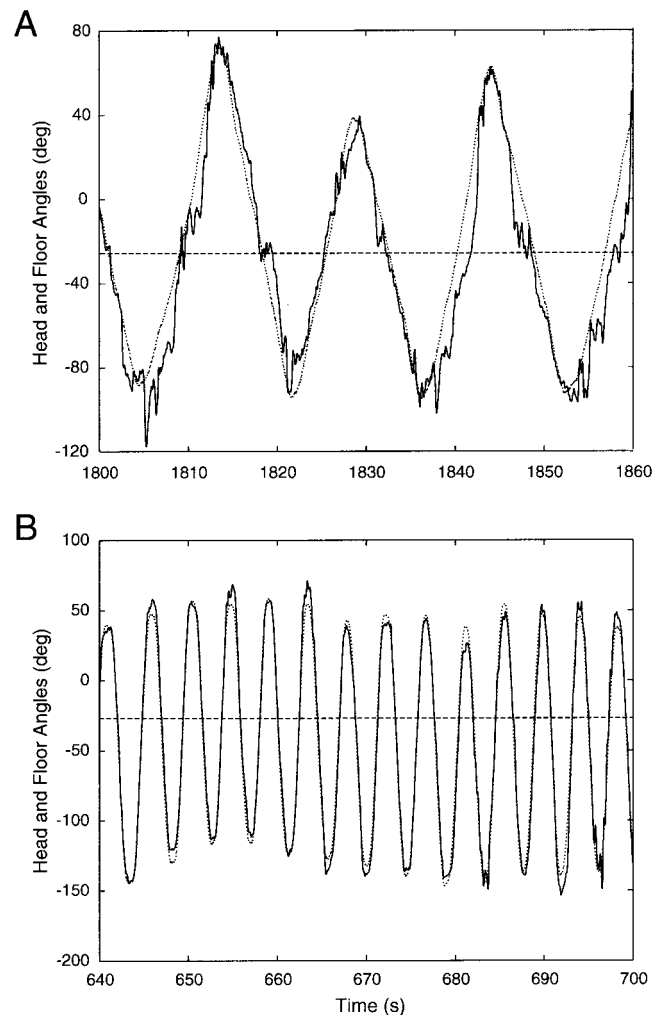

FIGURE 2. Instantaneous floor angle (dotted curves) and head orientation of the rat (continuous curves), during slow (A) and fast (B) rotations. The preferred direction of the head direction (HD) cell recorded in this session was −27° (dashed lines). A: During slow rotations, the maximum head angular velocity was 30°/s (reached each time the rat was oriented in the preferred direction). B: During fast rotations, the maximum head angular velocity was 140°/s.

(43%) increased their peak firing rates by more than one-third–and in three cases by more than 50%. On average, the peak firing rates increased by $36 \pm 6\%$ (SEM; range: $+11\% \sim +100\%$) from the slow to fast passive rotations (Fig. 5, continuous line).

This did not depend on turning direction: the ratios of peak firing rates during the fast versus slow passive rotations were not significantly different between clockwise (CW) and counterclockwise (CCW) turns (Wilcoxon matched-pairs test, N = 14, NS).

In cells recorded in two or more sessions, the increase of the peak firing rate during faster passive rotations did not vary significantly between the successive sessions (Wilcoxon matched-pairs test, N = 9, NS). In the few sessions where more than one HD cell were recorded simultaneously, the changes in peak firing rates between slow and fast rotations were not significantly different in the respective neurons (Wilcoxon matched-pairs test, N = 4, NS).
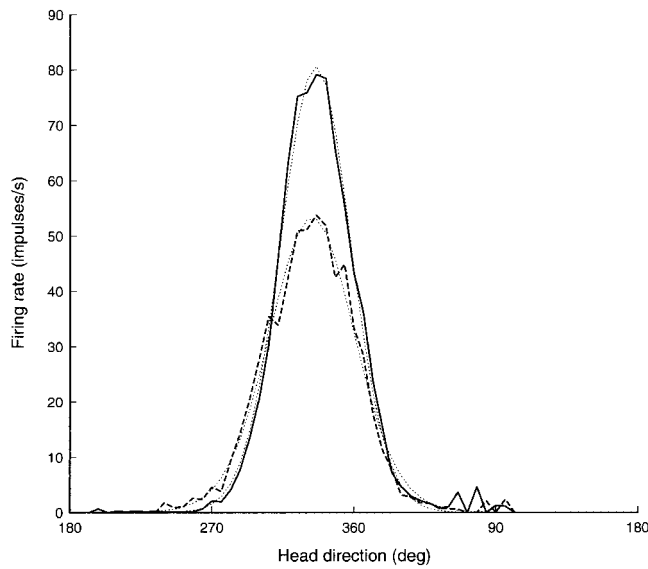
FIGURE 3. Response curves of a typical head direction (HD) cell, recorded during slow (dashed curve) and fast rotations (continuous curve). Analytical fits are represented as dotted curves.

Velocity independence of preferred directions, angular response ranges, and baseline firing rates

The preferred directions remained stable between slow and fast rotations (mean shift: 5 ± 7°, SD; see also Fig. 3). The ranges of the angular responses were 115 ± 11° (SEM, range: 70–193°) during the slow passive rotations, and 100 ± 7° (range: 74–169°) during
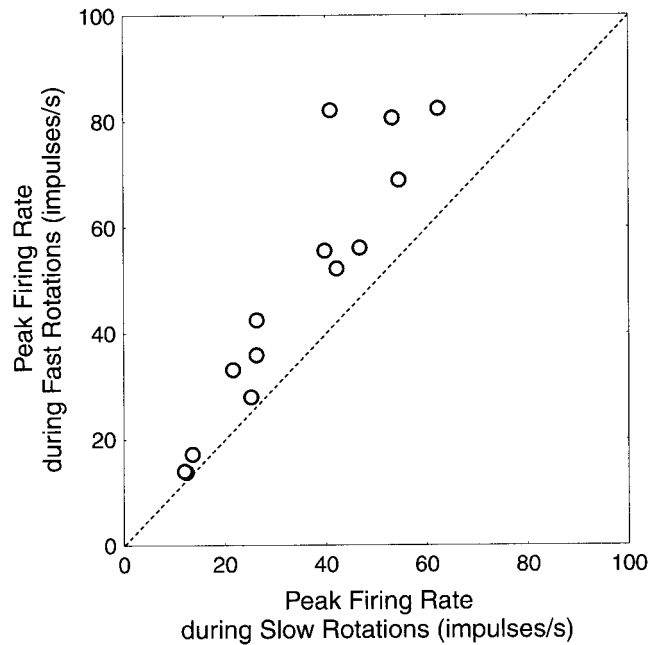

FIGURE 4. Peak firing rates during fast versus slow passive rotations for all neurons. Because unchanged peak firing rates would fall on the dashed line, virtually all neurons showed an increase in peak firing rates during rapid passive rotations.
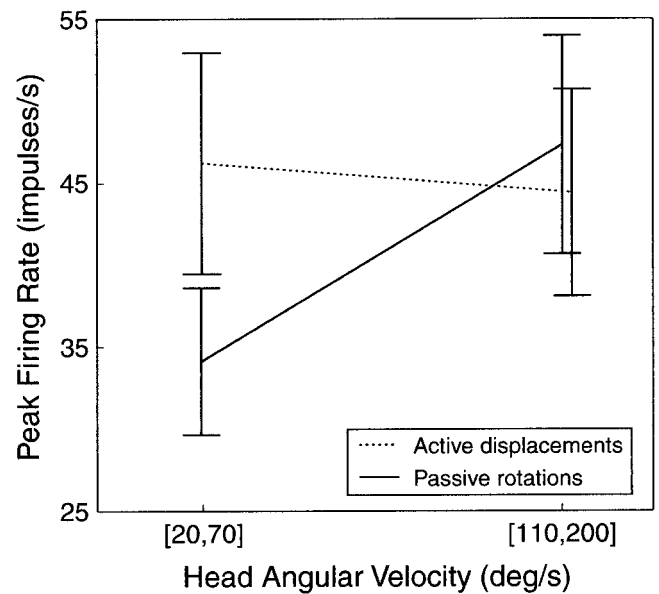

FIGURE 5. Mean peak firing rates (± SEM) during passive rotations (continuous line) and active displacements (dotted line) at slower and faster head angular velocities.

the fast passive rotations. These values were not significantly different (Wilcoxon matched-pairs test, NS, N = 14). The baseline firing rates were 0.4 ± 0.3 impulses per second (range: 0–3.1 impulses per second) during the slow passive rotations, and 0.7 ± 0.4 impulses per second (range: 0–6.2 impulses per second) during the fast passive rotations. These values were not significantly different (Wilcoxon matched-pairs test, N = 14, NS).

The skewness of the angular response curve is unchanged between CW and CCW turns

One possible factor contributing to increased peak firing rates during fast rotations could be deformation of the response curve. There is controversy concerning the changes in the shapes of the angular response curves of AD HD cells during CW versus CCW head turns. Blair et al. (1997) suggested that the response curves of AD HD cells were distorted during head turns. This was inferred from the finding that the preferred directions of the CW and CCW response curves were shifted relative to one another, but that their angular ranges were not significantly different from that of the overall response curve (combining all head turns). To test this, Taube and Muller (1998) measured the ratios of the slopes of the left and right edges of the response curves. This direct comparison of CW and CCW response curves failed to demonstrate a significant difference. Here, the asymmetry of the response curves (measured as skewness) was compared in CW versus CCW response curves from fast passive rotations. This failed to show significant differences (Wilcoxon matched-pairs test, N = 14, NS). For comparison purposes, this analysis was also repeated for data recorded during the active displacements phase, and again no significant difference in skewness was found (Wilcoxon matched-pairs test, N = 14, NS).

Are peak firing rates also modulated by angular velocity during active displacements?

As mentioned in the Introduction, it remains unclear whether (and to what extent) peak firing rates of AD HD cells are modulated by angular velocity during active head turns. Although this was not the principal focus of the present study, this data analysis was made for comparison purposes. The peak firing rates of the cells were not significantly different between slow (20–70°/s) and fast (110–200°/s) active head turns (Wilcoxon matched-pairs test, N = 14, NS). This is shown in Figure 5 (dashed line). However, peak firing rates varied from −16% to +33% (mean: −2 ± 3%) in the two conditions. This raises the question whether there are two subpopulations of AD HD cells, which are or are not modulated by sensory signals of self-motion during both passive and active rotations. To test for this, fast/slow ratios of peak firing rates were computed for each cell in the two conditions. The pairs of ratios for each cell were then sorted in two clusters using a K-means clustering procedure. This procedure is analogous to an analysis of variance (ANOVA) "in reverse": starting with two random clusters, pairs of ratios are moved between the clusters in order to minimize variability within clusters and maximize variability between clusters. This yielded two subgroups, with significantly different ratios for passive rotations ($F(12,1) = 24.66$, $P < 0.001$), but not for active movements ($F(12,1) = 1.21$, NS). Thus, the data provide no evidence that AD HD cells can be divided into two groups based upon the presence or absence of modulation by head angular velocity during both active and passive rotations.

DISCUSSION

The principal result here is that when rats are passively rotated, the peak firing rates of the AD HD cells are greater at higher angular velocities. This was not due to variations in responses of the cells related to turning direction, as the velocity-dependent increase in peak firing rates was similar for left and right rotations, and CW and CCW response curves had indistinguishable skewness.

This experiment was designed to test the influences of sensory signals arising from self-movements in the absence of locomotor signals. Because the rats were rather immobile during the rotations, it is unlikely that the responses of the cells were due to differences in motor efferent copy or corollary discharge signals. Thus, the peak firing rate increase observed during faster rotations was more likely due to velocity signals of sensory, rather than motor origin. These would include vestibular, somatosensory, and dynamic visual inputs. Because the rats were stationary and drinking in both conditions, neck and limb proprioceptors would not have provided accurate information about the velocity of ongoing rotations. Somatosensory signals are thus unlikely to underlie the velocity-dependence of the peak firing rates of the HD cells. In contrast, both the vestibular and the dynamic visual signals provide precise information useful for computing head angular velocity.

These signals are likely candidates to mediate the increase in peak firing rate of the HD cells during faster rotations.

One possible alternative explanation of the increase in peak firing rates during the faster passive rotations is that the rats may have been more attentive or aroused than during the slower passive rotations. However, this seems unlikely, in particular because one would expect that changes in attention or arousal would also correspond to variations in the baseline firing rate of the cells, which was not observed here. Also, the rats were involved in the same attentive drinking behavior during slow and fast passive rotations, suggesting that their level of attention and arousal was comparable in the two conditions.

The increase in peak firing rates during faster rotations could be related to the finding that the power of hippocampal rhythmic slow activity (RSA) at θ frequencies (~8 Hz) increases with angular velocity in passively rotated rats (Gavrilov et al., 1996). However, enhanced θ RSA is unlikely to directly mediate the increase in the peak firing rates of the AD HD cells during faster passive rotations, because there is little evidence of θ-rhythmic activity in AD (Wertes et al., 2001). Nonetheless, sensory signals arising during self-movement could independently influence both the amplitude of θ RSA as well as HD cell discharge rates.

Variability in the velocity dependence among individual neurons indicates that different cells may receive different levels of modulation by the sensory signals arising during passive rotations. However, there was no evidence that a subpopulation of AD HD cells is particularly sensitive to angular velocity during both active and passive rotations while another population is less responsive.

Consistent with the recent report that discharge rates of AD HD cells are, at best, weakly correlated with head angular velocity in freely moving rats (Taube and Muller, 1998), here in the active displacements condition, the peak firing rates of the cells were not higher during faster head turns. While this appears to contradict other reports (Taube, 1995; Blair and Sharp, 1995; Blair et al., 1997; Stackman and Taube, 1997; Blair et al., 1998), it must be emphasized that in those studies where peak firing rates, rather than mean firing rates, were compared (Blair et al., 1997; Blair et al., 1998), the increase during faster head turns was only on the order of 5–10%. Besides, as mentioned in the Introduction, the responses of the HD cells may not be directly comparable between active head turns at high versus low velocities when rats are engaged in the foraging task. Future studies should examine in a more appropriate manner whether the peak firing rates of AD HD cells increase with angular head velocity during active locomotion. This could be achieved by recording HD responses during well controlled active head turns at different velocities.

In summary, the peak firing rates of the AD HD cells were modulated by angular velocity when the rats were passively rotated (but not while they actively moved on the same platform). This is likely due to sensory signals arising during self-motion, such as vestibular and dynamic visual signals. Higher firing rates would transmit more information (Brunel and Nadal, 1998) during faster movements to downstream structures, such as the hippocampus.

Acknowledgments

REFERENCES

Blair HT, Sharp PE. 1995. Anticipatory head direction signals in anterior thalamus: evidence for a thalamocortical circuit that integrates angular head motion to compute head direction. J Neurosci 15:6260–6270.

Blair HT, Sharp PE. 1996. Visual and vestibular influences on head-direction cells in the anterior thalamus of the rat. Behav Neurosci 110:643–660.

Blair HT, Lipscomb BW, Sharp PE. 1997. Anticipatory time intervals of head-direction cells in the anterior thalamus of the rat: implications for path integration in the head-direction circuit. J Neurophysiol 78:145–159.

Blair HT, Cho J, Sharp PE. 1998. Role of the lateral mammillary nucleus in the rat head direction circuit: a combined single unit recording and lesion study. Neuron 21:1387–1397.

Brunel N, Nadal JP. 1998. Mutual information, Fisher information, and population coding. Neural Comp 10:1731–1757.

Gavrilov V, Wiener SI, Berthoz A. 1996. Whole-body rotations enhance hippocampal theta rhythmic slow activity in awake rats passively transported on a mobile robot. Ann NY Acad Sci 781:385–398.

Goodridge JP, Taube JS. 1995. Preferential use of the landmark navigational system by head direction cells in rats. Behav Neurosci 109:1–12.

Khabbaz A, Fee MS, Tsien JZ, Tank DW. 2000. A compact converging-electrode microdrive for recording head direction cells in mice. Soc Neurosci Abs 26:984.

Muller RU, Kubie JL, Ranck JB Jr. 1987. Spatial firing patterns of hippocampal complex-spike cells in a fixed environment. J Neurosci 7:1935–1950.

Ranck JB Jr. 1984. Head-direction cells in the deep cell layers of dorsal presubiculum in freely moving rats. Soc Neurosci Abs 10:599.

Robertson RG, Rolls ET, Georges-François P, Panzeri S. 1999. Head direction cells in the primate pre-subiculum. Hippocampus 9:206–219.

Stackman RW, Taube JS. 1997. Firing properties of head direction cells in the rat anterior thalamic nucleus: dependence on vestibular input. J Neurosci 17:4349–4358.

Taube JS. 1995. Head direction cells recorded in the anterior thalamic nuclei of freely moving rats. J Neurosci 15:70–86.

Taube JS. 1998. Head direction cells and the neurophysiological basis for a sense of direction. Prog Neurobiol 55:1–32.

Taube JS, Muller RU. 1998. Comparisons of head direction cell activity in the postsubiculum and anterior thalamus of freely moving rats. Hippocampus 8:87–108.

Vertes RP, Albo Z, Viana di Prisco G. 2001. Theta-rhythmically firing neurons in the anterior thalamus: implications for mnemonic functions of Papez's circuit. Neurosciece 104:619–625.

Wiener SI. 1993. Spatial and behavioral correlates of striatal neurons in rats performing a self-initiated navigation task. J Neurosci 13:3802–3817.

Zugaro MB, Tabuchi E, Wiener SI. 2000. Influence of conflicting visual, inertial and substratal cues on head direction cell activity. Exp Brain Res 133:198–208.

Zugaro MB, Berthoz A, Wiener SI. 2001a. Background, but not foreground, spatial cues are taken as references for head direction responses by rat anterodorsal thalamus neurons. J Neurosci 21(RC154):1–5.

Zugaro MB, Tabuchi E, Fouquier C, Berthoz A, Wiener SI. 2001b. Active locomotion increases peak firing rates of anterodorsal thalamic head direction cells. J Neurophysiol 86:692–702