The *TINS* Lecture
The parietal association cortex in depth perception and visual control of hand action

H. Sakata, M. Taira, M. Kusunoki, A. Murata and Y. Tanaka

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Recent neurophysiological studies in alert monkeys have revealed that the parietal association cortex plays a crucial role in depth perception and visually guided hand movement. The following five classes of parietal neurons covering various aspects of these functions have been identified: (1) depth-selective visual-fixation (VF) neurons of the inferior parietal lobule (IPL), representing egocentric distance; (2) depth-movement sensitive (DMS) neurons of V5A and the ventral intraparietal (VIP) area representing direction of linear movement in 3-D space; (3) depth- rotation-sensitive (RS) neurons of V5A and the posterior parietal (PP) area representing direction of rotary movement in space; (4) visually responsive manipulation-related neurons (visual-dominant or visual-and-motor type) of the anterior intraparietal (AIP) area, representing 3-D shape or orientation (or both) of objects for manipulation; and (5) axis-orientation-selective (AOS) and surface-orientation-selective (SOS) neurons in the caudal intraparietal sulcus (cIPS) sensitive to binocular disparity and representing the 3-D orientation of the longitudinal axes and flat surfaces, respectively. Some AOS and SOS neurons are selective in both orientation and shape. Thus the dorsal visual pathway is divided into at least two subsystems, V5A, PP and VIP areas for motion vision and V6, LIP and cIPS areas for coding position and 3-D features. The cIPS sends the signals of 3-D features of objects to the AIP area, which is reciprocally connected to the ventral premotor (F5) area and plays an essential role in matching hand orientation and shaping with 3-D objects for manipulation.

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THE PREHENSILE HAND and binocular stereopsis are two major functional features of primates[1], and the arms and hands working under close binocular visual guidance are the most important instruments in the rise of human intellect[2], especially for tool-using and tool-making[3]. Recently, the visual-predation theory of primate evolution[4] has postulated that the common ancestor of living primates was a small, big-eyed, nocturnal creature that relied on vision for hunting insects, such as the small primates tarsiers do today. Tarsiers have long fingers with flattened nails and large frontal eyes with foveas[5]. The emergence of these features coincided with an expansion of the parietal association cortex in tarsiers in contrast to tupaias, the closest infraprimate mammals[6]. Therefore, the most probable site of integration of binocular vision and skilled hand movement is the parietal association cortex.

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The earliest evidence for the relation of the parietal cortex to visually guided hand movement and depth perception was obtained in a number of clinical studies[7–16]. In 1909, Bálint[7] reported on the occurrence of optic ataxia together with psychic paralysis of visual fixation in a patient with bilateral parietal lesions who had difficulties in pointing, grasping and drawing. Later, disturbances of visual orientation were described in patients with gunshot wounds of the parieto-occipital cortex[8]. The most remarkable symptoms of these patients were difficulty in judging distance and perceiving depth movement, symptoms also observed in more recent clinical studies[9,10]. Other workers described cases of patients with parieto-occipital lesions who exhibited a deficit in stereopsis[11,12], although it has been reported that global stereopsis, as tested by a random-dot stereogram, is impaired by right temporal lobectomy[13]. There are cases of three-dimensional constructional apraxia in patients with parietal lesions (often bilateral) who showed gross abnormalities in their ability to assemble blocks into 3-D patterns, but not much difficulty in 2-D drawing or block design[14]. More recently, disturbances in preshaping the hand according to the shape of the object to be grasped[15] and errors in adjustment of hand orientation due to parietal lesions[16], have been identified.

The symptoms of optic ataxia were replicated in monkeys as misreaching[17] and loss of hand preshaping ability[18] by parieto-occipital lesions. It has been proposed that the dorsal or occipitoparietal pathway is

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specialized for spatial perception (locating where an object is), in contrast to the ventral or occipitotemporal pathway being specialized for object perception (identifying what an object is)[19]. More recently, the visual projection system to the parietal cortex has been postulated to provide action-relevant information about the structure and orientation of objects[20]. However, the impairment of depth perception due to the parieto-occipital lesion in monkeys is not clear.

Since the first single-unit analyses of parietal neurons in alert behaving monkeys[21,22], a number of studies aimed at investigating the neural mechanisms of visually guided eye and hand movements, as well as space vision and selective attention, have been performed[23,24]. However, only a few investigators have paid attention to the dimension of depth in space vision and spatial control of movements. Since the 1980s we have been studying the parietal neurons that are related to binocular depth perception and skilled hand movements. The results of these studies are summarized in this review in an effort to illustrate how the neural subsystems in the parietal cortex integrate visual and non-visual signals for depth perception, and how these perceptual signals are incorporated in the guidance of goal-directed hand movements.

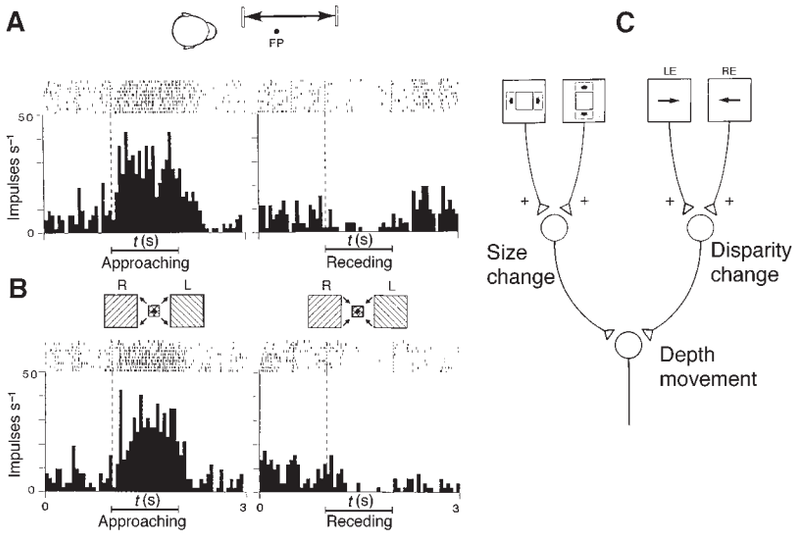

Fig. 1. ***Depth-movement-sensitive (DMS) neuron responses.*** **(A)** *Left: response to approaching plate (real object). Right: inhibitory response to receding plate.* **(B)** *Left: response to combination of stimulus size increase and increase of crossed disparity [opposed motion of the stimuli for the right eye (R) and the left eye (L)], simulating approach of a square. Right: inhibitory response to stimulus contraction and decrease of crossed disparity, simulating receding of a square.* **(C)** *Schematic diagram of the hypothetical neural circuit for a depth-movement-sensitive neuron receiving converging inputs from a size-change detector and a disparity-change detector.* Modified from Ref. 32.

Visual-fixation neurons and the discrimination of distance

Initial studies on parietal neurons in alert monkeys, showed two classes of eye movement-related neurons[21,22]. One, visual-fixation (VF) neurons that were activated during fixation of a static target in certain positions[25], and the other, visual-tracking (VT) neurons that were activated when the monkey tracked the moving target with smooth pursuit eye movement[26]. We recorded these two types of eye movement-related neurons together with visual neurons sensitive to depth movement and rotary movement in the inferior parietal lobule (IPL), and studied their selectivity to the position or direction of movement, not only in the frontoparallel plane but also in the plane of depth[27]. We found that VF neurons were distributed widely in area 7a and the lateral intraparietal (LIP) area whereas VT neurons were concentrated in the anterior bank and fundus of the superior temporal sulcus, in and around V5A, or the medial superior temporal (MST) area.

Most of the VF neurons we recorded were selective for fixation point position or direction of gaze[25] and many were also selective for fixation point distance[25,27]. The majority of the depth-selective VF neurons preferred a near target, and their activity increased gradually as the distance of the target from the eyes decreased with increasing angle of convergence and degree of accommodation. A smaller proportion of the depth-selective VF neurons preferred a distant target, and their activity increased gradually as the distance of the target from the eyes increased within the range of two to three meters. Therefore, depth-selective VF neurons are likely to receive an efference copy or corollary discharge of accommodation and vergence eye movement systems, although extraocular muscle proprioceptors cannot be excluded as alternative sources of extraretinal signals of convergence[28]. Moreover, some of the VF neurons we recorded appeared to receive retinal signals from the fovea, since their activity decreased sharply when the target light was switched off during the fixation. There is psychophysical evidence that convergence and accommodation play crucial roles in the estimation of absolute distance[29,30]. Therefore, it is highly likely that VF neurons play a crucial role in the perception of egocentric distance of the visual target. Recently, Gnadt and Mays[32] found that the level of activity of many eye movement-related neurons in area LIP changed as a function of visual target depth, according to the up-coming convergence and accommodation rather than the depth of a visual target; they speculated that this increased activity represented motor intention. Thus the perception of distance and the control of accommodation and convergence are linked tightly within the parietal cortex.

Depth-movement-sensitive neurons

We recorded many VT neurons and movement-sensitive visual neurons in the posterior part of the IPL. Some of these VT neurons were activated during visual tracking of a target moving in depth, and were thus considered likely to code depth movement of a visual target[26].

In addition, we identified a group of neurons that responded to approach or receding of a visual stimulus other than the target of fixation. Many of them were sensitive to size change of the visual stimulus[26]. We then set up an optical stimulator with polarizing filters to enable us to change the binocular disparity of the stimulus as well as its size. The depth-movement-sensitive (DMS) neurons were sensitive to either size change or disparity change, or to a combination of these two[32] (see Fig. 1A,B). The DMS neuron responded strongly to the approach of a luminous plate, and its activity was suppressed during receding of the plate (Fig. 1A). The same cell was activated equally strongly when a pair of squares for both eyes on the screen were moved to the opposite sides and

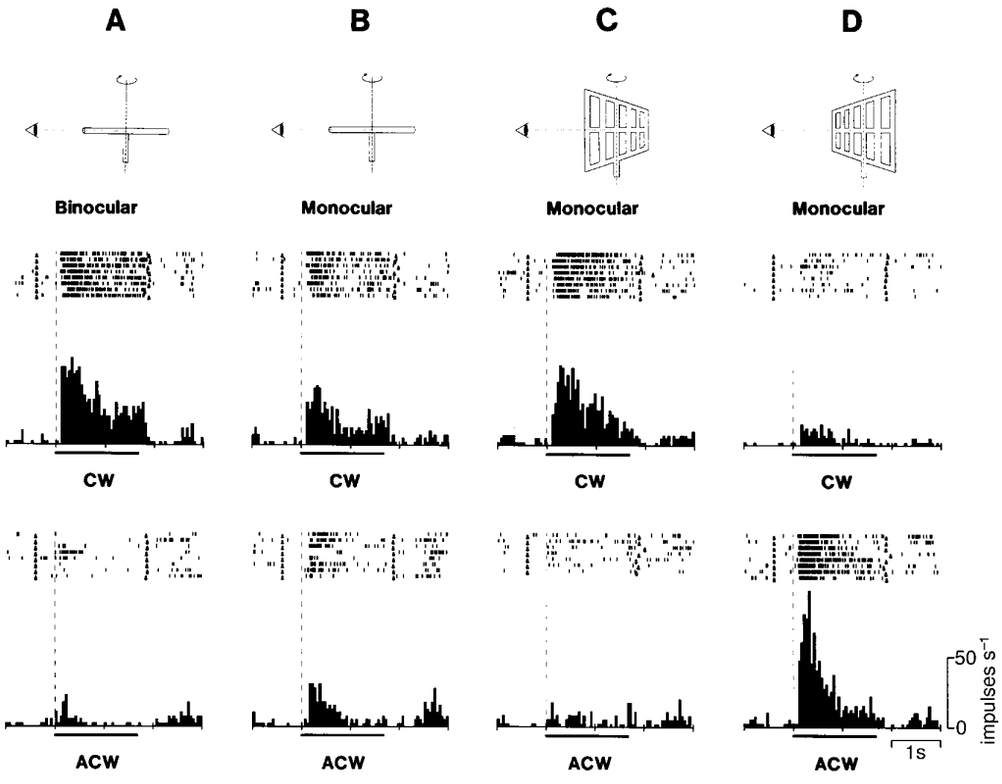

Fig. 2. ***Responses of a depth-rotation-sensitive (RS) neuron to rotation of a trapezoidal window.*** **(A)** *Response to rotation of a bar in binocular viewing conditions.* **(B)** *Responses to rotation of a bar under monocular viewing conditions.* **(C *and* D)** *Response to rotation of a trapezoidal (window-shaped) plate around an axis parallel to the base of the trapezoid, under monocular viewing conditions, with the longer edge moving in front of* (C) *or behind* (D) *the axis. The range of rotation was half a turn (180°) and the viewing distance was 150 cm for all recordings. Note a reversal of preferred direction of rotation in* D. *Stimuli were rotated in the sagittohorizontal plane, although the diagrams are drawn in the horizontal plane for simplicity*[43].

the squares were simultaneously expanded for a combination of disparity change and size change, to simulate the movements of retinal image during approach of a real object (Fig. 1B). Some of the DMS neurons were sensitive predominantly to the size change and some to disparity change; a considerable number of the cells were not activated strongly by either one of these stimuli alone, but were activated strongly by a combination of the two, similar to the case for visual neurons in the Clare–Bishop area of the cat[33]. The neurons sensitive to the size change of the squares were activated partially by paired movement of two edges in opposite directions, similar to previous findings[34], but most of them responded more strongly to the combined movement of two pairs of edges that produced a size change without a change in shape. Thus, the response of typical DMS neurons that responded only to combination of size change and disparity change was the outcome of several steps of hierarchical processing of visual motion signals (Fig. 1C). These results are consistent with the results of psychophysical studies indicating the existence of two separate filters for size change and disparity change[35].

The recording sites of the DMS neurons were located in two regions, one in area V5A (MST) in the fundus of the superior temporal sulcus (STS) and the other in the ventral intraparietal (VIP) area in the fundus of the IPS. Other workers have recorded neurons in the dorsal part of area V5A that are sensitive to radial movement of optical flow stimulation[36,37]. These properties were similar to the opponent vector or radial organization of directionalities of the parietal visual neurons reported previously in other studies[38,39]; although, the visual stimuli used in the former two studies were more likely to be related to the self-motion of the animal than to the motion of objects because they covered a wide field of the background. Colby *et al.*[40] recorded visual and polysensory (visual and somatosensory) neurons in the VIP area that responded to approach of a stimulus towards some part of the face or body. Those neurons preferred oblique rather than straight-ahead movement. Similarly, some of the DMS neurons we recorded[41] also preferred oblique movement to either the left or the right side of the face. Thus DMS neurons are likely to represent various directions of movement of objects in 3-D space.

Depth-rotation-sensitive neurons

We often recorded visual neurons in the anterior bank of the STS that preferred rotary movement to linear translational movement[42,43]. The majority of these rotation-sensitive (RS) neurons preferred depth rotation, in either a horizontal, a sagittal or a diagonal plane, and thus we called them depth RS neurons. These neurons were activated by the depth rotation of a pair of spots or even a single spot. Moreover, most of the RS neurons had large receptive fields and did not show a change in the preferred direction of rotation upon a change in stimulus position within the receptive field. Therefore, it was concluded that sequential changes in the direction of movement are essential for activation of RS neurons. Rotation-sensitive neurons have been recorded in the dorsal part of area V5A (dMST; Refs 36 and 37). However, in both cases large field optical flow stimuli were used, and therefore the activity of these dMST neurons was likely to be related to the perception of self-motion rather than the movement of external objects. The recording sites for the depth RS neurons we identified were located mainly in the lateral part of area V5A (lMST), but were also in adjacent posterior parietal (PP) area[44].

There is a peculiar illusion for depth rotation called the Ames window illusion[45]. It is caused by the rotation of a trapezoidal window-like plate which appears to be a rectangular window viewed from an oblique angle. When it is rotated around an axis parallel to the base of the trapezoid and viewed with one eye from a distance (a couple of metres), its direction of movement appears to reverse every half turn. Example recordings were obtained from a depth RS neuron displaying a reversal of preferred direction in response to rotation of a trapezoidal window under monocular viewing conditions (Fig. 2). The cell responded preferentially to clockwise rotation of a bar in a diagonal plane, that is, between sagittal and horizontal planes (Fig. 2A,B). The preferred direction of the rotation of the trapezoidal window was the same

when the longer edge moved in front of the axis of rotation (Fig. 2C), but was reversed when the longer edge moved behind the axis of rotation (Fig. 2D). This corresponds closely to the reversal of perceived direction of rotation in the Ames window illusion. The longer edge always appears to move in front of the axis of rotation (perhaps because it appears nearer than the shorter edge). The fact that the activity of the parietal neurons corresponded so closely to the perceived illusion strongly suggests that cortical neuronal activity at the level of the association cortex is closely related to the subjective experience of perception.

Hand manipulation task-related neurons

Cortical neurons related to visually guided reaching and manipulation when first recorded in the IPL (Refs 21,22) were classified into two groups: arm-projection (reaching) and hand-manipulation neurons. Further analytical studies of reaching neurons in the parietal cortex revealed that the superior parietal lobule (SPL: area 5) played an important role in reaching[46,47], although reach-related neurons were also recorded in area 7a of the IPL (Ref. 48). More recently, the neurons involved in hand movement were found to be concentrated in a small zone within the rostral part of the posterolateral bank of the IPS, designated the anterior intraparietal (AIP) area[49,50]. This area is strongly interconnected with area F5 of the ventral premotor cortex[52], in which grasping-with-the-hand neurons have been recorded. We recorded the activity of neurons in this area in monkeys that had been trained to manipulate various types of switches: push button, pull lever, pull knob and pull knob in a groove[49,53]. Many of these hand manipulation task-related neurons (we now call them 'manipulation-related' neurons) were highly selective and were preferentially activated during the manipulation of one of four routinely used objects.

Separation of visual and motor components

In order to determine the contribution of visual signals to the activation of these neurons, we let the monkeys perform the same task in the dark, guided only by a small spot of light on the object[49,53,54]. We then classified the manipulation-related neurons into three groups according to the difference between the levels of activity during manipulation of objects in the light and in the dark. Motor-dominant neurons (Fig. 3A) did not show any significant difference in the level of activity between the two conditions. Visual-and-motor neurons (Fig. 3B) were less active during manipulation in the dark than during that in the light; and visual-dominant neurons (Fig. 3C) were not activated during manipulation in the dark. Many of the latter two visually responsive neurons were activated by the sight of objects during fixation without grasping (object-type, Fig. 3B,C). The other visually responsive neurons were not activated during object fixation (non-object type) but seemed to require other visual stimuli for activation, such as the sight of the moving hand.

Almost all of the highly selective visual-and-motor neurons preferred the same object for manipulation and for fixation, showing precise correspondence between the pattern of hand action and the pattern of the object. This suggests that visual-and-motor neurons in the AIP area play an important role in matching the pattern of hand movement to the spatial characteristics of the object for manipulation[49]. These results correspond closely to the clinical evidence that parietal lobe lesions cause disturbances in preshaping of the hand according to the shape and orientation of the object to be grasped[15,16].

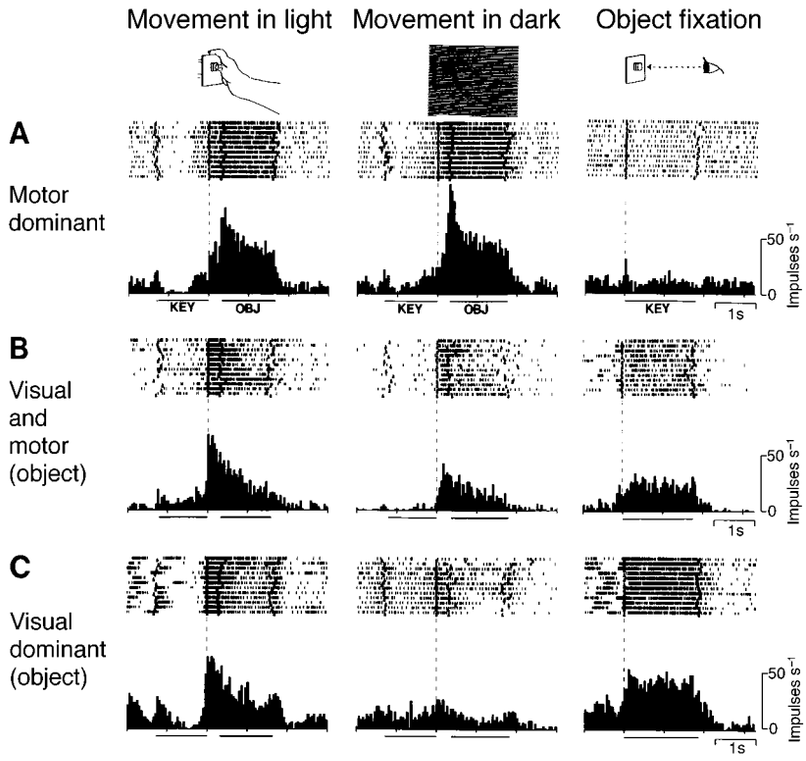

Fig. 3. ***Three types of manipulation-related neurons in the anterior intraparietal (AIP) area.*** *Activity of cells during manipulation in the light and in the dark, as well as during visual fixation of a push button is shown with rasters and histograms.* **(A)** *Motor-dominant neuron that showed almost equal levels of activity during manipulation in the light and in the dark, but was not activated during object fixation.* **(B)** *An object-type visual-and-motor neuron that was less active during manipulation in the dark than during that in the light, and was weakly activated during object fixation.* **(C)** *An object-type visual-dominant neuron that was not activated during hand movement in the dark but was strongly activated during object fixation in the light. KEY indicates the duration of pressing of the anchor key before movement towards the object. OBJ indicates the duration of holding of the object to keep the switch on.* Modified from Ref. 60.

Selectivity to the 3-D shape of objects

In more recent experiments on manipulation-related neurons we used six different objects of simple geometric shape: a sphere, cone, cylinder, cube, ring and square plate[55]. These objects were connected to microswitches, set in six sectors of a turntable and presented to the monkey in random order one at a time. The monkey was required to grasp and pull the object to turn the microswitch on or fixate the spot reflected on a half-mirror and superimposed on the object (Fig. 4A). More than one quarter of the manipulation-related neurons were highly selective for one particular object. The activity profile of one highly selective, object-type, visual-dominant neuron during object fixation is shown in Fig. 4B. The cell responded preferentially to the view of the square plate among the six objects. We found highly selective visual-dominant neurons for every one of the six objects. The square plate and circular ring were the most commonly preferred objects, and many of the cells that preferred these two objects showed selectivity to the orientation of the plane. We also found moderately selective neurons that responded to two or more objects equally strongly. Some of these moderately selective

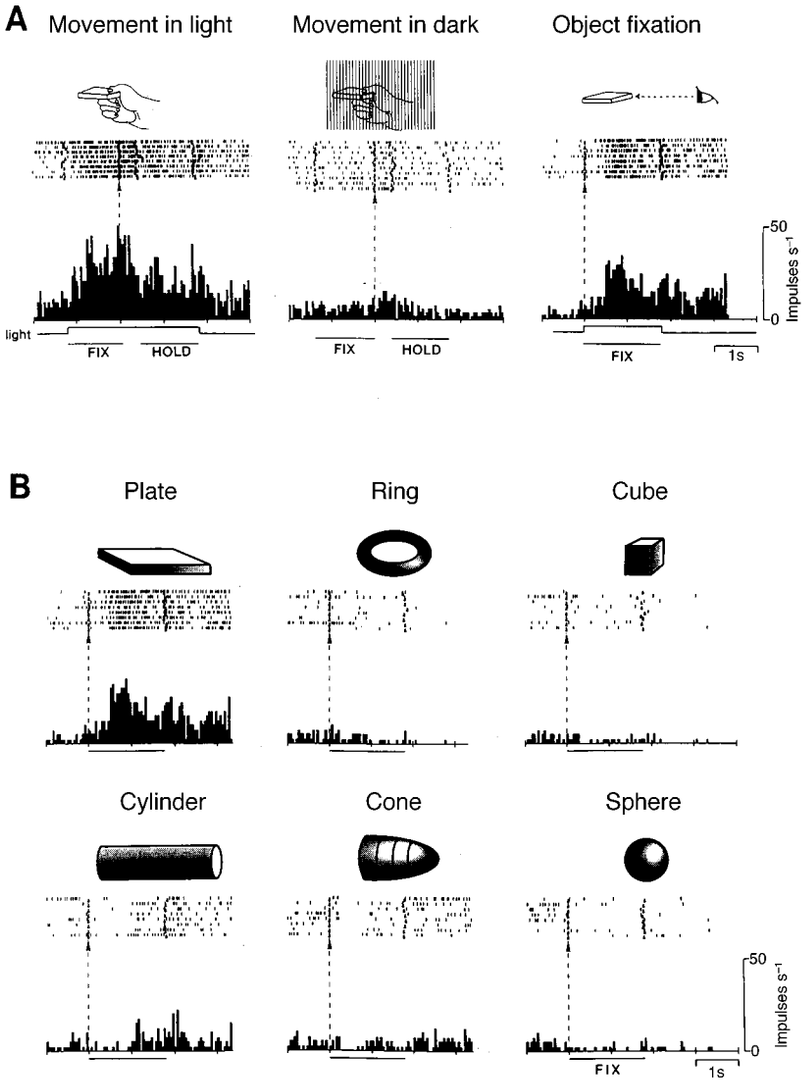

Fig. 4. ***Activity profile of an object-type visual-dominant neuron.*** **(A)** *Activity under three task conditions. Left: object manipulation in the light; middle: object manipulation in the dark; right: object fixation in the light.* **(B)** *Activity of the same neuron during fixation of different objects. The objects for fixation are shown above each raster and histogram pair. FIX, object fixation period; HOLD, object holding period.* Modified from Ref. 55.

neurons showed preference for a certain category of geometric shapes such as round objects (the sphere, cone and cylinder), angular objects (the cube and square plate), or flat objects (the plate and ring). These results suggest that the visually responsive neurons in the AIP area represent spatial characteristics of objects for manipulation, and that at least some of these neurons represent the 3-D shapes of the objects, which were categorized into a limited number of simple geometric shapes as suggested by Biederman[56] in his theory of recognition by components. However, it was not clear from where these neurons received signals of 3-D shape. Since the neurons of the inferior temporal cortex that play a major role in object vision did not differ much in response intensity to either 3-D objects or to 2–D images of the same objects[57], this area cannot provide adequate signals of 3-D shape for object manipulation.

Selectivity to 3-D orientation

Determination of the orientation of objects in a viewer-centred coordinate system is important for manipulation of objects with the hand. Thus, as anticipated, we found orientation-selective neurons during our study of manipulation-related neurons. This led us to find a group of visual neurons specifically selective to axis- and surface-orientation in space.

Axis-orientation-selective neurons

We found that most of the cells that preferred the pull-lever were selective for the axis orientation of the lever. During a further investigation, we found a group of neurons in the lateral bank of the cIPS that showed selectivity to the orientation of a luminous bar in space. We designated these neurons as axis-orientation-selective (AOS) neurons[58,59]. Most of these AOS neurons were binocular visual neurons, responding much less strongly under monocular viewing conditions than under binocular viewing conditions. The discharge rate of most of the cells increased monotonically with increasing length of the stimulus, and most of the cells preferred a thinner stimulus to a thicker one. However, the AOS neurons showed typically the same orientation preference across a wide range of change in stimulus thickness and length, as well as across wide receptive fields. These results suggest that AOS neurons represent the orientation of the longitudinal axes of objects in 3-D space. A few AOS neurons showed maximum responses to the stimulus with intermediate thickness. Some of these neurons preferred a cylinder to a square column, showing selectivity to shape in addition to orientation selectivity[60].

Bender and Jung[61] reported that in human parietal patients, vertical and horizontal axes are tilted considerably to the contralesional side. A similar finding in several cases of patients with right occipitoparietal lesions has been described[62]. Similar deficits in the perception of line orientation due to parietal lobe lesions have been reported[9]. Therefore, the discrimination of axis orientation is one of the prominent functions of the parietal cortex in the domain of space perception.

Surface-orientation-selective neurons

According to Marr's theory of vision[63], the main purpose of vision is object-centred representation of the 3-D shape and spatial arrangement of an object. The main stepping stone towards this goal is representation of the geometry of the visible surface. Therefore, there should be some area in the visual cortical pathways to represent surface orientation and curvature, if 3-D shape is to be represented somewhere in the cerebral cortex. In our recent experiments on hand manipulation task-related neurons, we found that some visual-dominant neurons that preferred the square plate showed selectivity to the orientation of the plate. This suggests that some parietal visual neurons can discriminate for surface orientation. Since a disparity gradient is the most important cue for perceiving the orientation of a surface in depth, we used a stereoscopic display of 3-D computer graphics and performed an extensive study of binocular neurons in the cIPS that were sensitive to changes in surface orientation[64].

Since we found parietal visual neurons that responded to a square plate or luminous checkerboard in the same region as the AOS neurons, we first compared the responses of the cells to a flat stimulus with those to an elongated stimulus. Most of the cells that preferred the flat to the elongated stimulus (presented on a stereoscopic display screen) were selective for the orientation of the flat surface and defined as surface-orientation-selective (SOS) neurons. The orientation

tuning of a SOS neuron to a square plate tilted 45 degrees to the left was recorded (Fig. 5A). No response was obtained when a stimulus was presented to either the left (Fig. 5B) or the right eye. Almost all SOS neurons responded more strongly to a binocular than to a monocular stimulus. The intensities of their responses increased with the width of the stimulus. Most of the SOS neurons showed no change in response intensity with a change in stimulus shape (for example, disc *vs* square plate) or even thickness, suggesting that coding of surface orientation in space is independent of shape. However, some of them preferred a thin to a thick plate, and a square plate to a disc, showing selectivity to both the shape and stimulus orientation.

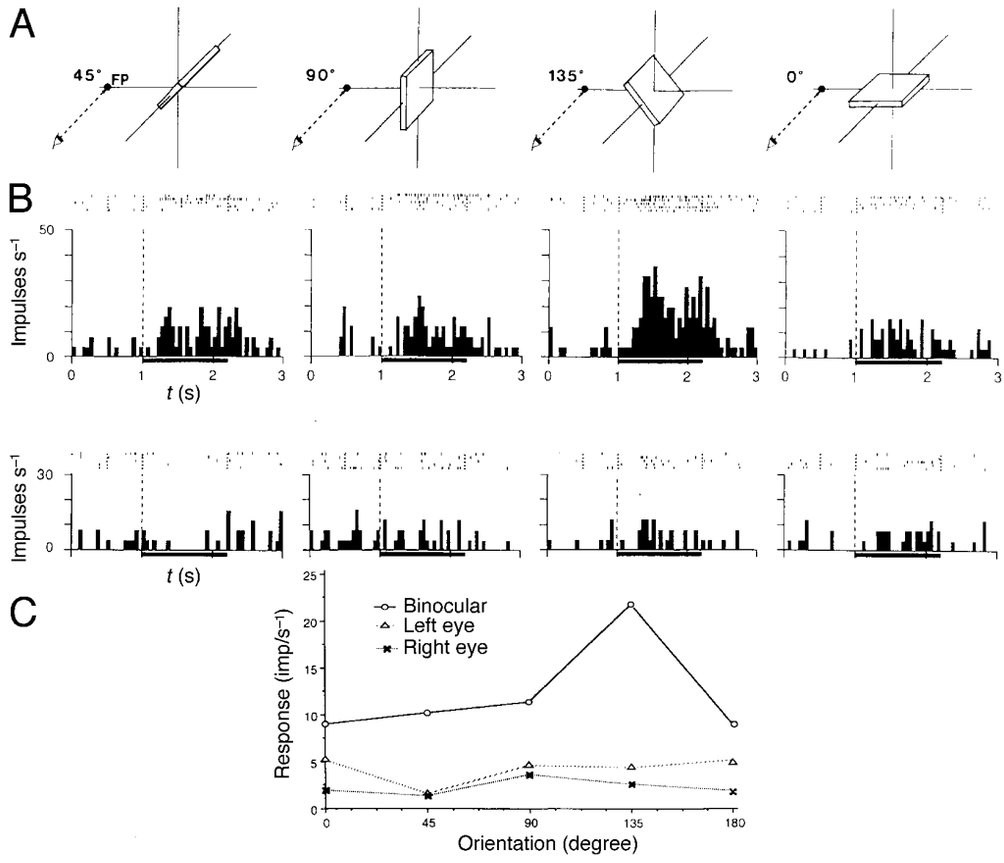

Fig. 5. ***Orientation tuning of a surface-orientation selective (SOS) neuron.*** **(A)** *Responses to a square plate shown in the stereoscopic display in various orientations around the sagittal axis in 45° steps, under binocular viewing conditions.* **(B)** *Responses to the same set of stimuli under monocular viewing conditions (left eye).* **(C)** *Orientation response curves for binocular and monocular viewing conditions*[64].

These findings regarding AOS neurons and SOS neurons in the cIPS suggest that this area, adjacent to area V3A, is a higher center of stereopsis for coding of the 3-D orientation and possibly the 3-D shape of objects. Although Cowey and Porter[65] found that lesion of the inferior temporal cortex caused impairment of global stereopsis, as tested by use of a random-dot and random-line stereogram, the impairment was observed only in random-line stereograms. More recently, the performance of a visual agnosia patient with relatively intact parieto-frontal cortical function was studied in a task of matching of the orientation of a plate in hand to that of the plate presented in front[66]. The patient performed very poorly in this task under monocular viewing conditions, suggesting that the parietal cortex depends on crucial binocular input for discrimination of surface orientation when the information from the ventral visual pathway is unavailable.

Subsystems of the dorsal visual pathway

So far, we have described functional properties of several classes of visual neurons in the IPL. These neurons are located mainly in two separate regions of the IPL: (1) in and around the area V5A, where we recorded DMS neurons, depth RS neurons and depth selective VT neurons, and (2) the lateral bank of the IPS, where we recorded visual-dominant manipulation-related neurons, AOS and SOS neurons and many depth-selective VF neurons. Those in the former region represent motion in depth, and those in the latter represent 3-D shape and orientation, as well as 3-D position.

Therefore, the function of the parietal cortex in the dorsal cortical visual pathway is not limited to the perception of position and movement, but also includes the perception of 3-D features of objects mediated by stereopsis. Binocular disparity signalling for stereopsis is mediated mainly by the magnocellular system of the dorsal visual pathway through thick stripes of the V2 and V3–V3A complex, in which many disparity-sensitive neurons have been recorded[67–70]. However, the possibility of contribution of projections from the TE and TEO areas of the ventral visual pathway to the lateral bank of the IPS (Ref. 71) can not be excluded.

The dorsal cortical visual pathway projecting to the parietal cortex may be subdivided into two subsystems (Fig. 6A). One subsystem contains a relay at area V5 (MT) and terminates in the V5A (MST) and VIP areas, subserving motion vision in extrapersonal and peripersonal space. The other subsystem contains a relay at the V3–V3A complex and terminates in the areas around the parieto-occipital and intraparietal sulci (V6, cIPS, LIP and AIP areas), subserving the perception of spatial position and the 3-D features of objects. The V6, LIP and 7a areas are concerned with the representation of position in egocentric space[74,75], whereas the cIPS is important for the higher-order processing of stereopsis for the perception of 3-D orientation and shape. The AIP area is pivotal for visual control of hand action and receives visual input from the cIPS concerning 3-D features of objects. It also has reciprocal connections with area F5 of the premotor cortex which sends command signals to the motor cortex (F1; Fig. 6B).

Concluding remarks

Depth is the third dimension beyond the 2-D image on the retina. We need binocular vision to perceive real depth, although monocular cues such as texture gradient, motion parallax, shading and linear perspective may be used for the perception of 3-D shape and relative distance. In this review we presented some

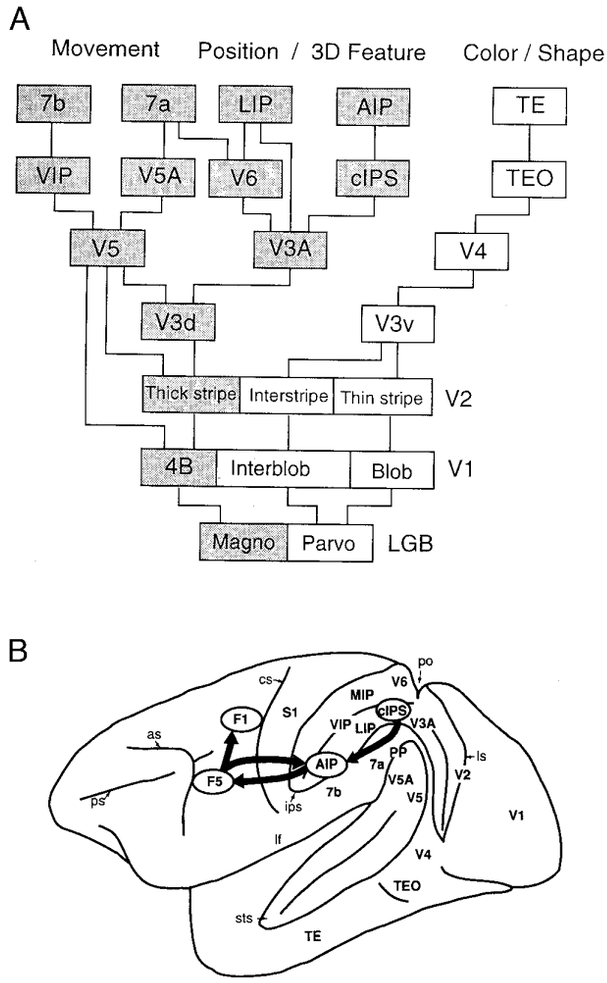

Fig. 6. ***Schematic diagram of the hierarchical connections of visual cortical areas.*** **(A)** *Hierarchy of visual areas*[72,73]. **(B)** *Lateral view of the monkey cerebral cortex showing the inside of the IPS, STS and lunate sulcus. The locations of visual areas along the dorsal visual pathways are shown in the diagram. The visuomotor stream for hand action is indicated by thick arrows. as, arcuate sulcus; cIPS, caudal intraparietal sulcus area; cs, central sulcus; F1, primary motor area; F5, hand region of ventral premotor area; ips, intraparietal sulcus; lf, lateral fissure; LIP, lateral intraparietal area; ls, lunate sulcus; MIP, medial intraparietal area; po, parieto-occipital sulcus; PP, posterior parietal area; ps, principal sulcus; sts, superior temporal sulcus; VIP, ventral intraparietal area; V1–6, primary, secondary, third, fourth, fifth and sixth visual areas.*

neurophysiological evidence that the parietal association cortex plays important roles in depth perception, by processing binocular signals such as ones related to disparity and its change, and extraretinal signals of convergence and accommodation. In primates, including humans, neural representation of 3-D objects with real physical dimensions and their egocentric positions and movements seems to occur in the parietal association cortex. The major purpose of this 3-D representation is the visual guidance of goal-directed hand action, in which the parietal cortex plays an essential role.

Acknowledgements

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Hematolymphopoietic and inflammatory cytokines in neural development

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It is now clear that cytokines traditionally viewed as immune modulators participate in inflammatory responses within the adult nervous system. However, in the developing nervous system hematolymphopoietic cytokines also play a role unrelated to neural–immune interactions. Instead, many of these factors subserve primary regulatory functions related both to the morphogenesis and to the cellular maturation of the central and peripheral nervous systems. This article focuses specifically on cytokine actions in neural development.

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THERE ARE NUMEROUS parallels between the hematolymphopoietic and the nervous systems in terms of mechanisms regulating their development[1,2]. In both systems, multipotent stem cells proliferate and undergo progressive lineage restriction under the influence of signals in the cellular microenvironment[3,4]. In view of these similarities, it is perhaps not surprising that many of the same cytokines regulate the development of both systems[1,4]. In addition to controlling the cellular processes of activation, proliferation, differentiation and survival, cytokines modulate anteroposterior regionalization and the development of dorsoventral domains in the nervous system[3–7]. In this review we will examine the functions of hematolymphopoietic ('hemopoietic') cytokines and specific transforming growth factor-β (TGF-β) superfamily factors in the regulation of neural development (Table 1). Additional receptor tyrosine kinase-mediated signaling molecules [neurotrophins, neuregulins, Eph family factors, orphan tyrosine kinase receptors and putative ligands, including Tie/Tck, Tyro 3 and Axl-mediated ligands and basic fibroblast growth factor (bFGF), platelet-derived growth factor (PDGF) and insulin-like growth factors (IGFs)] with important roles in neural development[8–14] will be covered in other forums.

CNS lineage commitment, proliferation and survival

Neural tube-derived stem cells (NTSCs) are derived from the developing neural tube along its entire anteroposterior axis and undergo initial symmetric cell divisions to increase the number of self-renewing progeny within periventricular generative zones from the spinal cord to the cerebral cortex (Fig. 1)[3,15]. Early CNS mitogens (epidermal growth factor, bFGF) and related factors program the proliferation, survival and early fate restrictions of these multipotent progenitors (MPs)[3,15]. The neuropoietic cytokines (CNTF, LIF, OM) potentiate astroglial lineage commitment from early neural progenitor cells; in cultures of early embryonic spinal cord neural progenitors, LIFβR-blocking antibodies effectively attenuate this cellular action[16]. CNTF and LIF also promote the elaboration of radial glia, a cellular species that acts as a scaffold for migrating neuroblasts in embryonic development, from murine and rodent embryonic subventricular zone (SVZ) multipotent progenitors, *in vitro*[17]. Oligodendroglial progenitors (OPs) develop from multipotent progenitors under the influence of non-hemopoietin 'oligotrophins' (such as PDGF, NT-3 and IGF-1) in late embryonic and early postnatal development in a caudal–rostral gradient[18]. CNTF and IL4 mediate the survival of early rodent OPs *in vitro*, while long-term survival requires the application of growth factors from two additional non-hemopoietin subclasses (NT-3 and IGF-1) in addition to the neuropoietic cytokines[19]. The requirement for combinatorial cytokine interactions to potentiate a CNS developmental process is a recurring theme in neural progenitor cell biology. The proliferation of early rat OPs *in vitro* is promoted by IL2 and IL4, and negatively regulated by TGF-β superfamily factors[18,20–23]. Finally, for the neuronal lineage, IL5,7,9 and 11 have been shown to enhance the elaboration of neuroblasts from a conditionally immortalized cell line derived from embryonic murine hippocampal multipotent progenitor cells; this developmental effect was associated with neurofilament expression, decreased cellular electrotonic coupling and the development of physiologically immature sodium channels and action potentials, the hallmark of the early neuronal lineage[24]. Thus hematopoietic cytokines may participate in the differentiation of all three major cell types in the developing brain.

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