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Visual–vestibular interactive responses in the macaque ventral intraparietal area (VIP)

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Abstract

Self-motion detection requires the interaction of a number of sensory systems for correct perceptual interpretation of a given movement and an eventual motor response. Parietal cortical areas are thought to play an important role in this function, and we have thus studied the encoding of multimodal signals and their spatiotemporal interactions in the ventral intraparietal area of macaque monkeys. Thereby, we have identified for the first time the presence of vestibular sensory input to this area and described its interaction with somatosensory and visual signals, via extracellular single-cell recordings in awake head-fixed animals. Visual responses were driven by large field stimuli that simulated either backward or forward self-motion (contraction or expansion stimuli, respectively), or movement in the frontoparallel plane (visual increments moving simultaneously in the same direction). While the dominant sensory modality in most neurons was visual, about one third of all recorded neurons responded to horizontal rotation. These vestibular responses were typically in phase with head velocity, but in some cases they could signal acceleration or even showed integration to position. The associated visual responses were always codirectional with the vestibular on-direction, i.e. noncomplementary. Somatosensory responses were in register with the visual preferred direction, either in the same or in the opposite direction, thus signalling translation or rotation in the horizontal plane. These results, taken together with data on responses to optic flow stimuli obtained in a parallel study, strongly suggest an involvement of area VIP in the analysis and the encoding of self-motion.

Introduction

Unequivocal interpretation of self-motion by the nervous system requires converging multisensory information that takes into account rotational and translational displacements of eyes, head and body in three-dimensional space. It also necessitates a comparison of congruent and conflicting input originating from different sensors. In the neocortex, self-motion detection has been mostly studied from the perspective of optic flow field representations. In such a case, neuronal responses to the variations of retinal image velocity encode information about self-motion such as the direction of heading (Duffy & Wurtz, 1991a,b; see also Bremmer *et al*., 2002). However, for higher cortical processing, a single sensory quality by itself can no longer be of perceptual importance, because every displacement of the head in space will stimulate labyrinthine receptors detecting either rotational (semicircular canals) or linear (otoliths) accelerations, in addition to the visual, auditory and somatosensory peripheries. Furthermore, multisensory input could be used to clarify otherwise ambiguous monosensory information. Thus, signals carrying meaningful messages are certain to contain multisensory information.

The principal objective of this study was to understand how sensory inputs leading to movement-in-space perception/representation are combined at the level of single neurons in the primate neocortex, in particular the ventral intraparietal area (VIP). This area is located in the fundus of the intraparietal sulcus (Maunsell & Van Essen, 1983), neighbouring the medial and lateral intraparietal areas (MIP and LIP, respectively). Its neurons have been shown to respond selectively to the direction and speed of moving visual stimuli (Duhamel *et al*., 1991, 1998; Colby *et al*., 1993). Many of these neurons also have tactile sensitivity. In such cases, location and response properties of visual and somatosensory receptive fields were congruent and codirectional (Duhamel *et al*., 1998). Within the intraparietal sulcus, area VIP has been defined as the principal projection area from the medial temporal area (MT) (Maunsell & Van Essen, 1983), and thus can be considered intimately related to self-motion detection and analysis. It is therefore a good candidate when searching for the existence of other sensory inputs which may interact for this purpose, such as from the vestibular endorgans. Indeed, we found that many neurons in VIP have vestibular responses. Vestibular input, surprisingly, was always tuned in the same direction as the visual on-direction (codirectionality), i.e. noncomplementary.

The overall goal of our research is to describe detection and perception mechanisms of self-movement and object movement as occurring in our three-dimensional surroundings. This environment may normally be physically stable. At times, however, it may become physically unstable. In the natural habitat of nonhuman primates, such an event may occur when the animal is placed on moving branches in a tree. In such a case, questions of active vs. passive movement detection may also come into play.

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Preliminary reports have already been published (Bremmer *et al.*, 1995; Graf *et al.*, 1996; Bremmer *et al.*, 1997).

Materials and methods

Extracellular recordings were made in the left hemispheres of two female macaque monkeys, one rhesus *(Macaca mulatta*: monkey 1*)* and one fascicularis (*Macaca fascicularis*: monkey 2). Animal care (housing, nourishment, veterinary consultations, surgical procedures, postoperative care, daily care) conformed to French Government regulations (Ministries of Agriculture and Research, CNRS) and European Union standards (European Communities Council Directive 86/609/EEC), and were approved by a joint CNRS/ Ministry of Agriculture/Veterinary Services commission (approval #75–546). Most animal preparation, training and recording procedures have been described in detail in earlier publications (Ben Hamed *et al.*, 2001; Bremmer *et al.*, 2002), and are summarized briefly in the following.

Animal training

Head-fixed animals were initially trained to fixate on a small spot of light within a narrowly defined window (2° × 2°) for a certain time (usually 3.5 s) to receive a liquid reward. The fixation target was presented in darkness and in light to monitor a given neuron's resting activity, its firing rate during large-field visual motion to determine its selectivity for the direction and speed of stimulus motion, or during horizontal whole-body rotations in light and in darkness to determine its activity during VOR suppression. To determine a neuron's eye position sensitivity, the spot was located in random order at nine different locations on the tangential screen.

Surgical procedures

For all surgical interventions, animals were initially anaesthetized with an intramuscular injection of ketamine (10 mg/kg). Subsequently, venous access was established and an intravenous anaesthetic (propofol: induction dose 10 mg/kg, maintenance dose 15 mg/kg/h) was administered for the duration of the procedure via a syringe pump. The animals were intubated, but typically respired spontaneously. An electrocardiogram was monitored routinely. All surgical manipulations were under sterile conditions.

The monkeys' heads were fixed in a stereotaxic head-holder via ear bars and a mouth clamp. At first, scleral coils made of Teflon-coated silver wire were implanted. The ends were led under the skin to the top of the head and soldered to prefabricated plugs. These were later anchored with dental acrylic to the skull. The skin over the skull was opened and small self-tapping screws were implanted into the bone. Onto these, a head-holding device was attached with dental acrylic. At the coordinates of the intraparietal sulcus (centred at P 3.5, L 12 mm), a trepan hole was made into the skull without opening the underlying dura. A prefabricated stainless steel cylinder was mounted over the opening and fixed to the skull with acrylic. Into this cylinder, a Teflon grid for electrode placement was inserted, and a hydraulic motor-driven microdrive (Narishige) was mounted on it during the recording sessions. The grid allowed reproducible electrode penetrations with a 500-μm resolution.

Recordings

Single cells were recorded extracellularly with glass-coated tungsten microelectrodes (F. Haer Inc., Bowdoinham, USA) in area VIP in the left hemisphere in each monkey. The animals were awake, and performed several oculomotor tasks. A total of 186 cells were recorded. Neurons were classified as located in area VIP on the basis of the recording sites within the intraparietal sulcus and with respect to their response properties (Colby *et al.*, 1993; Duhamel *et al.*, 1998). Neurons in VIP differ from those in neighbouring areas MIP (in the medial bank) and LIP (in the lateral bank of the intraparietal sulcus) regarding a strong preference for the direction and speed of moving visual stimuli (see also Ben Hamed *et al.*, 2001; Bremmer *et al.*, 2002). In a typical recording session, the passage of the electrode into VIP was marked by a distinct change in background and resting activity of the recorded neurons.

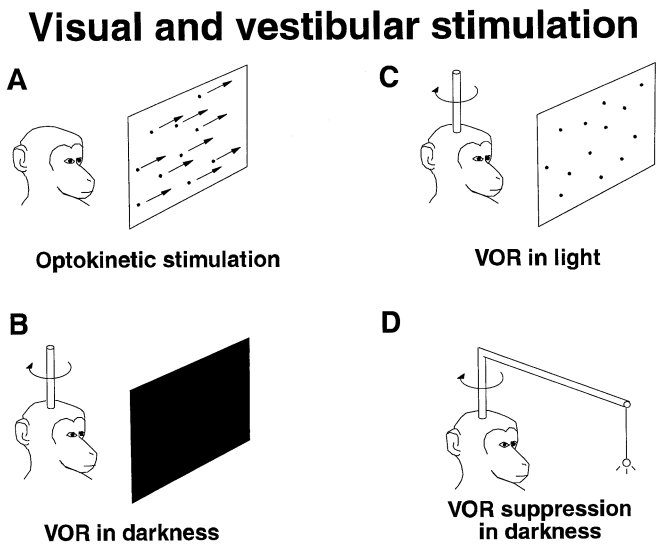


FIG. 1. Visual and vestibular stimulation paradigms. (A) Optokinetic stimulation: the animal was seated, stationary, in front of a random dot pattern. In order to assess the directional selectivity of a given neuron, the random dot pattern was moved in eight cardinal linear directions while the monkey was either fixating on a central fixation spot or was allowed to perform eye movements (optokinetic nystagmus). An abbreviated method to determine visual directional selectivity was to move the random dot pattern along a circular pathway that constantly changed the direction of the visual increments while the monkey was fixating (see Fig. 2B, 1 and 2). The random dot pattern could also be used to deliver optic flow stimulation, i.e. expanding or contracting visual stimuli. (B)Vestibulo-ocular reflex (VOR) in darkness: the animal was rotated sinusoidally about the horizontal axis in the darkened laboratory, eliciting vestibular nystagmus. (C) VOR in light: the animal was rotated sinusoidally about the vertical axis in front of the stationary random dot pattern under reflex eye movement conditions. (D) VOR suppression in darkness: the animal was rotated sinusoidally about the vertical axis in the darkened laboratory environment, fixating on an LED fastened to the turntable. Thus reflex eye movements were suppressed.

Stimulation and characterization of neuronal responsiveness

Visual stimuli as well as fixation targets were back-projected onto a translucent tangential screen covering an area of 90° (horizontal) × 80° (vertical) at a viewing distance of 57 cm (Fig. 1A and C). Visual neuronal responses were initially explored with a hand-held projection lamp displaying spots and bars. Sensitivity to large-field motion was assessed quantitatively by presenting a computer-generated moving random dot pattern (240 dots) that covered the whole tangential screen. The dots could be driven to mimic forward or backward linear self-motion, i.e. displaying an expansion or contraction pattern, respectively (see Bremmer *et al.*, 2002), or represent leftward, rightward, up, down etc. movements to determine a given neuron's visual directional selectivity in the frontoparallel plane (Fig. 1A). Usually, visual patterns on the retina resulting from any form of self-motion are termed optic flow pattern. Yet, in order to

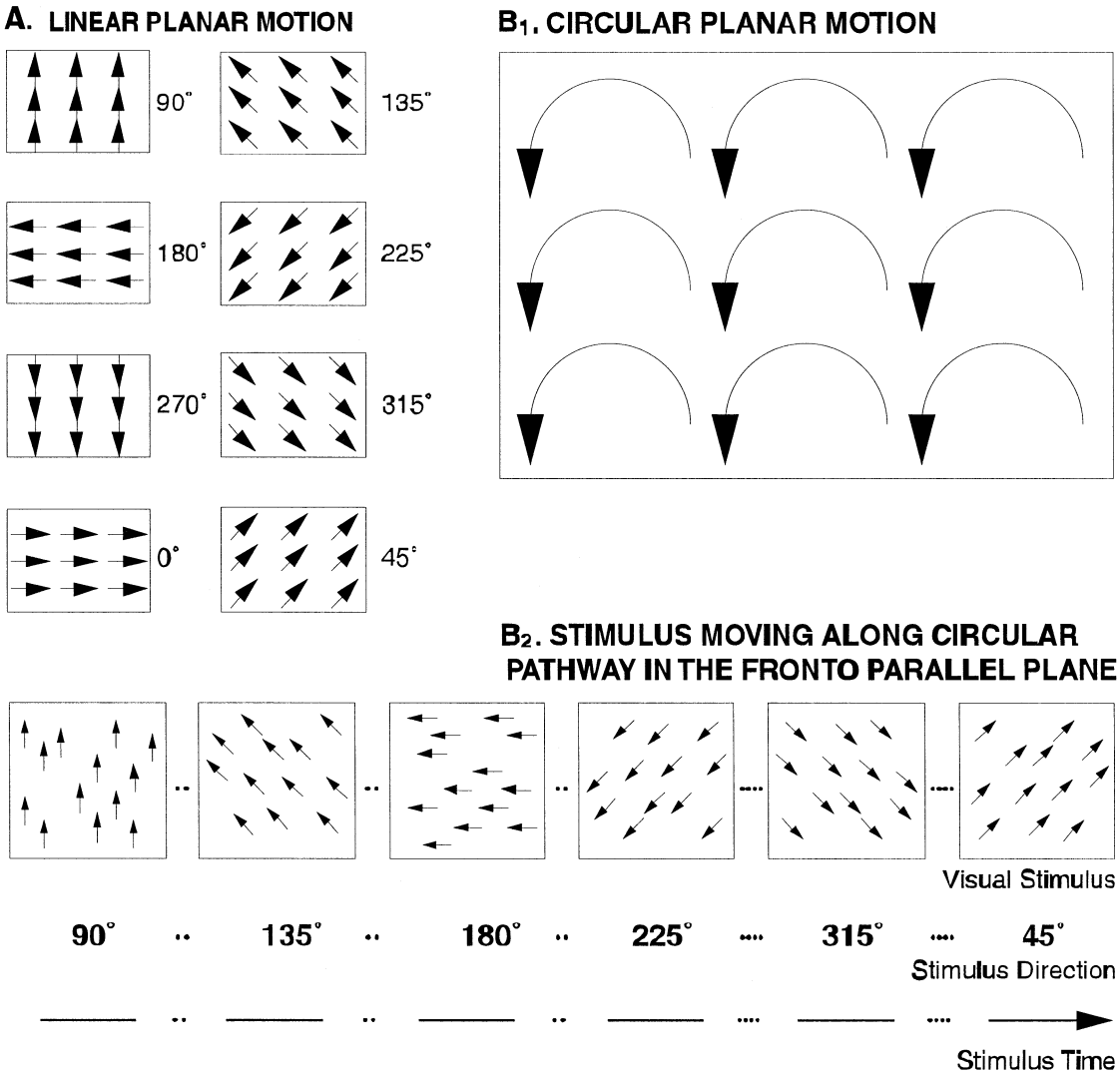


FIG. 2. Visual stimulation paradigms to determine visual directional selectivity. (A) Linear planar stimulation (classical testing method). Visual stimuli were moving across the projection screen in the eight shown directions, i.e. up (90°), up and left (135°), etc. (B) Circular pathway visual stimulation. (B1) The random dot pattern was moved along a circular pathway of 5–10° eccentricity. At each moment, the dots would follow a different linear trajectory moving around a respective circle of stimulation. (B2) Effective stimulus directions during circular pathway stimulation. At each instance of circular pathway stimulation, a different linear direction would be stimulated, including the eight principal stimulus directions used for linear planar motion stimulation. By contrast to the linear planar motion stimulation pattern (depicted in A), where each of only eight directions would be stimulated individually and one at a time, the stimulation directions during circular planar motion would be continuous and successive during a given movement cycle (symbolized by the dots in-between each panel). It has to be emphasized that the circular planar motion stimulus constitutes not a rotation testing but a linear direction testing.

distinguish easily the two modes of stimulation (forward/backward motion vs. frontoparallel motion), we termed the first type of movement pattern 'optic flow' (OF), because it produces a visual flow pattern occurring during linear forward or backward motion (i.e. a translation along the *z*-axis). The second type of visual stimulation was termed 'directional selectivity' (DS) stimulus. In essence, such a movement pattern could simulate either linear movement to the left, right, up, down etc. (a translation along the *x* or *y* axis, or any axis in between these), or eye and head rotations about the respective axes (e.g. about the vertical rotation axis for left–right movements). During both types of stimulation (OF and DS), optokinetic nystagmus would typically be elicited when the animal was not fixating.

Visual directional selectivity was assessed in two ways. The random dot pattern was either moved in eight different directions at 45° intervals as described above (linear planar motion) under fixation or optokinetic nystagmus conditions (Figs 2A and 3), or along a circular pathway (Fig. 2B1). For circular planar motion, the speed of the pattern was kept constant at either 40 or 27°/s throughout a stimulus trial (cycle), but stimulus direction changed continuously (0° to 360°) within a complete stimulus cycle (Fig. 2B2). In such cases, the monkey had to maintain fixation throughout the trial. With this kind of stimulation, a neuron's directional vector could be determined during a single trial without the need to test a critical number of unidirectional pattern movements (Schoppmann & Hoffmann, 1976; see also Bremmer *et al.*, 2002). It should be mentioned that the circular planar motion stimulus does not constitute a rotation testing, but a linear direction testing. The visual stimuli that drive the neuronal responses move linearly; only the stimulus pattern moves about a circle to cover all possible linear directions. Neither of them,

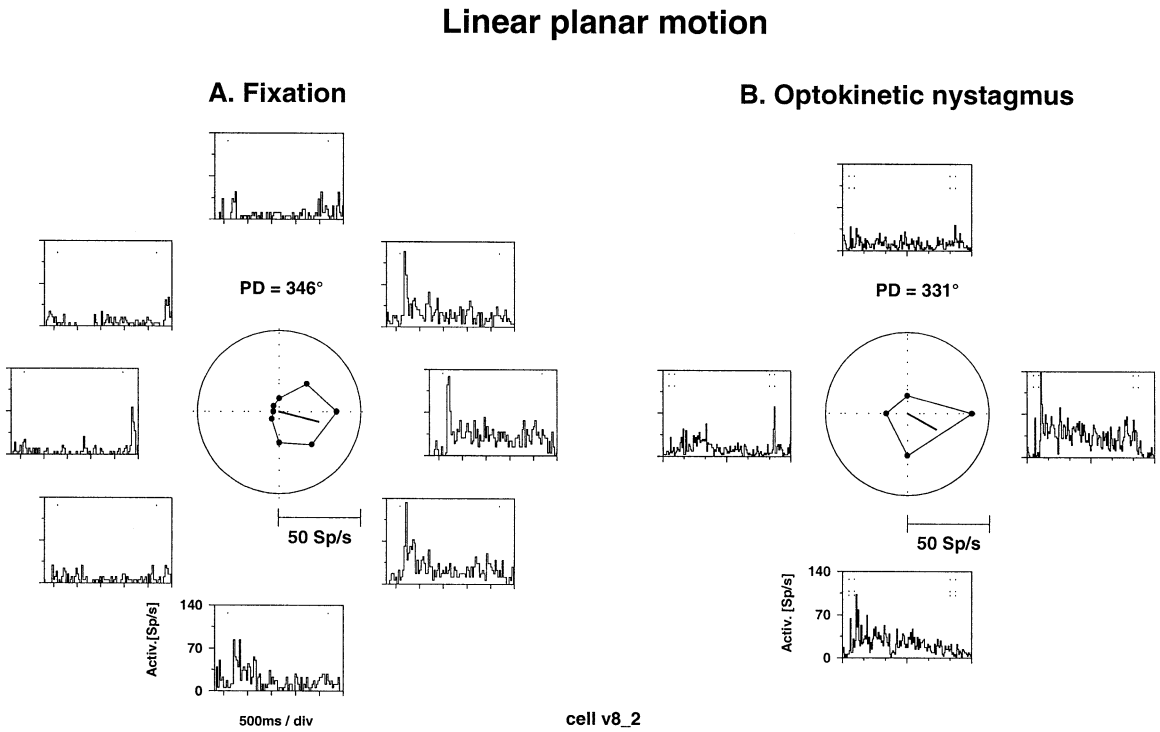


FIG. 3. Visual preferred directions during (A) linear planar motion under fixation conditions and (B) during optokinetic nystagmus. Under fixation conditions, eight principal directions were tested (45° intervals); under optokinetic nystagmus conditions only stimuli into the four cardinal directions were used to avoid directional uncertainties during oblique eye movements. Neuronal response profiles for identical stimulation directions under the two stimulus conditions were similar (e.g. there is no significant difference between the respective optimal responses: Mann–Whitney, $P > 0.256$), although different retinal slip velocities of the stimulus pattern may have occurred. In any case, the general directional selectivity of the neuron remained the same, although the increased number of tested stimulus directions under fixation conditions clearly sharpened the neuron's directional selectivity vector (bin width 25 ms).

in any case, would provide a true rotation, i.e. turn about a defined axis of rotation. For testing a neuron's responsiveness when the animal was free to make optokinetic eye movements, a four-direction paradigm was used. In such cases, determination of the directional selectivity vector, naturally, was less accurate (Fig. 3B).

Visual receptive field contours were first delineated manually ($n = 109$) with a hand-held projector displaying bars and spots. Quantitative mapping of the full receptive field was accomplished for a number of neurons ($n = 52$) in later stages of the experiments using computer-generated stimuli while the monkey fixated the central fixation spot (Duhamel *et al*., 1997). Mapping stimuli consisted of a white bar moving in the optimal direction at constant velocity. The bar was always orientated perpendicular to the direction of movement. Receptive field maps were constructed off-line by counting the total number of spikes evoked by stimulating a given area within the total stimulation surface using a shifted temporal window adjusted to the cell's response latency. A detailed description of the mapping procedure may be found in Duhamel *et al*. (1997) and Bremmer *et al*. (2002).

Vestibular stimulation was delivered via a vertical axis turntable (horizontal rotation) that could be moved manually or via a servo controller (Fig. 1B–D). The monkey was placed on the turntable in such a way that the virtual axis of rotation intersected the interaural axis at the centre of the head. Typically, the stimulus profiles were a series of sinusoids of 0.25 Hz with a +30° amplitude. The animals were rotated either in darkness (Fig. 1B) or in light (Fig. 1C). They were either left free to make compensatory eye movements (vestibulo-ocular reflex, VOR) (Fig. 1B and C), or they had to suppress the VOR by fixating a chair-mounted light-emitting diode (LED) (Fig. 1D). For testing of VOR conditions in darkness, the laboratory was darkened in addition to covering the animals' eyes and head with a light-tight and wind-shielding material. There was no auditory signal produced by the movement of the turntable.

Finally, somatosensory responsiveness was tested qualitatively with an electronic signal brush or cotton tip applicators, touching different parts of head, body and limbs, and by passive rotation of single joints of arms and hands. The signal brush gave an approximate indication of the time of contact with the skin. However, in this study we were only interested in the placement of the tactile receptive fields and the tactile directional sensitivities therein.

Data analysis

Preferred directions of visual stimulus motion were determined using the weighted average method. Average firing rates of a cell's response to a circular pathway stimulus usually were determined over a 500-ms period centred in the temporal domain on a point corresponding to the cell's preferred direction. An 80-ms latency was introduced to determine the directional vector at peak firing rate in order to account for the delay in the neuronal response. Average firing rates of a cell's response to expansion or contraction stimuli were computed from the full response period. Vestibular and visual–vestibular responses were averaged over several stimulation cycles. Stimulus–phase relationships of vestibular responses were determined by Fourier transformation.

When needed, differences in activity were tested for statistical significance with a Kolmogorov–Smirnov test, a Mann–Whitney rank test or a distribution-free ANOVA.

TABLE 1. Response properties of all 186 recorded VIP neurons, with breakdown of visual responses

	VIP neurons (*n*)	
Sensitivity	All cells	Visual responses
Visual		
DS	138	
OF	134	
DS only		34
OF only		30
DS + OF		104
Total		168
Vestibular	57	
Somatosensory	44	
Eye position (Fix)	59	

DS, directional selectivity; OF, optic flow sensitivity. Not all cells were tested for all parameters.

TABLE 2. Response properties of 82 VIP neurons tested for visual, vestibular and somatosensory sensitivity, either qualitatively or quantitatively, with breakdown of visual responses

	n	Totals
Vestibular responses		35
Vest. only	1	
Vest. + DS + OF	17	
Vest. + DS + OF + somat.	14	
Vest. + DS + somat.	3	
Visual only		30
DS	3	
OF	4	
DS + OF	23	
Somatosensory		17
Somat. only	1	
Somat. + DS	4	
Somat. + DS + OF	12	
Grand total		82
Overall responsiveness		
Vest.	35	
DS	76	
OF	70	
Somat.	34	
All visually responsive cells		80
DS but not OF	10	
OF but not DS	4	
DS + OF	66	

DS, directional selectivity; OF, optic flow sensitivity; vest., vestibular sensitivity; somat., somatosensory sensitivity.

Histology

The recording sites have been verified in the rhesus monkey (*M. mulatta*) used in this study (for details, see Bremmer *et al*., 2002). The other animal (*M. fascicularis*) is still used in ongoing experiments. To mark key recording sites, electrolytic lesions were placed within the VIP area of the rhesus monkey.

The histological procedures have been described in detail in earlier publications (Ben Hamed *et al*., 2001; Bremmer *et al*., 2002). In brief, the animal was anaesthetized and perfused. After the initial fixation (see Bremmer *et al*., 2002, the preceding paper), the head was removed from the trunk and placed into a stereotaxic frame. Marker pins were inserted with a microdrive through the periphery of the recording grid to outline the extent of the volume of brain tissue where electrode penetrations had been made. The brain was then postfixed by immersion, inside the cranium, in 4% buffered paraformaldehyde for several days. After removal of the brain, a block of cortex containing the intraparietal sulcus was removed, cut into serial sections of 50 μm on a freezing microtome and stained with Cresyl violet and a myelin stain (Schmued, 1990). To be able to follow the entire length of a given electrode penetration within single brain sections, the tissue was cut not in stereotaxic coordinates but along planes parallel to the marking pins. The topography of the intraparietal sulcus and the placement of the electrode tracks was reconstructed with computer-aided light microscopy (MicroBrightfield, Neurolucida) and camera lucida drawings. The topography of the area around the intraparietal sulcus and the relevant recording sites have been documented in Bremmer *et al*. (2002).

Results

A total of 186 recorded cells (109 cells from monkey 1 and 77 cells from monkey 2) were tested for various parameters of visual, vestibular and somatosensory stimulation as well as eye movements (Tables 1 and 2).

Visual responses

Optic flow

As mentioned in the Materials and methods, we termed a visual stimulation an 'optic flow' (OF), when the dots of the random dot pattern were moved to simulate forward or backward linear self-motion (translation along the anterior–posterior axis), i.e. showing an expansion or contraction pattern, respectively. Neurons reacted either to expansion or to contraction in 80% of the test cases (134/168; Table 1). A detailed description of their visual response characteristics may be found in Bremmer *et al*. (2002).

Directional selectivity

To determine the directional selectivity (DS) of a neuron within the frontal plane, the dots comprising the visual stimulus would be moved simultaneously in the same direction across the projection screen, and optokinetic nystagmus would typically be elicited when the animal was allowed to make eye movements. As assessed with the linear planar motion (Figs 2A and 3) or the circular planar motion paradigm (Fig. 2B1 and 2; see also Figs 4D, 5D, 6D, 7D), directional selectivity showed a DS vector distribution across the neuron population in basically all directions (shown in Fig. 9B).

The vast majority of cells were strongly selective for the direction of a moving stimulus (138/168, i.e. 82%; Table 1). Overall directional selectivity did not change in the case where the animals were allowed to make optokinetic eye movements. However, the accuracy of the directional selectivity vector was reduced in such cases because only the four cardinal movement directions were used (the oblique directions were eliminated) (Fig. 3B). For some neurons, there was no difference in activity under fixation and optokinetic nystagmus conditions for identical stimulus directions (Fig. 3 and Fig. 4A and D) whereas, in others, the presence of eye movements introduced a steep reduction in activity (Fig. 5A and D). Whether this difference in activity between the two conditions, i.e. with and without optokinetic nystagmus, is due to a difference in retinal slip velocity or due to eye movements remains to be determined (see also Bremmer *et al*., 1999a). In this context, it should be noted that peak neuronal activity for preferred direction stimulation during linear planar and circular planar testing was about the same under fixation conditions (nonsignificant differences in five such tested neurons; see also Bremmer *et al*., 2002).

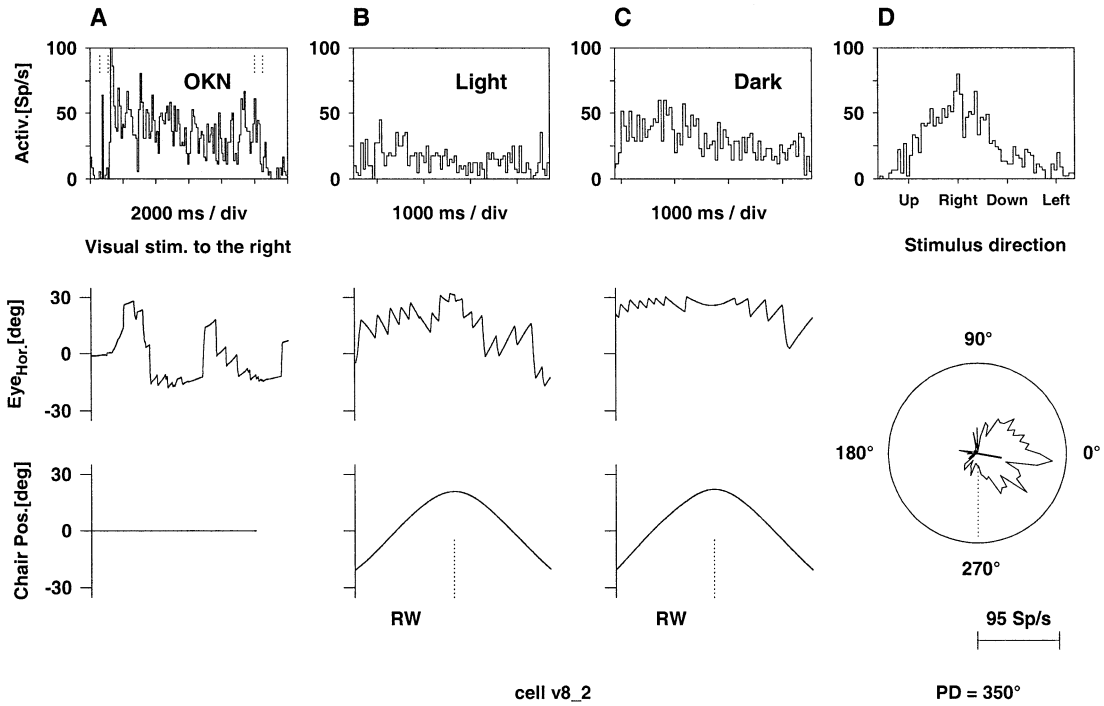


FIG. 4. Responses of a single neuron (same neuron as in Fig. 3) to visual (optokinetic nystagmus (OKN) and fixation), vestibular (Dark) and combined visual–vestibular (Light) stimulation. The first three columns (A–C) show the neuronal responses in the top row (bin width 50 ms), horizontal eye position in the middle row and horizontal turntable position in the bottom row (upward is to the right). The neuron's preferred direction for vestibular and visual–vestibular stimulation is to the right. The last column (D) depicts the neuronal response to large-field visual stimulation along a circular pathway in a PSTH and in a polar plot representation, including the visual preferred direction. In A–C the animal was allowed to make eye movements whereas in D the animal had to fixate on a fixation spot. Note that peak firing rates for optokinetic nystagmus and fixation conditions (A and D, respectively) are approximately equal (see also Fig. 3). The preferred direction of this neuron for visual stimulus motion was to the right with a slight downward component. Thus, preferred directions for vestibular and visual stimulation were noncomplementary, i.e. during combined visual–vestibular stimulation, a sensory conflict situation would occur (during a rightward rotation of the animal in light, the virtual visual world movement in fact is to the left). (B; Light) This conflict situation is reflected in the respective reduced neuronal response during combined visual–vestibular stimulation. (A and D) Also note that this neuron had a relatively strong response during visual stimulation. Associated compensatory eye movements were as expected, i.e. (A) optokinetic nystagmus to the left during optokinetic stimulation to the right, and (B and C) vestibular nystagmus to the right during rightward turns (RW) and vice-versa (following the convention of defining direction according to the fast phases).

Vestibular responses

Self-motion detection includes both linear displacement (as simulated by the above described visual stimuli) and rotational displacements of the eye–head systems and of the whole body. We thus tested vestibular responsiveness of the recorded neurons while the animal was rotated sinusoidally on a vertical-axis turntable in light or in darkness. The animal was either free to make compensatory eye movements, i.e. VOR, or had to suppress the VOR by fixating a chair-mounted LED (Fig. 1B–D, respectively).

Rotation in darkness

There was a sizable proportion of the recorded neurons which responded to vertical axis rotation, i.e. about one third of the entire studied population (57/186, 31%; $P < 0.05$, distribution-free ANOVA) (Table 1). The existence of the vestibular sensory quality in VIP neurons had not been reported in previous publications (Colby *et al.*, 1993; Schaafsma & Duysens, 1996; Schaafsma *et al.*, 1997; Duhamel *et al.*, 1998). The majority of these cells (52/55) had a clear preference for rotation to the right or to the left (Type I, on-direction ipsilateral to the recording site; type II, on-direction contralateral to the recording site; Duensing & Schaefer, 1958) (e.g. Figs 4C, 5C, 6B and 10A). Two neurons were biphasic, i.e. they responded with activation during rotation in both directions (so-called Type III). One neuron's activity seemed to be more related to the position of the turntable than to the direction of its movement. The remainder of the cells (2/57) could not be tested to the extent necessary to allow classification.

There were indications for oculomotor-related modulation in the signal content in some neurons but not in others. For instance, in one population (Fig. 6C), no significant differences could be discerned between firing rates comparing stimulation in darkness allowing VOR eye movements, and stimulation under VOR-suppression conditions. In others, the presence of eye movements influenced a given neuron's firing rate significantly (Fig. 7C). A subset of neurons was tested quantitatively for eye-movement-related response modulation. Within this population, 7/10 neurons showed significant differences in firing rates under VOR and VOR-suppression conditions, while 3/10 did not. When tested for eye position effects under fixation conditions in darkness and in light, all neurons that had vestibular signals also had eye position effects, i.e. 24/24. However, in the case of the above two examples (Figs 6C and 7C), an added-on eye position signal could not account for the difference in firing behaviour because both neurons had eccentric eye position maxima (Bremmer *et al.*, 1999a).

A wide variety of vestibular response dynamics was observed in the neurons that underwent vestibular testing. First of all, vestibular responses could be vigorous or relatively weak. The prototypical examples reflect well the nature of vestibular responses that could be considered vigorous (e.g. Figs 6B and 7B), in contrast to responses

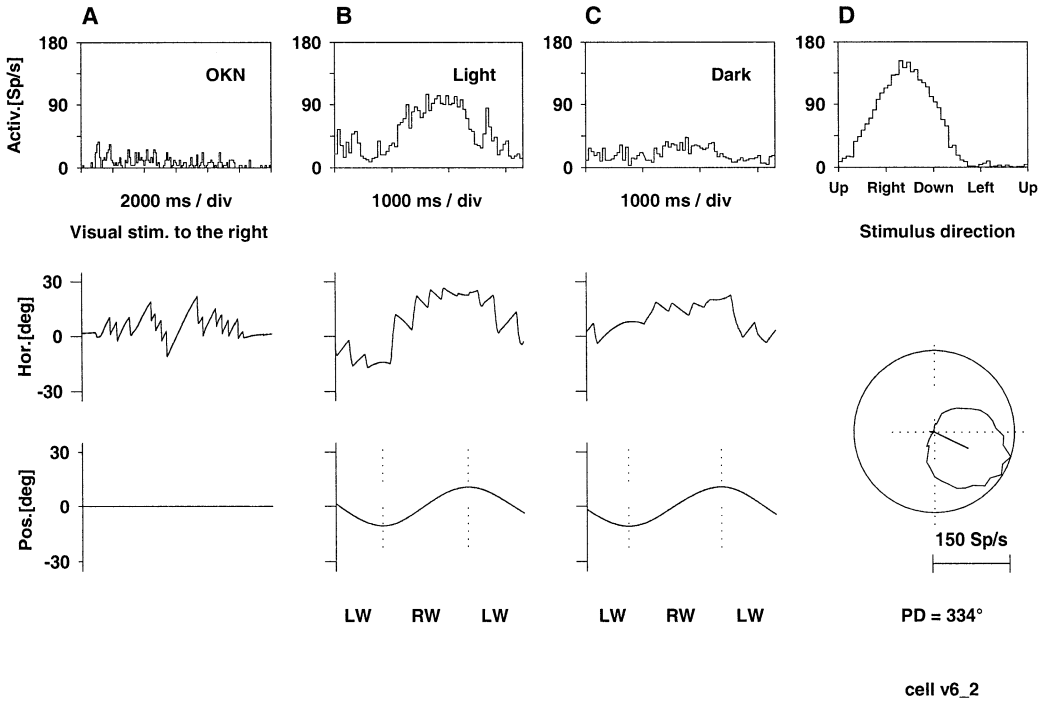


FIG. 5. Responses of a single neuron to visual [optokinetic nystagmus(OKN) and fixation], vestibular (Dark) and combined visual–vestibular (Light) stimulation. Data presentation is as in Fig. 4 (bin width 50 ms). The neuron's preferred direction for vestibular and visual–vestibular stimulation was to the right (LW, leftward; RW, rightward). In (A–C) the animal was allowed to make eye movements whereas in (D) the animal had to fixate on a fixation spot. Note marked difference in neuronal responses between A (during optokinetic nystagmus) and D (during fixation). In any case, the preferred direction of this neuron for visual stimulus motion was to the right with a downward component. Thus, preferred directions for vestibular and visual stimulation were noncomplementary, i.e. during combined visual–vestibular stimulation, a sensory conflict situation would occur. While the vestibular responsiveness of this neuron was low, the combined visual–vestibular response, in fact, exceeded it, although now the visual stimulation component occurred in the off-direction, i.e. to the left. Associated compensatory eye movements were as expected, i.e. (A) optokinetic nystagmus to the left during optokinetic stimulation to the right, and (B and C) vestibular nystagmus to the right during rightward turns and vice-versa.

that could be considered relatively weak (e.g. Figs 4C and 5C). Quantification of the data in this respect is presented below.

Second, vestibular responses could be categorized according to their peak firing rate–phase relationship (Fig. 8). The great majority of neurons were found to be in phase with the velocity of the turntable, i.e. head velocity (Figs 4C and 5C). Some neurons had their phase shifted such as to suggest integration to position (Fig. 6B). Others showed a phase advance towards acceleration coding (Fig. 7B). Quantification of the responses (Fig. 8) clearly demonstrates the head velocity coding of the majority of neurons (≈ 90°), with a number of examples showing the already mentioned phase shifts towards acceleration and position.

Visual–vestibular interaction

As mentioned above, most of the visually driven cells were direction-selective, besides being responsive to optic flow stimulation (Table 1). All but three neurons with vestibular activity also had visual input (Table 2). Interestingly, the preferred directions for visual and vestibular stimulation of such neurons were noncomplementary, i.e. the neuron preferred visual stimulus motion and rotation of the head into the same direction. There were no exceptions (Figs 4–7 and 10B).

The importance of this finding can be appreciated in particular after the following brief description of visual–vestibular psychophysiscs and neurophysiology. Classical psychophysical experiments in humans (Dichgans & Brandt, 1978) and electrophysiological recordings in vestibular nucleus neurons (Dichgans *et al*., 1973; Henn *et al*., 1974; Allum *et al*., 1976) have demonstrated complementarity of vestibular and visual preferred directions. In other words, a head rotation to the right, for instance, entails an apparent movement of the visual scene to the left, i.e. into the opposite direction. A purely optokinetic stimulus may thus cause a strong sensation of actual physical rotation in the opposite direction, a so-called circular vection. Complementarity, i.e. oppositely directed, vestibular and visual stimuli usually lead to an augmentation of the combined, i.e. visual–vestibular, response. If vestibular and visual stimuli are directed in the same direction, under certain conditions a visual–vestibular conflict will arise, leading to a diminished overall neuronal response as shown in electrophysiological recordings (Henn *et al*., 1974; Allum *et al*., 1976; Waespe & Henn, 1978). In psychophysical experiments, such a situation may even cause vertigo and nausea. In this context, the noncomplementary on-directions of the recorded visual and vestibular responses in our population of VIP neurons, in essence, could also generate a visual–vestibular conflict situation.

This surprising noncomplementary response characteristic of visual and vestibular preferred directions was obtained in 52 neurons of the population which could be tested to the necessary extent. In 40 of these, where visual direction selectivity was quantified, visual preferred directions were distributed about the vestibular ipsilateral and contralateral horizontal on-directions (Figs 9A and 10B). In one instance, the preferred visual on-direction was ≈90° off of the vestibular on-direction.

We examined the full extent of visual–vestibular interaction characteristics in 26 of the recorded neurons (Table 3). Although

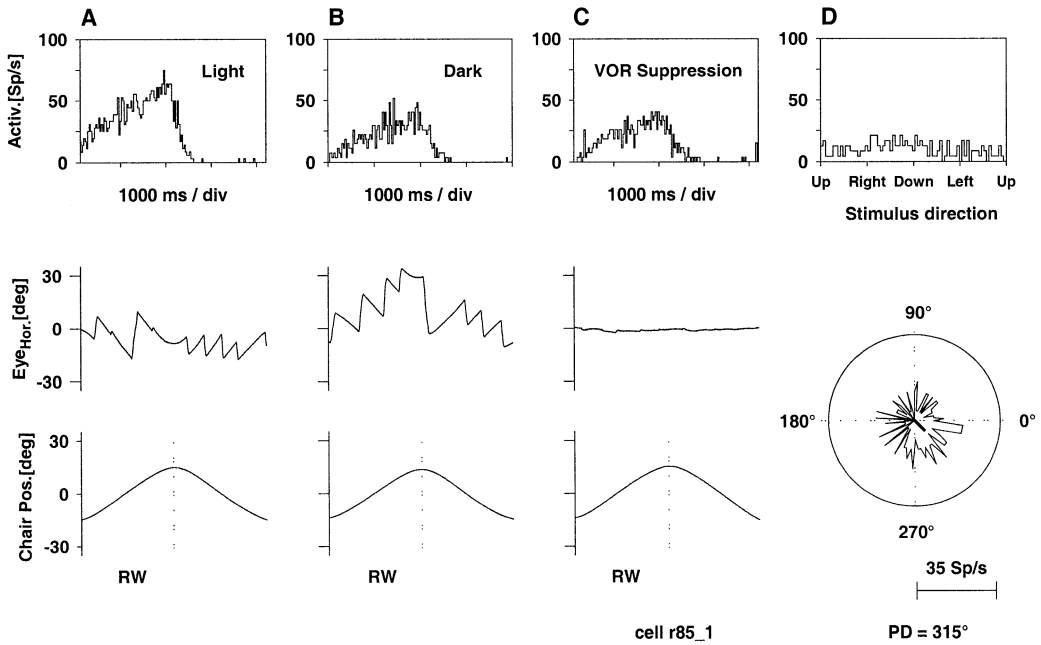


FIG. 6. Responses of a single neuron to (A) combined visual–vestibular (Light), (B) vestibular stimulation (Dark), (C) under VOR suppression conditions (VOR Suppression) and (D) to visual stimulation. Data presentation is as in Fig. 4 (bin width 25 ms). The neuron's preferred direction for vestibular and visual–vestibular stimulation was to the right (RW, rightward). In A and B, the animal was allowed to make eye movements whereas in C and D the animal had to fixate on a fixation spot. The preferred direction of this neuron's relatively weak response for visual stimulus motion was to the right with a sizable downward component. Thus, preferred directions for vestibular and visual stimulation were noncomplementary, i.e. during combined visual–vestibular stimulation, a sensory conflict situation would occur. Vestibular responsiveness of this neuron was strong, and there was no significant difference in neuronal discharge between VOR and VOR-suppression conditions (Kolmogorov–Smirnov, $P > 0.10$). The combined visual–vestibular response (A) exceeded the vestibular responses despite an initially weak visual response which, in addition, now occurred into the neuron's off-direction, i.e. to the left. Associated compensatory eye movements are as expected, i.e. (A,B) vestibular nystagmus to the right during rightward turns and vice-versa. Note that vestibular and visual–vestibular responses seemed to undergo integration towards position sensitivity.

visual inspection alone already revealed the depth of modulation of a given neuron during visual and vestibular stimulation, the responses were quantified according to a modulation index as defined in the following. The modulation index (I) calculation for vestibular (I_{vest}), visual (I_{vis}), and combined visual–vestibular stimulation (I_{VV}) took into account the maximal and minimal firing rates in the respective on- and off-directions after fitting an envelope to them (bin width 100 ms) [Modulation index (I) of the firing rate i: $I_{vest,vis,VV} = (i_{max} - i_{min})/(i_{max} + i_{min})$]. If a neuron's VOR suppression data were available (seven cases), this value was chosen to avoid any possibly biased classification for the vestibular sensory quality, although conflicting cases did not exist. Theoretically, the highest modulation index could be 1, the lowest 0. An index of 0.5, for instance, already signals low modulation. Surprisingly, neurons could be classified into 'high modulation' and 'low modulation' categories, with a cutoff between the two categories set at 0.76, for vestibular, visual and combined visual–vestibular responses. This cutoff point, D, was at 66% of the difference between the lowest (0.28) and the highest (1.0) modulation indices [$D = I_{min} + (I_{max} - I_{min})2/3$], and reflected a natural border between the two categories, i.e. there were relatively few borderline cases (see Fig. 11). From this classification scheme, we derived a table of visual–vestibular interaction characteristics for VIP neurons (Table 3).

The distinction between the two response types rested on the modulation differential between stimulation into the on- and the off-direction. For instance, 'low' modulation units never went into a cutoff phase, i.e. when the neuron reached a zero-firing rate during rotation in the off-direction, although the peak firing rate for both classes of units was ≈ 50 spikes/s (compare, e.g., Figures 4C and 6B). Differentiation into two such categories was considered necessary for interpreting the observations regarding visual–vestibular interaction (see below).

Prototypical examples for 'low vestibular' modulation are shown in Figs 4C ($I_{vest} = 0.61$) and 5C ($I_{vest} = 0.6$), for 'high vestibular' modulation in Figs 6B ($I_{vest} = 1$) and 7B ($I_{vest} = 1$), for 'low visual' modulation in Figs 6D ($I_{vis} = 0.49$) and 7D ($I_{vis} = 0.73$), and for 'high visual' modulation in Figs 4D ($I_{vis} = 0.88$) and 5D ($I_{vis} = 1$).

In a majority of the respective neurons, the visual–vestibular responses, indeed, showed the conflicting nature of the vestibular and visual sensory qualities, and the modulation depth was thus reduced (see Fig. 4B: $I_{VV} = 0.43$). Such responses were observed in 15/26 cases (Table 3: VV_{lo}). However, in a sizable minority of the recorded neurons (11/26; i.e. 42%), the discharge remained strong during vestibular stimulation in light compared to stimulation in darkness, despite the fact that the visual input was now opposed to the vestibular on-direction (Table 3: VV_{hi}). This observation was striking, in particular because in many neurons the seemingly conflicting visual and vestibular input in fact produced an amplification of the visual–vestibular signal.

These paradoxical visual–vestibular fusion responses are noteworthy in particular in the face of low vestibular and high visual modulation characteristics (see Fig. 5). In such case, the (now opposed and contradictory) visual input actually amplified the initially weak vestibular reaction, i.e. the neuron had a weak vestibular modulation ($I_{vest} = 0.6$) with an on-direction to the right,

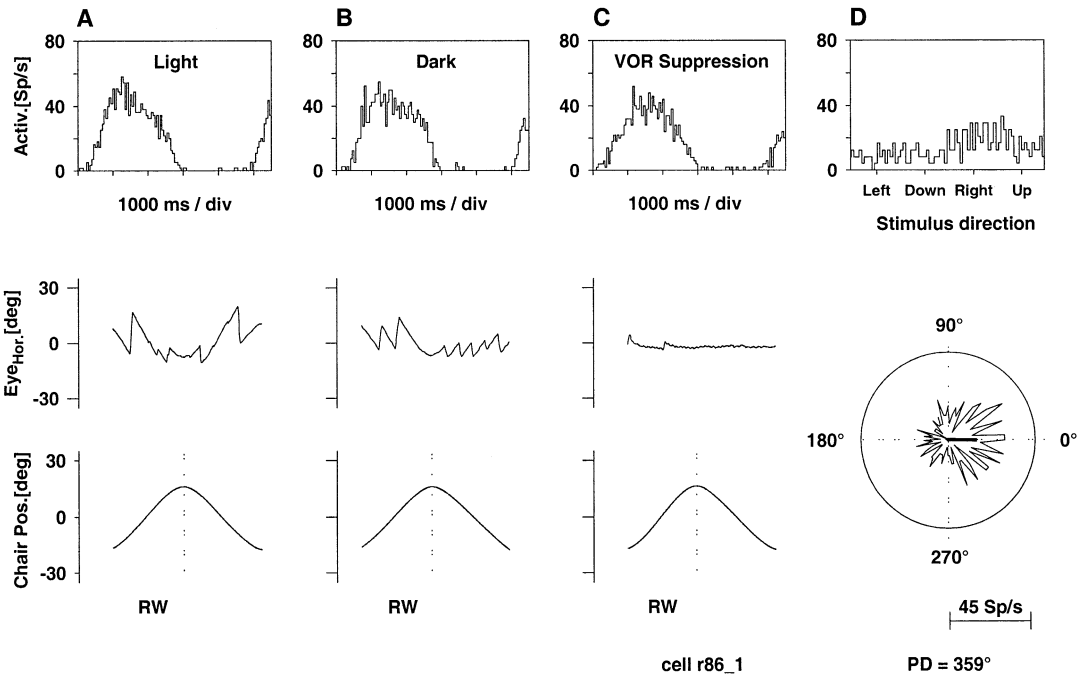


FIG. 7. Responses of a single neuron to (A) combined visual–vestibular (Light), (B) vestibular stimulation (Dark), (C) under VOR suppression conditions (VOR Suppression) and (D) to visual stimulation. Data presentation is as in Fig. 4 (bin width 50 ms). The neuron's preferred direction for vestibular and visual–vestibular stimulation was to the right (RW, rightward). In A and B the animal was allowed to make eye movements whereas in C and D the animal had to fixate on a fixation spot. The preferred direction of this neuron's relatively weak response for visual stimulus motion was to the right. Thus, preferred directions for vestibular and visual stimulation were noncomplementary, i.e. during combined visual–vestibular stimulation, a sensory conflict situation would occur. Vestibular responsiveness of this neuron was strong, and there was a significant difference in neuronal discharge between VOR and VOR-suppression conditions (Kolmogorov–Smirnov, $P < 0.005$). The combined visual–vestibular response (A) slightly exceeds the vestibular responses despite an initially weak visual response which, in addition, now occurred in the neuron's off-direction, i.e. to the left. Associated compensatory eye movements were as expected, i.e. vestibular nystagmus (A and B) to the right during rightward turns and vice-versa. Note that vestibular and visual–vestibular responses were shifted towards acceleration sensitivity.

while the visual component showed high modulation ($I_{vis} = 1$), also with a preferred direction to the right. The vestibular response was enhanced and amplified ($I_{VV} = 0.89$) despite the fact that, during vestibular stimulation in light to the right, strong visual inhibitory influence should come into play (see Fig. 5D); i.e. during stimulation in the vestibular on-direction (to right), the visual component was inhibitory, because an apparent visual movement to the left was thereby produced. Likewise, during stimulation in the vestibular off-direction (to left), the visual component was excitatory (apparent visual movement to the right). In both instances, although visual input was opposing the vestibular one it was, paradoxically, amplifying it (peak firing rate in darkness, 42 spikes/s; in light, 129 spikes/s; Mann–Whitney, $P < 0.00001$). The incoming vestibular signal in this condition thus clearly overruled the incoming visual signal and, in addition, reverses its inhibitory effect. The vestibular input thus indicates the true direction of a given head movement.

A similarly paradoxical multisensory fusion is observed in cases of initial strong vestibular and weak visual modulations. The examples of Figs 6 and 7, respectively, illustrate relatively weak visual modulations ($I_{vis} = 0.5$ and 0.73), strong vestibular modulation ($I_{vest} = 1$ and 1), and a strong visual–vestibular fusion signal ($I_{VV} = 1$ and 1). Although in these recordings the vestibular input clearly was dominant, the weaker visual signal would still be opposed to it. Thus, at least a reduced visual–vestibular response might be expected. Nevertheless, the overall response is paradoxical again, in particular in cell r85–1 (Fig. 6), where a strong amplification effect is observed that is not reflected in the maximum modulation index

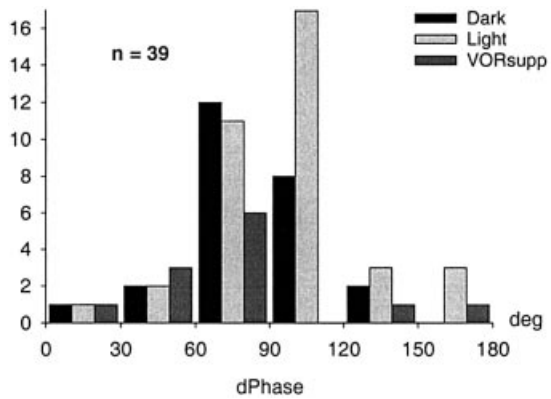


FIG. 8. Stimulus–phase relationships of neuronal responses following visual–vestibular (Light) and vestibular stimulation (Dark), and under VOR suppression (VORsupp). Responses are grouped in 30° intervals. The majority of neurons are clustered around velocity sensitivity (90°). Combined visual–vestibular stimulation shifted the phase distribution slightly towards acceleration (phase advance), i.e. to the left, VOR suppression towards position (phase lag), i.e. to the right.

(compare Fig. 6A and B; mean peak firing rates for vestibular stimulation in light and in darkness were 75 and 52 spikes/s, respectively; Mann–Whitney $P < 0.0039$). In the other example, cell r86–1 (Fig. 7 A and 7B), the effect is not as striking, because the responses for vestibular stimulation in light and in darkness are 'only'

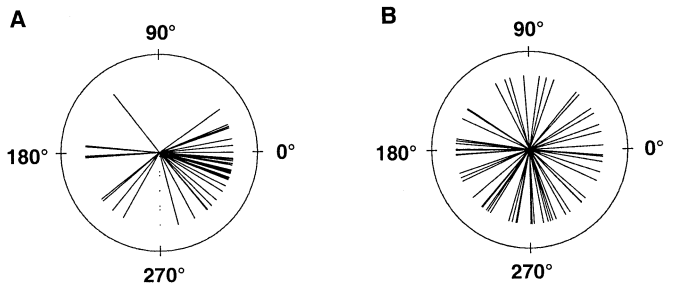


FIG. 9. Visual directional tuning of VIP neurons with and without vertical axis rotational sensitivity where directional selectivity was established quantitatively. (A) In neurons responding to yaw axis stimulation ($n = 40$), tuning directions formed two clusters, representing association with contralateral (≈ 0°) and ipsilateral (≈ 180°) vestibular on-directions (Type II and type I, respectively). The dotted line pointing towards 270° was the only example of a neuron whose visual tuning direction was 90° off the vestibular on-direction. (B) Visual tuning directions of neurons without vertical axis rotational sensitivity ($n = 57$) did not show a preferred distribution.

equal (mean peak firing rates are 63 and 55 spikes/s, respectively; Mann–Whitney $P < 0.86$).

Paradoxical amplification of visual–vestibular responses from a weak vestibular and a strong visual input, and from weak visual and strong vestibular input, as shown in the illustrated examples, was observed in four cases each. In the most unusual situation, weak visual modulation ($I_{vis} = 0.42$) and weak vestibular modulation ($I_{vest} = 0.57$) even resulted in strong visual–vestibular fusion ($I_{VV} = 0.86$) in one neuron (Table 3).

Tactile responses

Somatosensory responses were found in 44 neurons (Table 1). The majority of such neurons had tactile receptive fields located in the monkey's head region. In a minority, receptive fields were found to occupy shoulder, arm or hand. Many of these neurons only responded to movement of a tactile stimulus in one direction but not in the opposite direction.

A detailed analysis in 34 neurons of the entire test population showed that tactile responses could be associated either with optic flow, and/or with visual/vestibular direction-selective characteristics, although the populations are overlapping (see Table 2).

In the case of predominant optic flow responsiveness (6/34 cells), tactile receptive fields were usually large, covering the upper part of the face and the entire top and back of the head. A tactile flow field would originate from a focal point on the back (Fig. 12A), or the front (Fig. 12B) of the head with movement vectors emanating in parallel. This neuronal response could best be described as elicited by a backward (Fig. 12A) or a forward (Fig. 12B) movement of the animal through an environment rich in tactile cues, e.g. the leaves of a tree, or fast-moving air, with tactile directional vectors, i.e. the tactile vector space, directed towards the front or the back of the head, respectively. The input would thus generate a tactile flow pattern. The corresponding optic flow pattern was complementary in five cases, i.e. a forwardly directed tactile flow pattern would be associated with a contracting optic flow pattern, signalling backward movement (Fig. 12A), and vice versa (Fig. 12B). In one case, the tactile and optic flow directions were in the same direction, i.e. noncomplementary. Typically, these responses were never found to be combined with vestibular horizontal canal input. However, for these neurons a combination with otolith responses, i.e. linear forward/backward movement, would be most appropriate (Schlack & Bremmer, 2001).

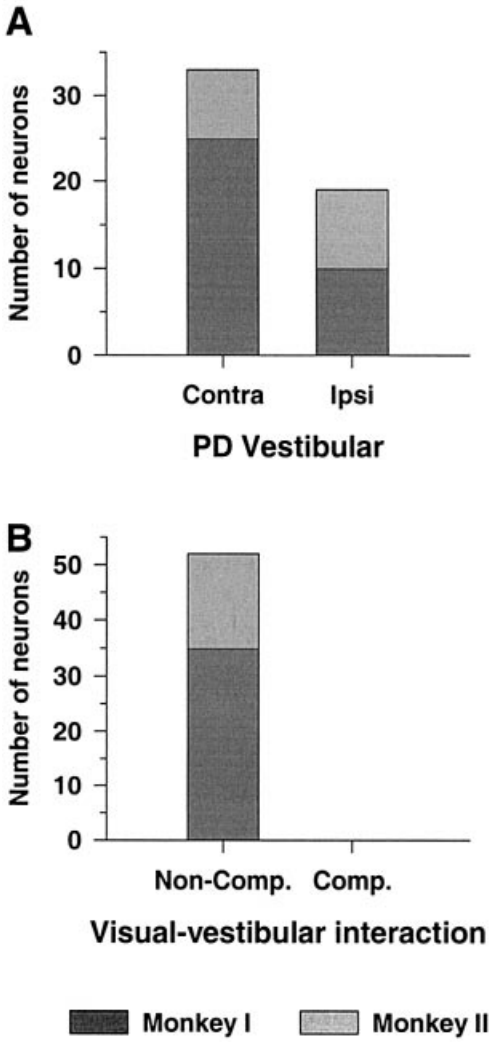


FIG. 10. Distribution of neurons where vestibular sensitivity was tested quantitatively. (A) Neurons sensitive to horizontal (vertical axis) rotation showed the classical pattern of type I and type II neurons (ipsilateral vs. contralateral on-directions). (B) Every single neuron with vestibular and visual sensitivity had a noncomplementary response pattern.

TABLE 3. Characterization of visual–vestibular responses ($n = 26$)

	Vis_{lo}		Vis_{hi}	
	VV_{hi}	VV_{lo}	VV_{hi}	VV_{lo}
$Vest_{lo}$	1	5	4	6
$Vest_{hi}$	4	3	2	1

Neuronal responses were classified according to the strength of their respective visual or vestibular modulation. The respective response strengths were quantified by a modulation index (see Materials and methods), but were also readily discernible in the prototypical examples given in the figures (vis_{lo}, low visual modulation, e.g. cell r85–1, Fig. 6D; vis_{hi}, high visual modulation, e.g. cell v6–2, Fig. 5D, and cell v8–2, Fig. 4D; $vest_{lo}$, low vestibular modulation, e.g. cell v6–2, Fig. 5C; $vest_{hi}$, high vestibular modulation, e.g. cell r85–1, Fig. 6B), and according to the resulting visual–vestibular interaction (VV_{hi}, high visual–vestibular modulation, e.g. cell v6–2: Fig. 5B, and cell r85–1: Fig. 6A; VV_{lo}, low visual–vestibular modulation, e.g. cell v8–2, Fig. 4B). VV_{lo} signals a visual–vestibular conflict situation, while VV_{hi} shows a paradoxical response conservation or even amplification. With respect to the latter cases, the constellations $vis_{lo}/vest_{lo}$, $vis_{hi}/vest_{lo}$, and $vis_{lo}/vest_{hi}$ leading to VV_{hi} are the most unusual ones.

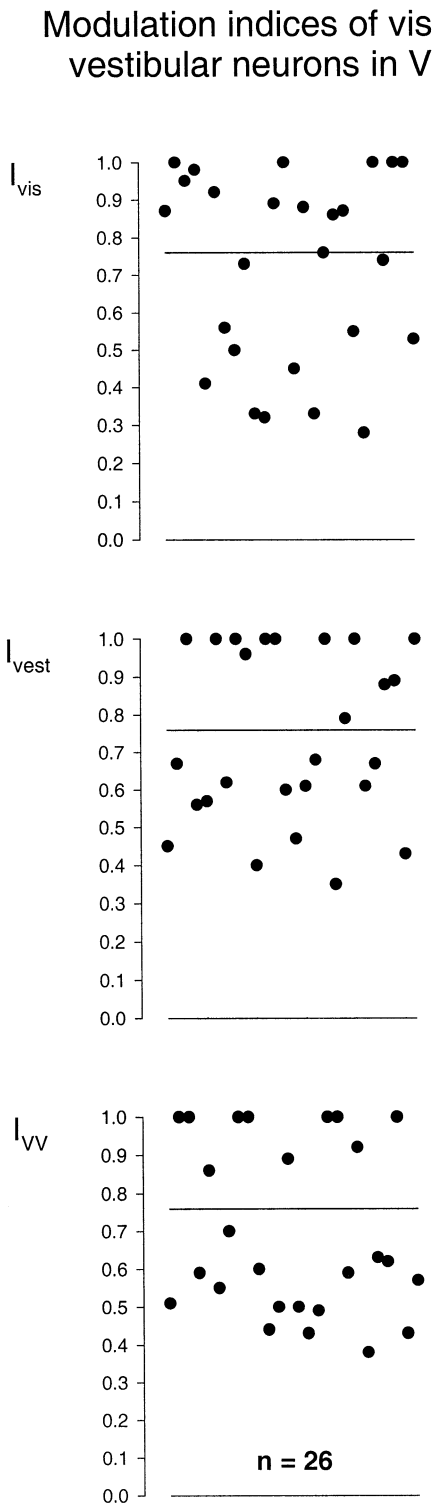


FIG. 11. Modulation indices of the 26 VIP neurons tested for visual (I_{vis}), vestibular (I_{vest}) and visual–vestibular interaction (I_{VV}). Horizontal lines inside the graphs indicate the 0.76 cutoff level between neurons of 'high' (above that level), and 'low' modulation (below that level). Note the remarkably few borderline cases (around the horizontal division lines), i.e. three neurons for I_{vis} and one case each for I_{vest} and I_{VV}. Otherwise, the values form essentially two distinct clusters for the 'high' and 'low' modulation categories in each instance. It should be emphasized that a modulation index of 1 cannot be exceeded (see Materials and methods), and thus the 'high modulation' cluster appears somewhat compressed.

In the case of a predominantly direction-selective tactile response (28/34 neurons), receptive fields were usually smaller and tactile directions were unidirectional with a given receptive field (Fig. 12C,D). Tactile and vestibular on-directions were either in opposite directions, i.e. complementary (4/28; Fig. 12C), or in the same direction, i.e. noncomplementary (11/28; Fig. 12D). Taking the example of complementary responses (Fig. 12C), the neuron's reaction could best be explained by a situation in which the animal makes a horizontal head movement to the left while a stationary object in its environment (or even air) touches its right cheek. The resulting tactile input (preferred direction to the right) would corroborate vestibular information about a head movement to the left. The neuron's visual directional selective response would, in any case, be noncomplementary. Furthermore, the optic flow response, i.e. contraction in the example of Fig. 12C, would be noncomplementary regarding the neuron's tactile preferred direction. In two cases where vestibular input was absent, visual and tactile on-directions were found to be opposite as well.

In the majority of cases, tactile and vestibular on-directions were similar, i.e. noncomplementary. In the example of Fig. 12D, vestibular, tactile and also visual preferred directions were to the right. The visual–vestibular paradox was thus now extended to also include the somatosensory quality. In another 11 cases, where vestibular input was absent or not tested, visual and tactile on-directions also coincided.

For the remainder of the total of thus examined neurons (10/44), no somatosensory preferred direction could be determined, i.e. the neuronal response was diffuse or it reacted only to touch *per se*, but not to movement in a particular direction.

Eye position sensitivity

Eye position sensitivity while fixating on a target in darkness or in light was found in 59 neurons (Table 1) (see Bremmer *et al*., 1999a, for detailed analysis). Of these, 24 neurons had vestibular signals and 25 did not. As mentioned above, all 24 neurons (100%) within the test population that had vestibular sensitivity also exhibited eye position sensitivity. We thus conclude that all vestibularly driven VIP neurons also have eye position sensitivity.

Visual receptive field structures

Initial testing with a hand-held light source projecting a bar or a circle had already revealed the approximate size and configuration of a given visual receptive field, including the directional sensitivity of the neuron (n = 109). After the initial qualitative manual evaluation, the receptive field parameters of a number of neurons (n = 59) were mapped quantitatively. Visual receptive fields were usually large, covering sometimes more than half of the animal's visual field (Fig. 13; see also Duhamel *et al*., 1991; Colby *et al*., 1993). Receptive fields could be of any shape. With regard to neurons responding to horizontal rotation, no discernable pattern could be identified that would link a particular receptive field shape or location to one or another neuronal response type, in particular visual–vestibular interaction. In particular, the receptive field location was not linked to the vestibular on-direction of a given neuron. In such cases, the area of highest activity within the receptive field could be located either contralaterally (Fig. 13A,B), ipsilaterally (Fig. 13C) or bilaterally (Fig. 13D), or it could be diffuse. As demonstrated previously, the location of visual and tactile receptive fields corresponded approximately (compare Figs 12D and 13B, and Figs 12B and 13D) (Duhamel *et al*., 1998). In the case in Fig. 13B, the tactile receptive field was located asymmetrically around the eyes

with a preponderance to the right; in the case in Fig. 13D, it was on the upper part of the head and face.

Multimodality of VIP neurons

An account of all observed responses may be found in Table 1. It should be noted, however, that not all cells could be tested for all parameters during the course of the experiments; thus the respective numbers in Table 1 indicate principally the variety of parameters to which neurons in VIP are related but do not necessarily show an absolute number of occurrences. Data to that effect are presented in Table 2. Regarding our entire neuron population (Table 1), we show visual, somatosensory, vestibular and eye movement related responses, with visual input figuring most prominently (90%). Of these, 104 neurons (62%) could be driven by large-field visual stimuli simulating self motion (OF and DS).

A rigorous testing with a finite number of parameters was undertaken in a limited number of neurons. In this population of 82 neurons, visual, vestibular horizontal rotational, and tactile inputs were tested systematically (Table 2). Slightly less than half of these neurons received vestibular input (35/82) while visual responsiveness was found in almost all of them (80/82; 98%). Almost all vestibularly driven neurons also had a visual component (34/35; 97%). Somatosensory responses were found in 34 neurons (42%). Typically, vestibular, visual and somatosensory responses were coaligned and codirectional (with four exceptions), and thus noncomplementary (Fig. 12D). The presence of all four sensory qualities [vestibular + direction selective (DS) + optic flow (OF) + somatosensory] was observed in 14 neurons, i.e. in 17% of the test cases. The combination of somatosensory and both visual (but not vestibular) response parameters (somatosensory + DS + OF) was found in 12 neurons, i.e. in 15%. Noticeably absent from the roster of responses were any combinations of somatosensory and optic flow, and vestibular–somatosensory and optic flow modulation (i.e. somatosensory + OF, and vestibular–somatosensory + OF). All the same, visual responsiveness was dominant in all test cases (in 80/82 neurons; 98%).

In a few neurons, auditory responses were tested and observed. However, the presence and characteristics of this sensory quality in VIP neurons was not further explored in this study (but see Schlack *et al*., 2000)

Visual response qualities

The vast majority of the observed VIP neurons in our study (168/186; 90%) had a visual component. When differentiating between additional sensory inputs (vestibular, somatosensory), purely visual neurons were found in 30/82 cases (i.e. 37%) (Table 2). Besides an on–off response, most visually driven neurons reacted to DS and OF stimulation (visual duality) (66/80; 82%). In the subpopulation of visual–vestibular responsive neurons, a similar proportion of dual visual responsiveness was present, i.e. in 31/35 neurons (89%). The data thus indicate a high proportion of dual visually responsive neurons, i.e. encoding translational (optic flow) as well as translational and/or rotational (directional selective) components.

Topography

During the course of the experiments, the entire area containing VIP in the two monkeys was mapped several times to the extent possible by the placement of the recording chamber and the electrode-positioning grid. However, in the rhesus monkey (Fig. 14A), a wider area could be explored than in the fascicularis monkey (Fig. 14B). Vestibular responses were found within a large volume of the examined area with distinct focal regions in both animals (arrows in Fig. 14A and B). Clearly, only the mapping in the rhesus monkey allows some limited conclusions about the topography of representation of the sensory qualities found in VIP. While visual responses were present throughout the entire explored area, vestibular information was more restricted and recorded predominately in a more anterior and medially placed region of the explored VIP volume. Such distribution would coincide with anatomical data of vestibular projections to VIP, which are indeed found in its anterior and medial portions (Lewis & Van Essen, 2000). However, in our experiments, we could test only responses presumably originating from the horizontal semicircular canals, but not from either of the vertical canals or the otoliths.

Discussion

Our results emphasize the nature of VIP as a multisensory area by adding a major sensory quality, vestibular, to the ones described there previously (Duhamel *et al*., 1991, 1998; Colby *et al*., 1993; Schaafsma & Duysens, 1996; Schaafsma *et al*., 1997). In fact, the observation of vestibular responses in area VIP was not entirely unexpected given the context of its presumed role in the processing of self-motion encoding. Any head or body movement will involve rotational or translational movements, or combinations thereof, and thus stimulate vestibular receptors. Entirely unexpected was the finding that the preferred directions for visual and vestibular stimuli were noncomplementary for essentially all investigated neurons. Regarding this aspect, area VIP differs remarkably from almost all other cortical areas, which are considered 'vestibular', and even more so from the classical vestibular brain stem centres (Dichgans *et al*., 1973; Henn *et al*., 1974; Allum *et al*., 1976).

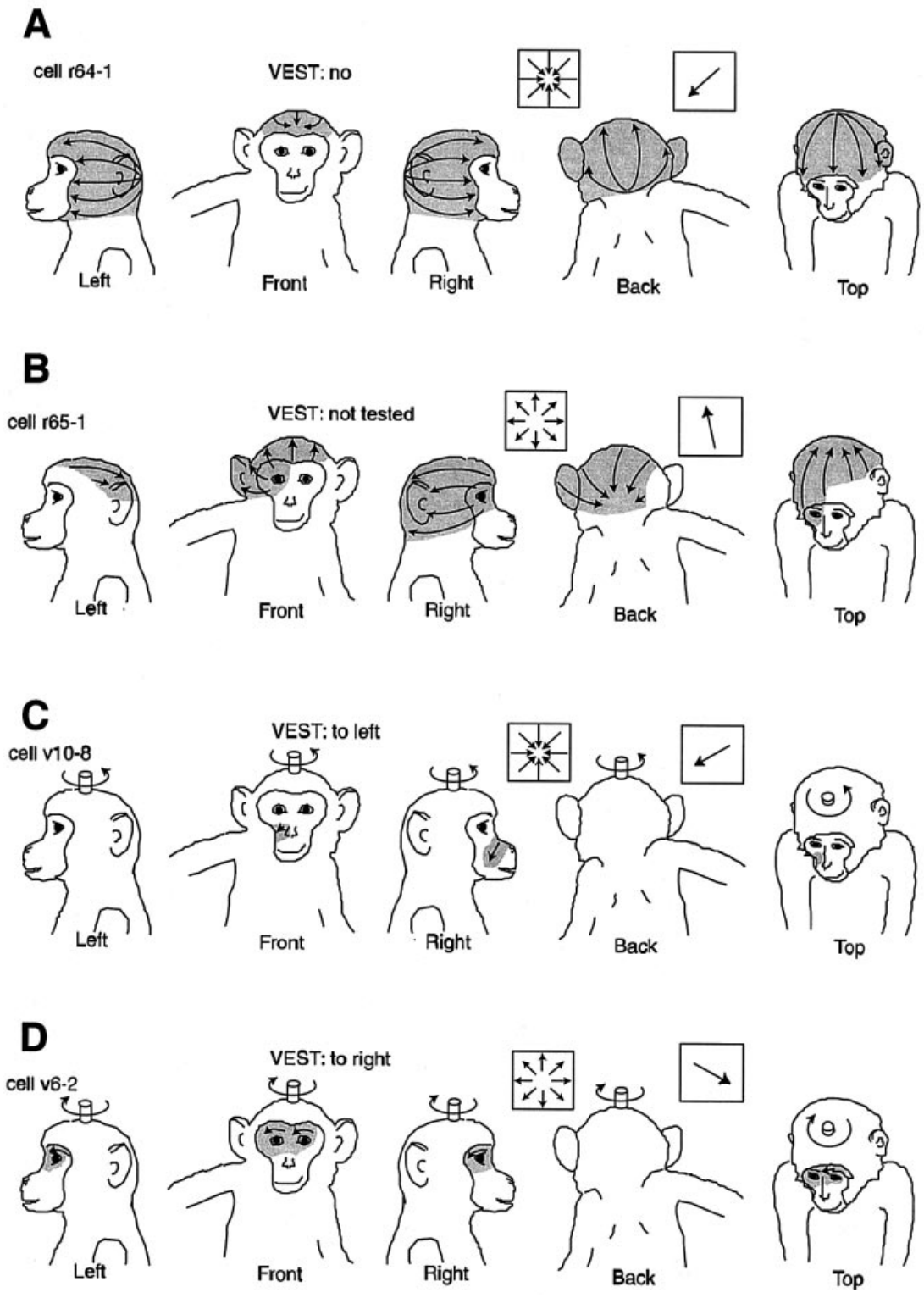
Vestibular responses in cortical and thalamic areas

Responses to vestibular stimulation so far have been reported in different regions of the macaque parieto-temporal cortex, such as the 'neck region' of somatosensory cortical area 3a (Ödkvist *et al*., 1974),

FIG. 12. Three-modal directional sensitivity in register. Prototypical examples of visual, vestibular and somatosensory directionalities in schematic renderings of different aspects of the experimental animals. Shading and arrows on the animal drawings indicate, respectively, the extent of the somatosensory receptive field and the directional preference of the tactile stimulus. Insets on top of the drawings indicate the cell identification, whether the neuron was tested for vestibular responses, the optic flow response (centripetal arrows, contraction; centrifugal arrows, expansion), and the directional selectivity vector. The placement of the latter two parameters on top of the drawing, showing the monkey from the back, represent the visual stimuli as actually seen by the animal during the experiments (i.e. an arrow pointing left indicates direction selectivity to the left). In the bottom two rows (C and D), the vestibular vertical rotation axis is indicated including the stimulation on-direction by the axis symbols on top of the monkeys' heads. Note coincidence of optic flow responses and tactile directional sensitivity in rows A and B (r64–1, complementarity of contraction and tactile response with linear backward movement; r65–1, complementarity of expansion and tactile response with linear forward movement). The visual directional selectivity vector would coincide only partially with the overall linear movement indicators. In C, vestibular and tactile responses were complementary, i.e. rotation to the left coincided with tactile stimulation to the right, and vice-versa. By contrast, the visual preferred direction would be noncomplementary to both the vestibular and the tactile responses. In D, vestibular and tactile responses were noncomplementary, as was the visual on-direction. The optic flow responses in C and D would signal simultaneous backward or forward translation, respectively.

vestibular area 2v at the anterior tip of the intraparietal sulcus (Schwarz & Fredrickson, 1971; Büttner & Buettner, 1978; Graf *et al*., 1995) and the parieto-insular vestibular cortex, located in the parietal operculum of the sulcus lateralis and the retroinsular region (Grüsser *et al*., 1990a,b). Interestingly, visual–vestibular responses were reported to be either complementary or noncomplementary in these publications. However, the functional role of the noncomplementary responses was not discussed. In addition, Büttner & Henn (1976) showed complementary and noncomplementary visual–vestibular interactive responses in neurons of the ventroposterior nucleus of the thalamus. All the above investigations had used only horizontal rotation stimuli.

Sakata *et al*. (1994) reported vertical vestibular responses in some neurons 'localized in the posterolateral part of area PG'. In this study,



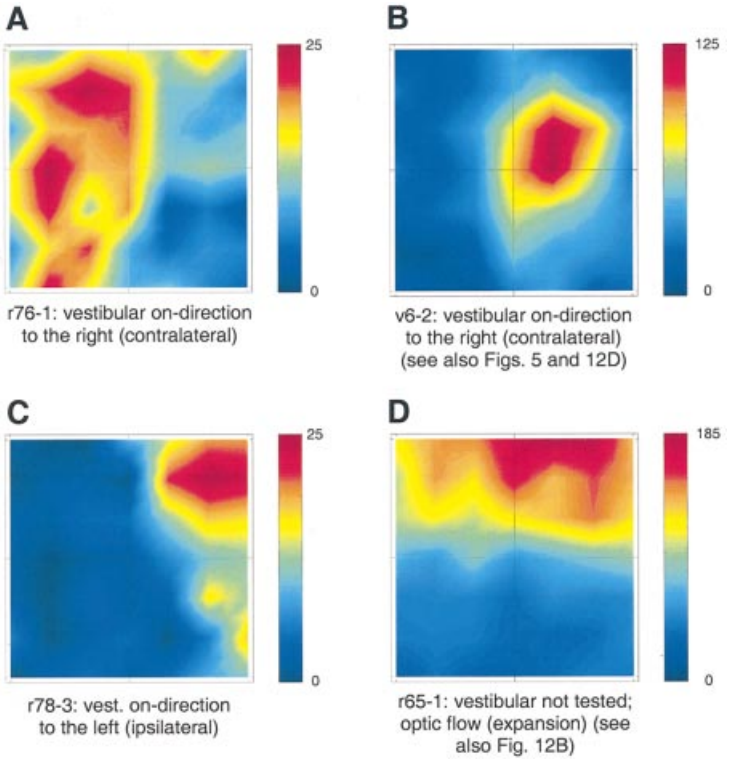


FIG. 13. Visual receptive field maps of VIP neurons. The individual panels depict colour-coded isofrequency contour maps in screen coordinates as seen by the animal. Scale bars next to individual panels indicate activity levels from low (blue) to high (red) spike discharges. In general, receptive field locations and shapes for horizontal rotation sensitive neurons were not correlated with vestibular on-direction or visual–vestibular interactive response. When tested, visual and tactile receptive fields were corresponding in spatial location (panels B and D).

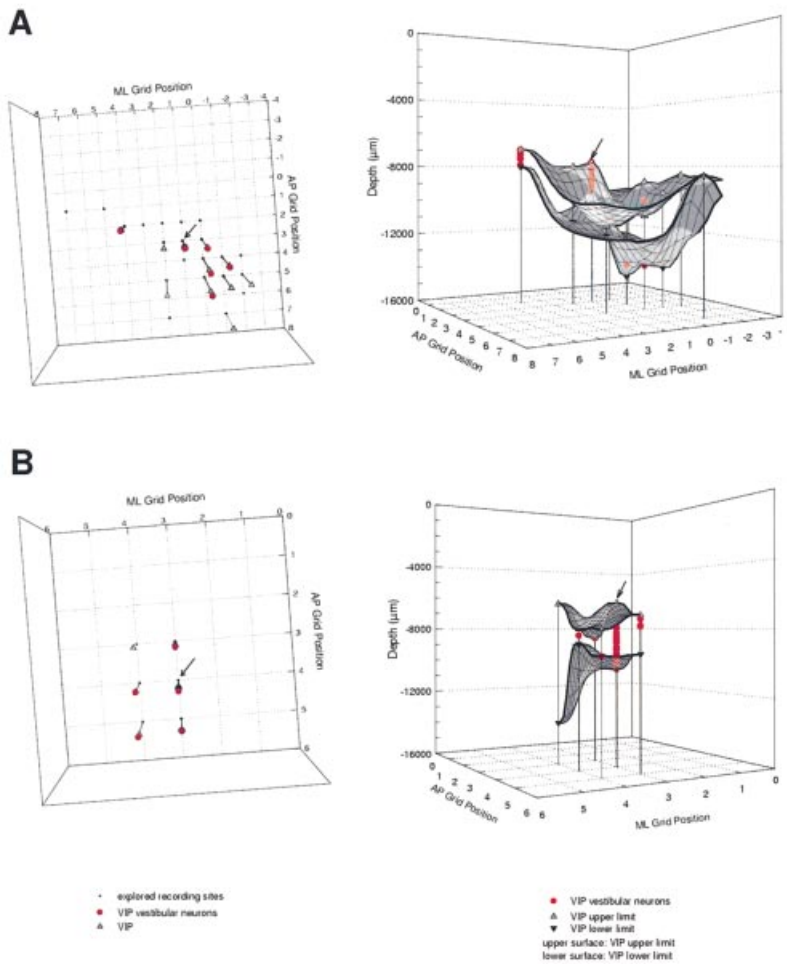


FIG. 14. Three-dimensional reconstruction of the two VIP recording sites in the two experimental animals in top view (all explored sites) and medio-posterior view (VIP sites only) within the recording grid (grid spacing 500 µm). (A) Rhesus monkey; (B) fascicularis monkey. Depth indicators refer to the surface of the brain. Open upward facing triangles and solid downward facing triangles indicate the upper and lower limits of VIP as encountered in the recordings, respectively. In order to illustrate the upper and lower surfaces, the respective data points were enveloped. Red circles mark sites where vestibular responses were encountered. In both animals, vestibular responses were found over a large portion of the explored VIP area, with a tendency to an anterior–medial placement in A. However, in certain penetrations, clusters of vestibular sensitivity were found (indicated by the arrows in all four three-dimensional plots). Note that in A (right), the major vestibular cluster is partially hidden behind the upper surface envelope.

rotations about the animal's anterior–posterior axis were applied, but not in any semicircular canal coordinates. Taken from a very limited sample ($n = 4$), all their neurons shared the exclusive noncomplementary response characteristics of area VIP neurons for preferred visual and vestibular directions.

The finding of exclusive or partial visual–vestibular noncomplementarity is puzzling, in particular because such a relationship has never been observed in vestibular nucleus neurons (Dichgans *et al*., 1973; Henn *et al*., 1974; Allum *et al*., 1976; Waespe & Henn, 1977, 1978), where visual–vestibular interaction is already occurring via the accessory optic system. In other contexts, neuronal responses resembling the described noncomplementary characteristics were found in cerebellar Purkinje cells (Belton *et al*., 2000); also, the signals of the eye movement related gaze-velocity Purkinje cells can be interpreted to carry information of conflicting nature (Lisberger & Fuchs, 1978a,b; Stone & Lisberger, 1990a,b).

VIP neurons and vestibular signals

Limitation to only yaw axis stimulation most probably led to an underestimation of the proportion of neurons responsive to vestibular stimulation. Within the neuron population not responsive to vertical axis rotation, no clear distribution of visual preferred directions could be discerned (Fig. 9B). These neurons could have either not received vestibular input at all, or they may have been connected with vertical canal or otolith systems, because vestibular-sensitive neurons were always also visually direction selective, including sensitivity to optic flow stimulation. Clearly, the majority of VIP neurons carry visual signals that encode both rotational and translational movement information (see Tables 1 and 2), and thus corresponding vestibular signals can be expected to be found once the necessary experiments are conducted.

We have to assume that VIP neurons may carry vestibular signals derived from all vestibular receptors, i.e. the three semicircular canals and the two otoliths (sacculus and utriculus). In such case, movement-related signals arriving at VIP neurons from the labyrinth would provide directional information encompassing all degrees of freedom, i.e. three rotation dimensions and three translation dimensions.

Movement-related encoding in visual signals

As mentioned in the companion paper (Bremmer *et al*., 2002), visual responses in cortical areas still need to be characterized according to their rotational vs. translational response properties. Although these differences may be subtle and not immediately obvious, differentiation of the two will be of fundamental importance for analysing multisensory interactions, in particular regarding the ubiquitous presence of vestibular components for motion and self-motion detection, in the form of the above-mentioned semicircular canal and otolith input, i.e. rotation- and translation-related signals. In lateral-eyed animals, where visual responses have been tested to that extent, a clear differentiation could be established (Graf *et al*., 1988; Graf, 1988; Wylie & Frost, 1990; Wylie *et al*., 1998). A number of cortical neurons, however, may have dual visual responsiveness, i.e. signal a combination of translation and rotation (see e.g. Duffy & Wurtz, 1991a,b; Lappe & Hoffmann, 2000; Lappe, 2000), as do most of our VIP neurons.

Projections to VIP

Anatomically and functionally, the motion areas in the parieto-temporal regions are situated at an intermediate stage between lower-level motion analysis and motor output, and are involved in multisensory integration and perceptual and motor decision-stage operations. Area VIP originally had been defined as the major input recipient of area MT in the intraparietal sulcus (Maunsell & Van Essen, 1983), but substantial visual projections also originate from the medial-superior temporal (MST) complex, besides others (Lewis & Van Essen, 2000). Interestingly, somatosensory input arrives largely from hand- and finger-related areas, and only to a lesser degree from face and head regions (Lewis & Van Essen, 2000), although our findings are weighted in favour of tactile receptive fields on the head and in the face in agreement with previous reports (Duhamel *et al*., 1991, 1998). Vestibular input comes from all cortical areas that are considered 'vestibular', notably parieto-insular vestibular cortex, 3a, and, to some extent, 2v (Lewis & Van Essen, 2000). In addition, vestibular input could be transmitted via MST as well (Thier & Erickson, 1992; Duffy, 1998; Bremmer *et al*., 1999b; Shenoy *et al*., 1999). The vestibular projections are predominantly found in the anterior and medial portion of VIP (Lewis & Van Essen, 2000), which is in agreement to some degree with our topographical analysis, although we clearly had not explored the full range of VIP in our preparations. VIP also receives input from the frontal eye fields (Lewis & Van Essen, 2000) and in turn also projects there (Stanton *et al*., 1998), and to the superior colliculus (Paré *et al*., 1999).

VIP and eye movements

Eye position effects in VIP neurons were present in all instances where vestibular responses were recorded. One of our earlier studies had shown eye position effects in about half of all recorded neurons (Bremmer *et al*., 1999a). These effects, however, cancelled within VIP when treated at the population level. Thus, local connectivity was interpreted as subserving encoding of visual information in a nonretinocentric reference frame (Duhamel *et al*., 1997). Nevertheless, some eye movement related signals could have an oculomotor function in light of the presence of significant eye movement signals (Figs 5A and D and 7B and C), and the described projections of VIP to the frontal eye fields and the superior colliculus. In fact, Colby *et al*. (1993) described motion-sensitive neurons in area VIP which also responded during smooth pursuit eye movements of small foveal targets. However, origin and functional context of such signals are still a matter of debate. In the vestibular nuclei, neurons related to head and eye movements subserving the VOR are found in a similar proportion as neurons that only signal head velocity, without any eye movement relatedness (Gdowski & McCrea, 1999). The latter are thought to be part of the vestibulo-cortical relay, although some vestibulo-ocular neurons project to thalamic units which, in turn, then project to the vestibular cortices (Matsuo *et al*., 1995). Vestibular thalamic and cortical units have been reported not to carry eye movement signals (Büttner *et al*., 1977; Magnin & Fuchs, 1977; Grüsser *et al*., 1990b). Because non-eye movement related vestibular nucleus neurons are always reported as being tuned to head velocity, in this context the presence of acceleration and position signals in our VIP neurons requires differentiation and integration by additional processing mechanisms.

Conclusions

Our data are in agreement with the established notion of area VIP being involved in multisensory analysis of movement, either of objects and/or of self-motion, in the context of representation of extrapersonal space and certain motor coordination functions. The majority of neurons respond to visual direction selective and/or optic flow patterns, simulating rotations or translations. Many neurons have tactile directional selectivity, and we have now discovered the presence of vestibular responses. In addition, preliminary data from

one of us give strong evidence for the presence of auditory sensory signals in area VIP (Schlack *et al*., 2000).

The peculiar noncomplementarity found in the vestibular and visual on-directions has been described in other vestibular-related areas together with the classical complementary visual–vestibular interactive response pattern, but exclusive noncomplementarity was only found in our study on VIP neurons, and in a very limited set of neurons ($n = 4$) in area PG (Sakata *et al*., 1994). However, the unexpected polarization of VIP neurons into 'high' and 'low' visual, vestibular and combined visual–vestibular responses *a priori* escapes a functional role in movement detection. In the light of the now evident change in firing behaviour of neurons within the basic rotational and linear vestibulo-ocular reflex arcs depending on viewing distance (Chen-Huang & McCrea, 1999a,b), additional experiments taking into consideration viewing distance and off-axis head rotations will have to be conducted.

For an overall interpretation of the role of VIP neurons, and of other regions thought to be involved in the detection and perception of self-motion, an understanding of the visual and vestibular sensory interaction characteristics is thus a key issue. This interaction could be interpreted in terms of an allocentric encoding scheme (Snyder *et al*., 1998; Andersen *et al*., 1999). In such a case, the resting firing rate of these neurons could be envisioned to signal that the world where the observer is located is stable. While, in all probability, in any biologically relevant situation for humans the world can be considered stable, there may be numerous instances of nonstable environments for arboreal primates. This allocentric interpretation of VIP function is supported *prima vista* by the finding that all neurons with vestibular sensitivity also exhibited eye position sensitivity. Thus, these neurons may code for external space and for orientation in three dimensions, because eye position sensitivity could be interpreted in terms of responses to external position of objects, and vestibular responses in terms of orientation of the head. The neurons would then code for orientation of eye, head and/or body to a given part of external space, or for attention directed to a given part of space (see e.g. Cook & Maunsell, 2002). Such an idea would gain credence if the same directional preference existed for eye and head position. However, within an appropriate test population of 19 horizontal neurons, in only eight neurons did vestibular and eye position directions coincide whereas in six cases they were oppositely directed and in five cases vertically displaced. Cleary, more experiments are needed to explore all possibilities in this regard.

Alternatively, observer-centred interpretations may be offered. Visual and vestibular signals of the same type as observed in our recordings would occur if, during a given head movement, the resulting VOR eye movements were overcompensatory. The combined visual–vestibular signal then would indicate a motor performance error of the VOR. Whether VIP responses have to be interpreted in a motor control function rather than in a perceptual context is questionable. In any case, our eye movement recordings showed that the VOR undercompensated rather than overcompensated. Although the animal made compensatory eye movements (VOR), the gain of the VOR was typically < 1.0. Thus, for instance, the resulting retinal slip signal during head rotation to the right was visual motion to the left, i.e. the nonpreferred direction of such a neuron.

Finally, envisioning self-motion of a monkey through its natural environment might give a meaningful answer to the question of visual–vestibular interaction in area VIP. Self-motion usually not only includes linear displacement into one direction with fixed gaze as simulated by our employed optokinetic and optic flow visual stimuli, but also comprises orientating and tracking of objects, i.e. movement of the eyes and of the head. Because we did not test systematically optokinetic or pursuit eye movements, we will consider only head movements here. If we now consider the visual information arriving at the retina during linear self-motion and a simultaneous head rotation, e.g. to track some object, it becomes clear that the direction of motion on the retina induced by objects in the environment depends on the location of these objects with respect to the fixation plane (Fig. 15A). Objects located beyond the fixation plane induce visual motion on the retina, motion which is opposite to the direction of head movement. However, many objects closer than the fixation plane induce visual motion in the same direction as the head movement. Approaching objects, such as leaves and twigs, could even touch the body surface such as to produce tactile flow, for instance, across the face. Some objects located in the near-extrapersonal space would indeed generate a noncomplementary visual movement pattern (Fig. 15B). Thus, the functional role of motion-sensitive neurons in area VIP could be to encode self-motion in the near-extrapersonal space (Bremmer & Kubischik, 1999). This interpretation appears appealing and, indeed, holds good for a large portion of the visual movement space, although not for its entirety, according to geometrical reconstruction.

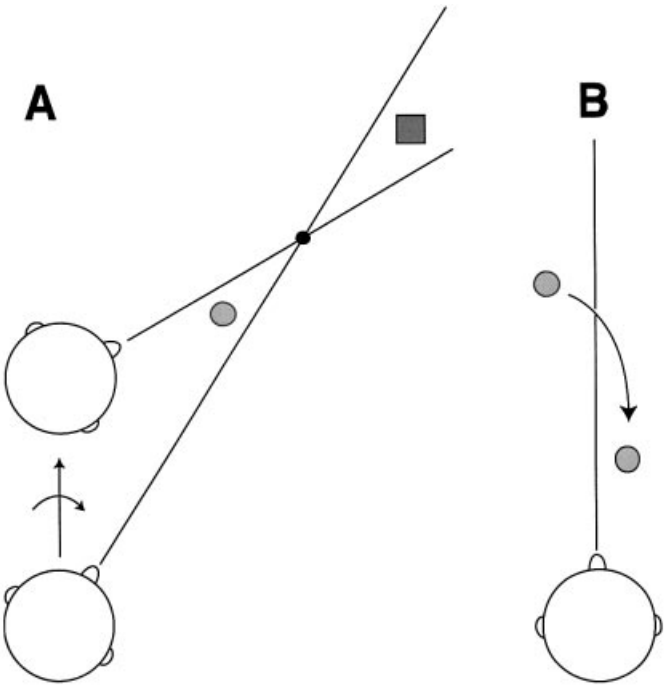


FIG. 15. Interpretation of noncomplementarity of visual and vestibular responses. (A) Allocentric situation: during forward translation, an observer may fixate on an object in a given focal plane (small solid circle), while a second object (shaded large circle) is located closer to the observer (by contrast with the squared object further away from the observer). In order to keep gaze on the object in the focal plane (small solid circle) during forward movement, a head rotation, in this case to the right, has to take place. (B) Observer-centric situation: during the rightward head movement while translating forward, the object near the observer (shaded large circle) would actually also undergo an apparent rotation to the right.

Self-motion detection in near-extrapersonal space could also be the key difference between movement processing in areas VIP and MST. The latter is widely considered to play an important role in heading detection (Lappe *et al*., 1996), i.e. in the encoding of visual information in the far extrapersonal space. However, further experiments in animals whose heads are unrestrained during linear forward and backward motion need to be conducted to verify this hypothesis.

In addition, we have to consider that vestibular input to a particular population of vestibular nucleus neurons changes substantially during active vs. passive head movements (McCrea *et al*., 1999), i.e. during active head movements the vestibular signal disappears entirely. There are clearly counter-examples, such as the so-called head-direction cells, where vestibular information is present during active head movements (Taube, 1995; Stackman & Taube, 1997, 1998). Thus, a final answer to a comprehensive interpretation of our noncomplementary visual–vestibular VIP neurons, and also those in other brain areas, will also have to take into account passive vs. active head- or even whole-body movements.

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Abbreviations

DS, directional selectivity; I_{vest}, modulation index for vestibular stimulation; I_{vis}, modulation index for visual stimulation; I_{VV}, modulation index for combined visual–vestibular stimulation; LED, light-emitting diode; LIP, lateral intraparietal area; MIP, medial intraparietal area; MST, medial superior temporal area; MT, medial temporal area; OF, optic flow; VIP, ventral intraparietal area; VOR, vestibulo-ocular reflex.

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