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Interaction of linear vestibular and visual stimulation in the macaque ventral intraparietal area (VIP)

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Abstract

Navigation in space requires the brain to combine information arising from different sensory modalities with the appropriate motor commands. Sensory information about self-motion in particular is provided by the visual and the vestibular system. The macaque ventral intraparietal area (VIP) has recently been shown to be involved in the processing of self-motion information provided by optical flow, to contain multimodal neurons and to receive input from areas involved in the analysis of vestibular information. By studying responses to linear vestibular, visual and bimodal stimulation we aimed at gaining more insight into the mechanisms involved in multimodal integration and self-motion processing. A large proportion of cells (77%) revealed a significant response to passive linear translation of the monkey. Of these cells, 59% encoded information about the direction of self-motion. The phase relationship between vestibular stimulation and neuronal responses covered a broad spectrum, demonstrating the complexity of the spatio-temporal pattern of vestibular information encoded by neurons in area VIP. For 53% of the direction-selective neurons the preferred directions for stimuli of both modalities were the same; they were opposite for the remaining 47% of the neurons. During bimodal stimulation the responses of neurons with opposite direction selectivity in the two modalities were determined either by the visual (53%) or the vestibular (47%) modality. These heterogeneous responses to unimodal and bimodal stimulation might be used to prevent misjudgements about self- and/or object-motion, which could be caused by relying on information of one sensory modality alone.

Introduction

Self-motion through a natural environment is encoded across different sensory systems. Along with somatosensory and auditory signals, visual and vestibular information can be used to estimate self-motion parameters. Relying only on the information of one of the latter sensory modalities can lead to perceptual misjudgements. A combination of visual information as provided by optic flow with vestibular-related information could solve this problem (Telford *et al*., 1995). Such a combination of sensory signals could be achieved most easily in areas in the brain receiving both kinds of sensory inputs. One appropriate candidate is the macaque ventral intraparietal area (VIP). Neurons in area VIP are responsive to optic flow stimuli (Schaafsma & Duysens, 1996; Schaafsma *et al*., 1997; Bremmer *et al*., 2002a) and to rotational vestibular stimulation (Bremmer *et al*., 1997a, 2002b). Area VIP is reciprocally connected to the medial superior temporal area (MST) which is also involved in the processing of visual and vestibular self-motion information (Duffy, 1998; Bremmer *et al*., 1999b; Froehler & Duffy, 2002). Additionally, Lewis & Van Essen (2000) have revealed direct connections to areas of the parieto-cortical network, which has been implicated in the processing of vestibular information (Büttner & Buettner, 1978; Guldin *et al*., 1992; Akbarian *et al*., 1993, 1994; Guldin & Grüsser, 1998). Most of the physiological studies of neuronal activity in these vestibular areas only tested for rotational vestibular signals, as provided by the semicircular canals. However, a large part of everyday self-motion consists of translational movements as detected by the otoliths. Many studies related to the otolith system only tested for steady tilt signals and concluded, from the absence of responses, that there are no otolithal influences present in the areas of the vestibular network (e.g. Guldin *et al*., 1992). However, Siebold *et al*. (2001) were able to show that 74% of the neurons in the fastigial nucleus respond to dynamic linear acceleration whereas static tilt of the head influenced only a minor proportion of the neurons. Thus, searching for head tilt signals might lead to an underestimation of the proportion of neurons related to the processing of linear translational signals (Angelaki & Dickman, 2000; Siebold *et al*., 2001). Similarly, recent studies have demonstrated linear translational signals in area MST (Duffy, 1998; Bremmer *et al*., 1999b; Froehler & Duffy, 2002).

In our present study we were interested in whether such linear vestibular information is also present in area VIP. Additionally, we wanted to address the question of how this information would interact with the visual information available. We recorded neuronal activity in area VIP during linear translation in darkness (termed 'pure vestibular stimulation'), during visually simulated forward and backward motion without additional vestibular stimulation (termed 'pure visual stimulation') and, finally, during bimodal stimulation (linear translation with additional visual input). Neuronal responses were analysed in order to determine the mechanisms of multimodal integration during self-motion processing.

Preliminary data of this study have been published in abstract form (Schlack & Bremmer, 2001).

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Materials and methods

We recorded neuronal activity in area VIP in two male awake behaving monkeys (*M. mulatta*, 9.2 and 9.5 kg). All treatment of the animals such as housing and surgical procedures were in accordance with German and international published guidelines on the use of animals in research (European Communities Council Directive 86/609/ECC).

Animal preparation and experimental equipment

Before the experimental period, the animal had a head-holding device implanted under general anaesthesia (for details of the surgical procedure see Bremmer *et al*., 1997b). Briefly, monkeys were pretreated with atropine and sedated with ketamine hydrochloride. Under general anaesthesia [pentobarbital sodium (Nembutal), 10 mg/kg iv] and sterile surgical conditions each animal was implanted with a device for holding the head. For the monitoring of eye movements, two scleral search coils were implanted. On the basis of previously measured MRI scans, we placed the recording chamber for microelectrode penetrations parallel to the intraparietal sulcus and orthogonal to the scull. In one animal we recorded from the left, in the other animal from the right cortical hemisphere.

During experiments, monkeys were seated in a primate chair with the head fixed. For each correct trial monkeys received a liquid reward. We used a PC running self-written software (NABEDA developed by M. Pekel) to control the stimulation and data acquisition. For each penetration we determined the location of area VIP by the position of the electrode in the chamber relative to the MRI scans and by physiological criteria (e.g. direction-selective responses to visual stimuli). After recording was completed, the monkey was given an overdose of sodium pentobarbital and, after respiratory block and cessation of all reflexes, transcardially perfused. Histological analysis from the first animal verified that recordings had been performed in area VIP.

Visual and vestibular stimuli

We used three types of stimulation: linear translation in darkness (termed 'pure vestibular stimulation'), visually simulated forward and backward motion without additional vestibular stimulation (termed 'pure visual stimulation') and bimodal stimulation (linear translation with additional visual input). For different cells, the three different types of stimulation were presented counter-balanced, i.e. in pseudo-randomized, order.

During all experiments the monkey's chair was fixed on a parallel swing. For the pure visual stimulation the swing was fixed in the frontal position 0.48 m away from a large tangent projection screen covering the central 90 × 90° of the visual field.

Visual stimuli were generated with a Silicon Graphics Workstation using Performer 2.1 software and back-projected onto the screen by a video projector (Elektrohome 4100). During visual stimulation the monkey fixated on a central target. The stimuli consisted of random dot patterns (white dots on a black background), simulating horizontal forward (expansion) or backward (contraction) motion of the animal at 14 cm/s. The singularities of these optic flow stimuli were located at the centre of the screen. Five hundred and six light points were used, each with a diameter of ≈ 1°. A stationary random dot pattern served as a control.

Vestibular stimulation was achieved by moving the parallel swing sinusoidally with a frequency of 0.25 Hz and a peak-to-peak amplitude of 1 m in forward and backward directions. The maximum acceleration was 1.22 m/s^2. In order to avoid sideways motion, the swing was stabilized by a guide rail on the ground. The maximal upward/downward component of the movement was 0.031 m with a maximal acceleration of 0.076 m/s^2, which is below the sensory threshold (Bremmer *et al*., 1999b). The position of the swing was recorded simultaneously with the spike data. In order to measure the baseline activity of the neurons, the spike rate of each cell was computed as the average activity across several trials (each being 3 s long) without movement of the swing. The pure vestibular stimulation was performed in total darkness. In order to exclude tactile stimulation on the monkey's head we covered the monkey's head with a light-tight windshield.

For bimodal stimulation we projected a stationary random dot pattern onto the screen and moved the monkey simultaneously on the swing. Thus visual and vestibular information about the monkey's movement in space was provided.

Data analysis

To determine the responsiveness of neurons to the pure visual, pure vestibular and bimodal stimulation, the cell's activity during the stimulation was compared with a stationary baseline condition. This was done with a Kruskal–Wallis analysis of variance. When the null hypothesis could be rejected ($P < 0.01$), the cell's activity was considered to be modulated by the stimulus. In these cases a method of multiple comparisons (Siegel & Castellan, 1988) was used to test which comparisons were significant.

In order to classify the pure visual responses we compared the cell's response for the stationary, the expansion and contraction stimulus. If the cell activity was significantly higher in the expansion condition than in the contraction condition the cell was considered to encode forward motion (and vice versa for backward motion).

As the neuron could either encode the direction of the vestibular stimulation and/or a certain velocity, acceleration or position in space, three different analyses were performed to take these different possibilities into account.

The first analysis aimed at determining whether the neuron was direction-selective. Three intervals were defined and tested against each other and against baseline activity. The first interval began with stimulus onset and lasted until the movement slowed down to < 0.001 m/s (i.e. forward motion). The period centred on the reversal point with velocities < 0.001 m/s was defined as the second time interval. The remaining time until the end of the trial formed the third time interval (i.e. backward motion). Neurons with significant differences in neuronal activity during forward vs. backward movement (first vs. third time interval) were classified as direction-selective. The direction-selective response could either be as long as the whole first or third time interval or cover only a part of the trajectory. Accordingly, the first kind of neuron was classified as 'broadly direction tuned', the latter kind as 'narrowly direction tuned'. A direction index (DI) was computed for all direction-selective neurons to quantify the strength of the direction selectivity:

$$DI = 1 - (mDND/mDPD) \quad (1)$$

In this equation, mDND is the mean discharge in null direction and mDPD is the mean discharge in preferred direction, the null direction being the direction opposite to the preferred direction. The DI quantifies the additional discharge during movement in the preferred as opposed to the null direction. According to this definition, a DI of 0.0 would indicate a similar strength of discharge during forward and backward motion. A DI of 0.5 would be achieved if the activity in the null direction was half that of the activity in the preferred direction. A

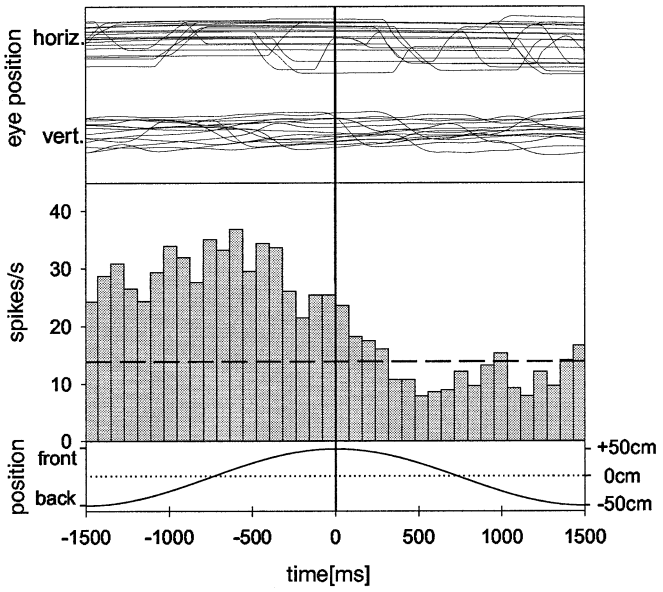

FIG. 1. Cell response for a specific stimulus direction. The lower panel shows the position of the swing between the front and the rear reverse point. The panel above depicts the corresponding neuronal activity of the neuron. Activity is aligned to the frontal reverse point of the trajectory of the swing as indicated by the vertical solid line. The horizontal dashed line shows the level of baseline activity. For this individual neuron activity was significantly increased during forward motion ($P < 0.01$) and tended to be inhibited (but not significantly) during backward motion. The top panel shows the horizontal and vertical eye movements the monkey made during the different trials. Because no systematic change of eye position was present among trials, the reproducible change of neuronal activity could not be related to eye movements.

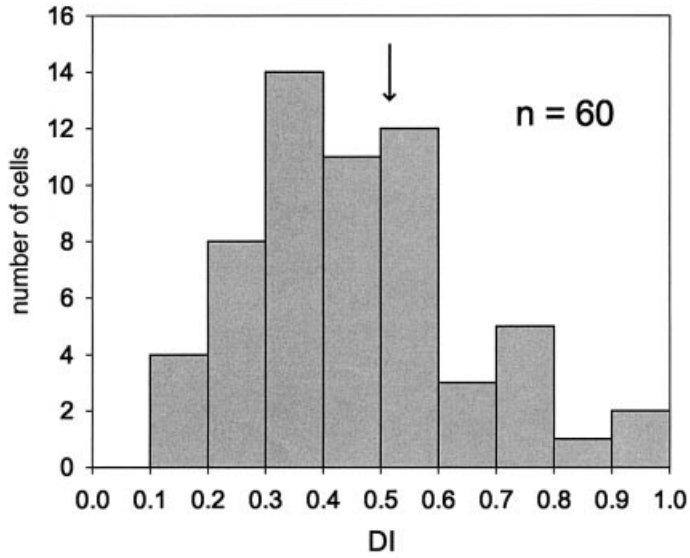

FIG. 2. Distribution of the direction index (DI) of the direction-selective neurons. DI was determined for the 60 direction-selective neurons. The arrow indicates the DI of the example neuron shown in Fig. 1 (DI = 0.51). The mean DI of the population of neurons was 0.45.

DI of 1.0 would indicate a null response during movement in null direction.

For the second analysis we divided the duration of the recording into 100-ms bins and performed a Kruskal–Wallis analysis over these samples and the baseline condition. This analysis was performed to reveal short-lasting effects such as a peak for a certain amount of acceleration.

In the third analysis three individual analysis windows were defined to access the responses of those cells which could not be described adequately by the two other procedures.

Neurons were considered to respond significantly to vestibular stimulation when at least one of the three analyses revealed a statistically significant effect ($P < 0.01$).

For each cell being responsive to vestibular stimulation, we were interested in the temporal relationship between the cell activity and vestibular stimulation. Hence, according to a standard procedure for analysing vestibular data (see, e.g., Berthoz *et al*., 1992), the differences between the phase of the first harmonic of a Fourier analysis of the neuronal response and the velocity profile of the swing movement were computed.

Results

Vestibular classification

We recorded from 133 neurons in area VIP of two awake behaving monkeys during linear vestibular stimulation. Of these neurons, 77% (102/133) responded significantly to vestibular stimulation. This response could not be caused by eye movements of the monkeys because the animals did not make any systematic eye movements among trials (as an example see Fig. 1). The response pattern varied, ranging from neurons clearly tuned for (Group 1) the direction of motion to (Group 2) the acceleration (or position) of motion to those (Group 3) with a more complex vestibular response. Eighteen per cent from the first two groups (18/102) belonged to both groups (1 and 2) because they were modulated by both the direction of movement and the acceleration (or position) of the monkey.

Encoding of stimulus direction

Fifty-nine per cent of the cells (60/102) showed direction selectivity to linear translation in darkness (termed 'pure vestibular stimulation'). Two-thirds (40/60) revealed a narrow direction-selective response. One third of the neurons (20/60) were broadly tuned to the direction of self-motion. Neurons from this latter group revealed a strong discharge, e.g. during the whole forward linear translation. During backward movement the firing rate remained at a significantly lower level (and vice versa for neurons encoding the backward movement). In addition, the activity of some of these broadly tuned direction-selective neurons was modulated by the velocity of the movement. For such neurons, activity was not constant during movement into preferred or nonpreferred direction but rather sinusoidally modulated, i.e. also related to the velocity profile of the movement. An example of such a broadly tuned cell with additional velocity tuning is shown in Fig. 1. During forward motion the cell's activity was significantly increased ($P < 0.01$) with regard to baseline; during backward motion the activity was slightly (but not significantly) lower than baseline. Hence, this cell coded for forward motion.

As a measure of the strength of the direction selectivity we computed the direction index DI for each of the 60 direction-selective neurons. The distribution of DI across the population of neurons is shown in Fig. 2. The mean DI was 0.45, indicating that on average the neurons' discharge during motion into the preferred direction was nearly twice as high as the discharge in the null direction.

Encoding of acceleration (or position) in space

Thirty-eight per cent of the neurons (39/102) did not encode the direction of self-motion but rather the acceleration of the movement

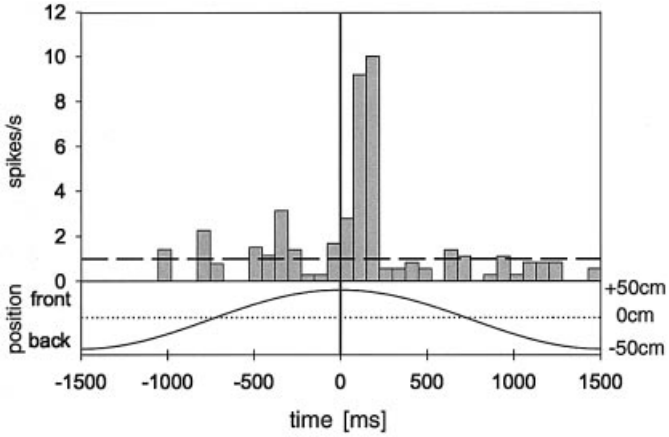

FIG. 3. Cell with a narrow response profile. Same data presentation as in Fig. 1. The neuronal activity of this neuron peaked at the frontal reverse point of the movement. During the remaining movement it was not significantly different from baseline activity ($P > 0.05$).

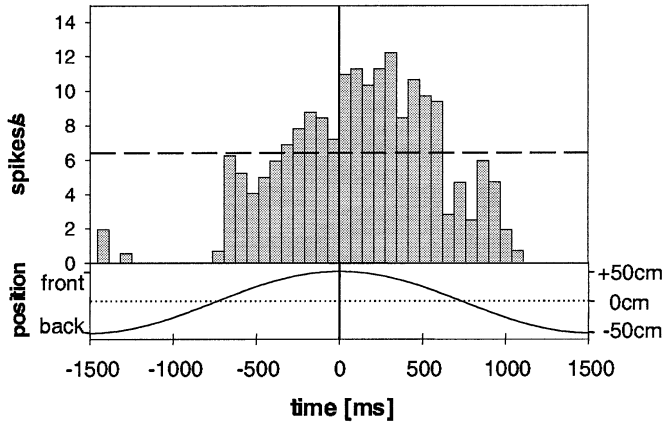

FIG. 4. Cell with a broad response profile. Same data presentation as in lower part of Fig. 1. The discharge rate of this neuron was increased during backward acceleration (or alternatively when the monkey was in front of the mid-position of his movement trajectory) and inhibited during forward acceleration (or alternatively when it was behind this mid-position).

or the monkey's position in space. Due to the sinusoidal movement trajectory it was not possible to dissociate between the two movement parameters because they have a fixed phase difference of 180°. Nevertheless, two different types of response profiles were distinguished.

(i) Fifty-six per cent of the neurons (22/39) showed a narrow tuning. For 68% of these neurons (15/22) the peak discharge was at a reverse point of the movement. As an example, Fig. 3 shows a cell that revealed a burst of activity with a latency of 80 ms after the monkey passed the frontal reverse point of the movement.

(ii) Forty-four per cent of the cells (17/39) had a rather broad response profile. This could correlate, for example, with the movement interval of backward acceleration or alternatively with the very part of the movement trajectory with the monkey being in front of the midline of the movement trajectory. Of these cells, 65% (11/17) preferred backward acceleration (or a position in front) and 35% (6/17) preferred forward acceleration (or a position behind the midline). Figure 4 shows an example of such a cell. Backward acceleration (or positions in the front hemifield of space) led to an increase in the spike rate, while forward acceleration (or positions in the back field) caused a strong inhibition of the cell's activity. Thus, this cell coded for either backward acceleration or anterior space.

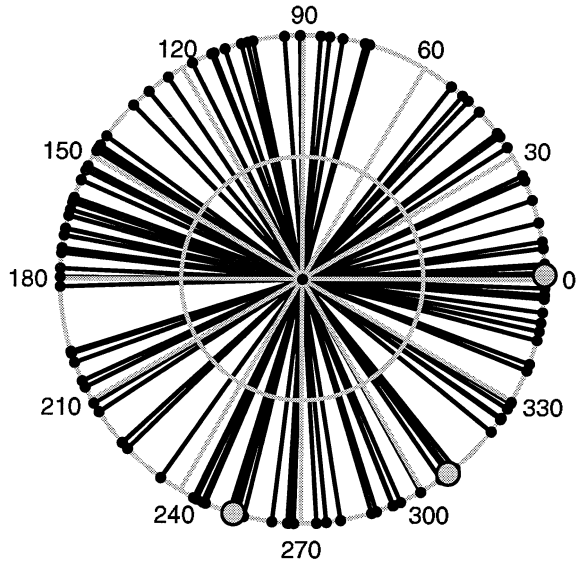

FIG. 5. Phase relationship between cell response and stimulus velocity for all vestibular-responsive cells ($n = 102$). The polar plot shows the distribution of phases between cell response and velocity of the movement. Each vector and dot corresponds to the phase of one single neuron. The large grey dots indicate the phases of the three neurons represented in Figs 1, 3 and 4. There was no bias for a particular phase amongst the population.

Complex vestibular response

Although significantly modulated by vestibular stimulation, the tuning of 20% of the neurons (20/102) could not be classified into a simple response scheme. These neurons' responses varied reproducibly among trials, but did not show any simple straightforward relationship between neuronal response and acceleration/spatial position or movement direction.

Phase difference between cell response and vestibular stimulation

Figure 5 shows the phase differences between cell activity and vestibular stimulation for the 102 vestibular-responsive cells. We related neuronal activity to head velocity. Because the vestibular stimulation was sinusoidal, selection of position or acceleration would have merely introduced a constant offset of –90° or +90°, respectively. Phase differences were uniformly distributed. Only the group of broadly direction-selective neurons showed a tendency for phase coupling with peaks at ≈ 0 and 180° (see Fig. 6).

Pure visual and pure vestibular stimulation: direction selectivity

All vestibular-responsive neurons responded also to visual stimulation. We thus addressed the question of whether the responses of neurons to unimodal stimulation (either pure visual or pure vestibular) were related to each other. Hence, 87 of the 102 vestibular-responsive neurons were additionally tested during pure visual stimulation with stimuli simulating either forward (expansion stimuli) or backward (contraction stimuli) motion. The direction selectivity of the neurons was computed and compared to the direction selectivity during the pure vestibular stimulation.

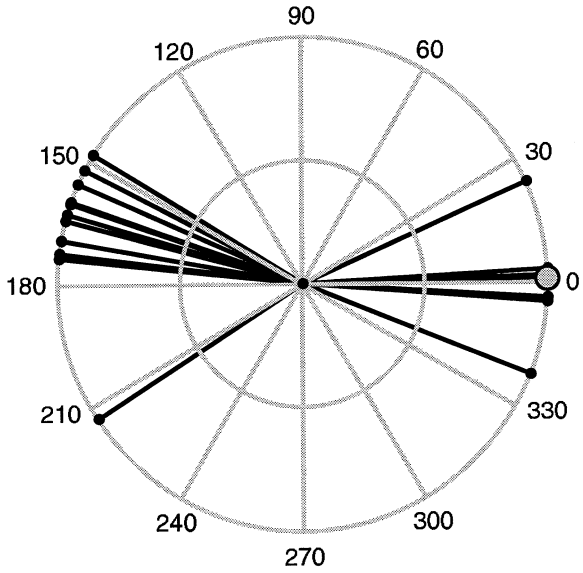

FIG. 6. Phase difference between cell response and stimulus velocity (n = 20). Only the neurons classified as broadly direction tuned were considered, i.e. those neurons whose response lasted for the whole movement time into one direction. For these neurons the phases were either 0 ± 45 or 180 ± 45°, corresponding to forward or backward movement, respectively. The observation that the clusters do not exactly centre on 0° or 180° is related to the fact that we performed the Fourier analysis on the raw data without latency correction. Given an average response latency of 80–120 ms this corresponds to a shift of ≈ 10–15°.

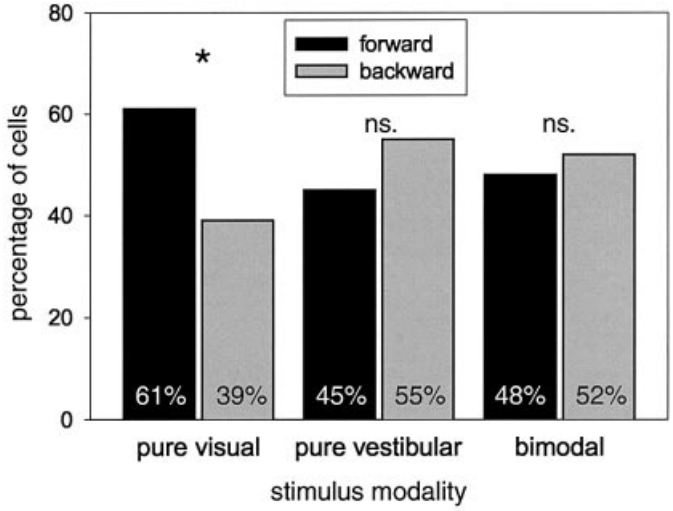

FIG. 7. Distribution of the preferred direction of direction-selective neurons under pure visual (n = 57), pure vestibular (n = 49) and bimodal (n = 23) stimulation (only vestibular-responsive cells). The height of the bars in this plot indicates the percentage of direction-selective neurons preferring forward (black bars) or backward (grey bars) motion. The proportion of cells with a preference for forward or backward motion was similar during pure vestibular or bimodal stimulation as indicated by the four bars on the right (not significantly different from a uniform distribution: $P > 0.05$, χ^2-test). However, there was a significant bias ($P < 0.05$, χ^2-test) for simulated forward motion compared to backward motion during the pure visual stimulation (two bars on the left). ns., not significant; *$P < 0.05$.

Thirty-seven per cent of the neurons (32/87) were direction-selective to stimuli of both modalities, 29% (25/87) only in the case of the visual stimulation and 20% (17/87) only during pure vestibular stimulation; 15% (13/87) of the neurons showed no direction-selective response to any of the two stimulus modalities.

For the cells with direction selectivity to stimuli of both modalities, the preferred directions in the two modalities were compared. Fifty-three per cent of these neurons (17/32) preferred the same direction. For 47% of the neurons (15/32), the preferred direction was opposite during stimulation in the two modalities.

Sixty-one per cent (35/57) of the bimodal neurons (i.e. significant responses to both modalities) with directional visual responses preferred forward motion; 39% (22/57) preferred backward motion. Considering all visually responsive cells, including those without a vestibular response, the ratio of cells preferring simulated forward motion to those preferring simulated backward motion was reduced to 53% compared to 47%. Thus, the number of cells preferring the one or the other (visually simulated) movement direction was almost balanced.

In contrast, the responses of vestibular direction-selective neurons were equally distributed between forward and backward motion. Similarly, during bimodal stimulation the proportions of direction-selective neurons preferring either forward or backward motion was almost the same (see Fig. 7).

Bimodal stimulation

In order to determine the interaction of the two sensory modalities we tested 33 neurons during bimodal stimulation. We found three types of interaction: (i) visual modality dominating the cell's response; (ii) vestibular modality dominating the cell's response; and (iii) similar direction encoding in all conditions.

Visual modality dominating a cell's response

For 30% of the neurons (10/33) the visual stimulus modality dominated the cell's response, i.e. the bimodal direction encoding was similar to that during pure visual and different from the pure vestibular stimulation. This influence of the visual modality is demonstrated for one neuron in Fig. 8. During vestibular stimulation in darkness the discharge of the cell was highest when the monkey moved backward (Fig. 8A). In the pure visual condition the cell preferred simulated forward motion (Fig. 8C) compared to backward motion (Fig. 8D). Bimodal stimulation led to strong discharge rates during forward motion of the monkey (Fig. 8B). Hence, the visual stimulation determined the cell's response during bimodal stimulation.

Vestibular modality dominating a cell's response

The response of 27% of the neurons (9/33) was determined by the vestibular modality. Figure 9 shows the activity of a neuron with a preferred direction of backward movement during pure vestibular stimulation (Fig. 9A). The cell preferred forward motion when stimulated purely visually (Fig. 9C and D). The response to bimodal stimulation was determined by the vestibular stimulus, i.e. the preferred direction under this stimulus condition was backward motion (Fig. 9B).

Similar direction encoding in all three conditions

Fifteen per cent of the neurons (5/33) had the same preferred direction during pure vestibular, pure visual and bimodal stimulation. We computed the direction index DI of these neurons for the pure vestibular, bimodal and pure visual stimulation. For all but one of the neurons the DI was higher during bimodal than during pure vestibular stimulation. Accordingly, the mean ratio of DI of bimodal vs. pure vestibular stimulation, $DI_{ratio\text{-}1} = DI_{bimodal}/DI_{vestib}$, was 1.6. For all

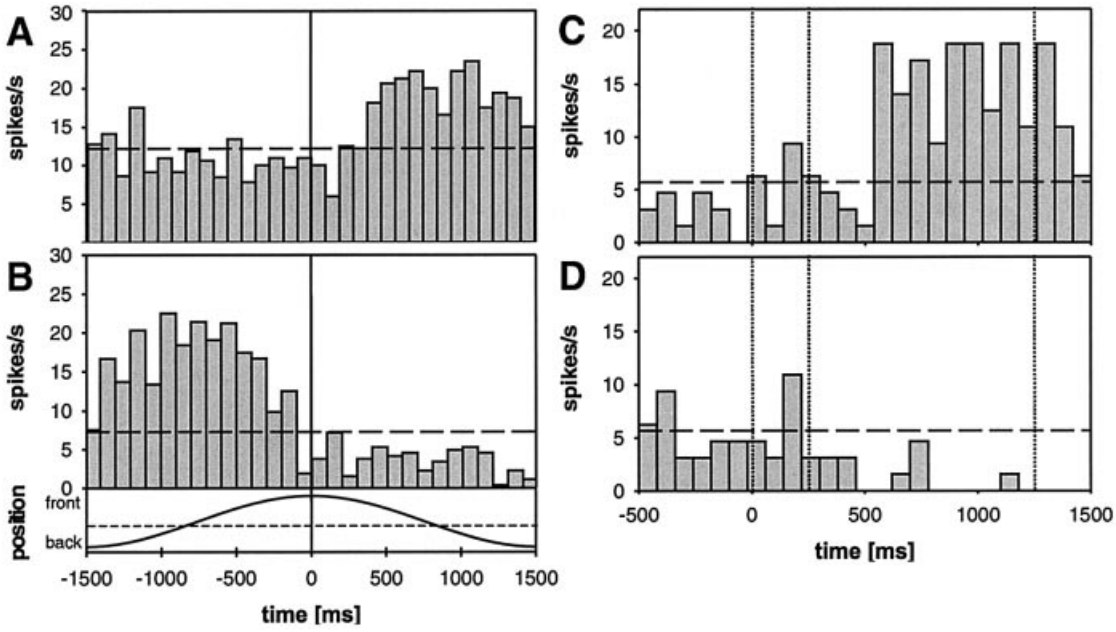

FIG. 8. Direction encoding under pure vestibular, pure visual and bimodal stimulation: the visual stimulus modality determines the cell's response to bimodal stimulation. The two panels on the right (C,D) show the activity of an individual neuron during pure visual stimulation. The first vertical dotted line indicates the onset of the stationary random dot pattern on the projection screen. The activity of the cell is aligned to this onset time. The remaining two dotted vertical lines correspond to the onset and the end of the movement. Panel C shows the activity of the neuron during simulated forward movement (expansion stimulus), while panel D corresponds to the cell's activity during simulated backward movement (contraction stimulus). For this neuron the discharge was significantly increased ($P < 0.01$) during expansion and decreased during the contraction stimulation. Hence, this neuron codes for visually simulated forward motion of the animal. (A) Response of the neuron to pure vestibular stimulation. During this condition the discharge was increased during backward motion of the animal; hence its direction preference was opposite to the pure visual direction encoding. (B) Activity of the neuron during bimodal stimulation. During this condition the activity of the cell was highest during forward motion of the monkey. Hence, the influence of the visual stimulation determined the response of the neuron during bimodal stimulation.

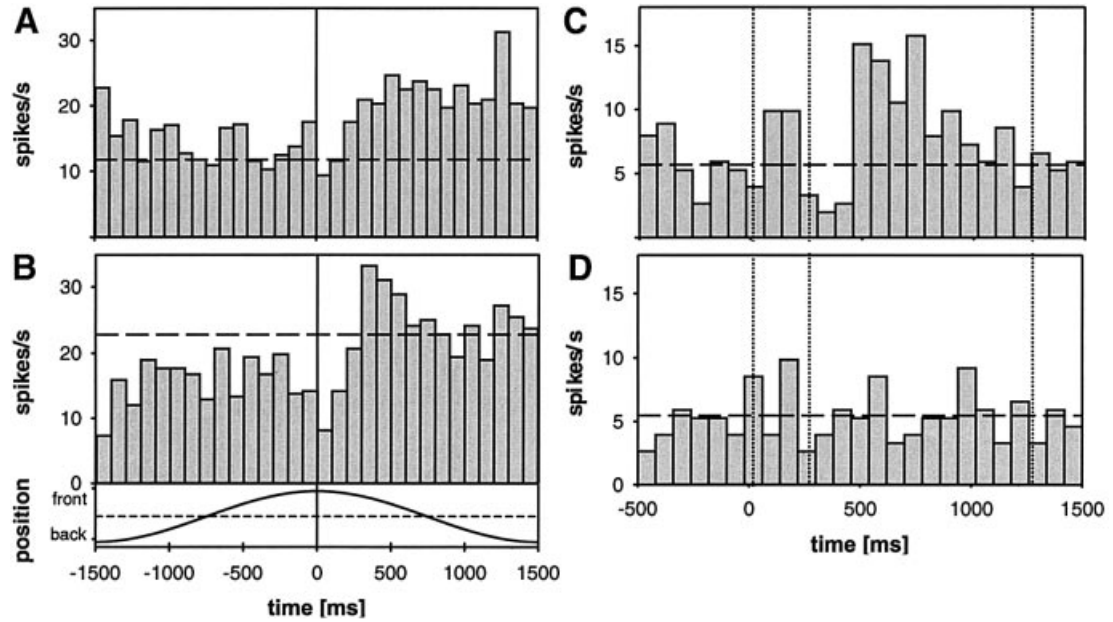

FIG. 9. Direction encoding under pure vestibular, pure visual and bimodal stimulation: the vestibular stimulus modality determines the cell's response to bimodal stimulation. Same data presentation as in Fig. 8. As before, this neuron responded best during visually simulated forward motion (expansion stimulus: panel C). During the simulation of backward motion the activity was not different from baseline activity. (A) The pure vestibular stimulation revealed a preference for backward motion. The preference of motion direction during bimodal stimulation was similar to the pure vestibular condition, i.e. backward motion. Hence the activity of this neuron is determined by the vestibular influence.

but one of the neurons the DI for the pure visual stimulation was slightly higher than for the bimodal stimulation, the mean ratio being $DI_{ratio\text{-}2} = DI_{bimodal}/DI_{vis} = 0.8$. Note, however, that the simulated movement trajectory and the velocity profile of the pure visual stimulation was different from the vestibular conditions. The absolute size of the DI may thus not be directly comparable. Nevertheless, our data imply an enhancement of a cell's response contrast by visual signals.

Of the remaining neurons, 80% (7/9) revealed direction selectivity neither to pure vestibular nor to bimodal stimulation. Twenty per cent (2/9) revealed opposite preferred directions during pure vestibular and pure visual stimulation but, when stimulated bimodally, the direction selectivity was lost. Hence, neither the visual nor the vestibular stimulus modality could dominate the other one to determine the cell's response. As this manner of crossmodal interaction occurred only in two neurons, we report this observation for completeness only.

Discussion

Diversity of vestibular responses to linear vestibular stimulation in area VIP

Our data clearly demonstrate responses to linear translational stimuli in monkey area VIP. The pattern of responses differed substantially between cells. Some neurons were modulated by the direction of movement, some by the acceleration and/or position of the monkey in space and the remaining neurons revealed a reproducible response which could not be unambiguously related to a specific parameter of the vestibular stimulus. This broad spectrum of responses is also reflected by the distribution of phase differences between vestibular stimulus and neuronal response. As there was no bias for specific phases, neurons in area VIP seem to code for a continuum of spatio-temporal patterns of vestibular stimuli.

Self-motion encoding in area VIP

One function of area VIP is thought to be the sensory-based guidance of head movements in near extrapersonal space (Lewis & Van Essen, 2000a; Bremmer *et al*., 2001a; Bremmer *et al*., 2001b). In order to fulfil such a function, the area must have access to a large set of multimodal information. Accordingly, spatial information about objects relative to the head are provided by the head-centred neurons and by the eye position signals available in this area (Duhamel *et al*., 1997; Bremmer *et al*., 1999a). In addition, information about positions and movements of the head in space is required. In the absence of visual feedback this information could be provided by the integration of inertial cues. In the present study we describe a class of cells encoding the acceleration or the position of the monkey's head in space. This class contained two subgroups of neurons with a rather broad or a rather narrow response tuning. With our experimental setup it was not possible to differentiate between acceleration and position signals. This is because the linear vestibular stimulation applied was sinusoidal and only orientated along one spatial axis. Because acceleration of the head is the primary pattern the vestibular system detects, it seems to be more likely that the responses observed in the present study were related to certain acceleration states.

However, space-encoding cells sensitive for particular positions have been described not only in the hippocampal formation (O'Mara *et al*., 1994) but recently also in area MST (Froehler & Duffy, 2002), an area which is heavily interconnected with area VIP. As the parietal cortex is connected to the hippocampus (O'Mara *et al*., 1994; Snyder *et al*., 1998), the pattern of responses in these brain regions could be related to each other.

The primate posterior parietal cortex provides spatial information in different frames of reference simultaneously (Andersen, 1997). The allocentric encoding provided by position cells in area MST (and possibly also in area VIP) seems to play an important role in the process of path integration and navigation (Bures *et al*., 1997; Fukushima, 1997). The output of these cells could, e.g., provide the underlying neuronal mechanism that allows determination and reproduction of the linear distance after passive transport (Berthoz *et al*., 1995; Israel *et al*., 1997). However, whether or not the kind of responsiveness observed in the present study reflects such encoding of allocentric space remains to be determined in future studies.

Encoding of object- and self-motion: visuo–vestibular interaction

Vestibular and visual direction encoding in area VIP

Some of the few earlier studies addressing responses of neurons to linear vestibular stimulation demonstrated direction-selective responses in macaque area MST (Duffy, 1998; Bremmer *et al*., 1999b). Similarly, more than half of the cells in area VIP (59%) recorded in the present study encoded the direction of linear vestibular stimulation. There was no bias for forward or backward motion, suggesting that both kinds of information are equally important (see Fig. 7). This matches the finding in area MST (Bremmer *et al*., 1999b). Additionally, it fits the proposed function of area VIP in the guidance and control of head movements in near extrapersonal space where either goal-directed movements toward objects of interest or the avoidance of obstacles are required and hence forward and backward movement are equally important.

However, in line with other studies (e.g. Schaafsma & Duysens, 1996; Bremmer *et al*., 2002a) the present VIP data show a strong bias for expansion stimuli in the responses to visual stimulation (see Fig. 7). This indicates that this sensory pattern is of great importance for the processes represented in this area. Interestingly, this bias was particularly strong if only bimodal neurons with an additional vestibular response were considered. The bias decreased if all visually tested neurons were considered regardless of whether they had a vestibular response or not. Thus, it seems that this bias plays an important role especially for bimodal neurons.

Both the vestibular and the visual stimuli could be used to determine the pattern of self-motion. Relying only on information from the visual modality could lead to a wrong estimation of the direction of self-motion because optic flow signals can be ambiguous (Lappe *et al*., 1999). As an example, self-motion to the side with gaze directed straight ahead results in the same visual flow on the retina as self-motion straight-ahead and gaze directed to the opposite side. Accordingly, the vestibular information can be used to remove ambiguities from the information provided by the visual modality (Cornilleau-Peres & Droulez, 1994; Hietanen & Perrett, 1996; Harris *et al*., 2000). In the present study, 53% of the neurons with direction-selective responses in both modalities preferred the same direction of movement. The remaining 47% of the direction-selective neurons had different preferred directions, suggesting that the direction-selective neurons in area VIP could be used to encode self-motion and all kinds of interaction between object- and self-motion. These interactions are crucial for the computation of goal-directed movement towards objects and obstacle avoidance (Bense *et al*., 2001). In the present study the information about the direction of self-motion provided by the two modalities during bimodal stimulation was synergistic. As either the visual or the vestibular stimulation could dominate the

responses of the neurons, one could expect a bias for forward motion during bimodal stimulation according to the visual influence. However, this was not the case and both directions of self-motion were encoded by about the same proportion of cells (see Fig. 7). This finding suggests that an integration of the signals must have taken place. Because of the corresponding bimodal information about the direction of self-motion the visual signal is in this case unlikely to cause a perceptual mismatch. A bias for forward motion during synergistic bimodal stimulation is therefore not necessary. It therefore would be interesting to test neurons in VIP during conflicting visual and vestibular stimulation and analyse the resulting direction encoding of bimodal neurons.

Visuo-vestibular interaction

As mentioned above, the vestibular information could be used to remove ambiguities from optic flow caused by object- and self-motion. In addition, vestibular information represents information about movement of the head in space, which could be different from the real amount of self-motion of the whole body (Telford *et al*., 1995). To estimate a goal directed movement the real amount of self-motion of the whole body must be known. This could be achieved by analysing additional information, for instance from the visual domain (Telford *et al*., 1995; Brandt *et al*., 1998). Inhibition of the visual system by vestibular stimulation and vice versa as recently demonstrated by several studies (Wenzel *et al*., 1996; Brandt *et al*., 1998; Bense *et al*., 2001) could form a fundamental scheme to avoid the possible perceptual mismatches as described above. This modulation of activity in the different sensory systems might cause in bimodal neurons either the one or the other modality to determine the cell's response to the stimulation applied, or the two inputs to extinguish each other's influence on the cell activity (Büttner & Henn, 1976). This matches the present results concerning cell activity caused by bimodal stimulation in area VIP.

In the case of different preferred directions in the pure vestibular and the pure visual stimulus condition, there occurred a conflict when information in both modalities was present. This was the case for a subpopulation of 21 neurons. For 43% of these neurons the vestibular stimulation dominated the cell activity, in 47% the visual stimulation was more influential and in 10% the influences of the two modalities were equally weighted so that the neurons lost their direction selectivity. Thus, the amount of bimodal cells relying either on the visual or on the vestibular information was similar. These neurons could be used to avoid perceptual mismatches caused by either the one or the other modality.

Neurons with synergistic encoding of motion direction in the two modalities showed an enhancement of the direction selectivity as indicated by a higher DI during bimodal than during pure vestibular stimulation. Such an enhancement could be used to enforce the 'vote' of a particular neuron for a certain self-motion direction. However, such an enhancement of directional selectivity was not observed for the comparison of bimodal with pure visual stimulation. This latter observation might be related to the fact that the visual signals were not identical in the 'pure visual' and the 'bimodal' conditions. Nevertheless, it indicates that supra-additive responses as observed, e.g., for crossmodal interaction in the superior colliculus (e.g. Stein & Meredith, 1990; Stein *et al*., 1993) is not always found for visual vestibular interactions in area VIP.

Functional implication

The integration of multimodal sensory information is crucial to generate a unique percept of the environment, the movements of objects relative to the body and the amount of self-motion. One region of particular importance for this task is the posterior parietal cortex, as has been implicated by lesion studies showing crossmodal neglect or extinction (for review see, e.g., Pouget & Driver, 2000). Several areas in this part of the brain are multimodal and could thus play a role in the integration of different sensory information. One area in this multimodal network is area VIP which receives input from the vestibular, auditory, visual and somatosensory systems as revealed by anatomical as well as functional studies (Colby *et al*., 1993; Duhamel *et al*., 1998; Lewis & Van Essen, 2000a; Lewis & Van Essen, 2000b; Schlack *et al*., 2000; Bremmer *et al*., 2001a). Additionally, this area has been shown to be involved in the processing of self-motion information. (Schaafsma & Duysens, 1996; Bremmer *et al*., 1997a; Schaafsma *et al*., 1997; Bremmer *et al*., 2002a,b).

Considering linear translational signals, we demonstrated in our study that there is a strong influence of the vestibular system on area VIP. Comparing the modulatory strength of the vestibular input to neurons in this area with that of area MST (Duffy, 1998; Bremmer *et al*., 1999b), we found that the importance of the vestibular modality seems to be even higher in area VIP than in area MST. This is reflected by several observations. Firstly, the proportion of vestibular responsiveness in the two studies was different: Duffy (1998) found only 24%, Bremmer *et al*. (1999b) 55% of the cells responsive to vestibular stimulation, while we found 78% of neurons sensitive to vestibular stimuli. Secondly, the strength of direction selectivity differs: in VIP we found about the same number of cells direction selective during pure vestibular as during pure visual stimulation. In area MST the amount of cells with direction selectivity in the pure vestibular was half that in the pure visual condition. Finally, we showed that both sensory modalities seem to be equally influential during bimodal stimulation such that both could determine the cell's response. In contrast to our findings in area VIP, there are only modulatory effects of the vestibular stimulus on MST neurons during bimodal stimulation. Hence the vestibular signals seem to be even more important in area VIP than in area MST. Even though the self-motion stimulus in our study was passive, qualitative and quantitative similarities in studies comparing passive and active transport suggest that both are driven by a common physiological process (Israel *et al*., 1997). This extends the relevance of our results to more natural conditions where active head displacements take place.

The posterior parietal cortex is involved in spatial analysis and contains neurons that encode space in different frames of reference (Vallar *et al*., 1999; Galati *et al*., 2000). This is the case either implicitly via gain field modulation or explicitly at the single cell level. Duhamel *et al*. (1997) showed that there exists a continuum of reference frames between retinocentric and craniocentric encoding of space in area VIP (Duhamel *et al*., 1997). The present study suggests that some neurons may encode allocentric space based on inertial cues. Thus, spatial information in different reference frames is present in area VIP. This information is provided by different sensory sources. By using this multimodal information (Colby *et al*., 1993; Duhamel *et al*., 1998; Schlack *et al*., 2000), the system could compute a reliable spatial representation of the environment with eliminating mismatches caused by one modality or another.

Taken together, our findings reveal that neurons in area VIP are capable of providing spatial information about the location and movement of the animal with regard to its environment taking into account information from different sensory sources. Additionally, neurons in area VIP tend to prefer visual stimuli in near extrapersonal space and somatosensory stimulation of the head region, and are connected to the premotor cortex (Colby *et al*., 1993; Duhamel *et al*.,

1998; Luppino *et al*., 1999; Lewis & Van Essen, 2000a; Lewis & Van Essen, 2000b). Together with the strong content of information about self- and object-motion all these findings reinforce the hypothesis that area VIP plays a crucial role in multimodal sensorimotor integration and possibly path integration. Thus, area VIP seems to be particularly important for the control and guidance of head movements in near extrapersonal space either during self-motion and object avoidance or goal-directed movements with the head towards objects of interest.

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Abbreviations

DI, direction index; MRI, magnetic resonance imaging; MST, medial superior temporal area; VIP, ventral intraparietal area.

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