



## The cortical visual area V6 in macaque and human brains

Patrizia Fattori<sup>a,\*</sup>, Sabrina Pitzalis<sup>b,c</sup>, Claudio Galletti<sup>a</sup>

<sup>a</sup>Department of Human and General Physiology, University of Bologna, Piazza di Porta San Donato 2, 40126 Bologna, Italy

<sup>b</sup>Department of Education in Sport and Human Movement, University for Human Movement "IUSM", Rome, Italy

<sup>c</sup>NeuroImaging Laboratory, Santa Lucia Foundation, Istituto di Ricovero e Cura a Carattere Scientifico, Rome, Italy

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### ABSTRACT

Single cell recording and neuro-anatomical techniques in the monkey have allowed to find a mosaic of visual areas in the temporo-parieto-occipital cortex. Thanks to neuroimaging methods, several of these areas have been mapped also in the human brain and named in humans based on homologies in their visuotopic organization with non-human primate areas.

We have recently found a new, retinotopically-organized cortical visual area, that we have called V6. Area V6 was first described in the macaque monkey and then, recently, in the human. In both primates, it is located in the medial parieto-occipital region of the brain. Like the other extrastriate areas, V6 contains a retinotopic map of the entire contralateral hemifield, but unlike other extrastriate areas, V6 lacks an emphasis of the central visual field. In macaque, area V6 receives visual information directly from V1 and from other extrastriate areas of the occipital lobe, and sends visual information to several parietal areas, all belonging to the so called dorsal visual stream. The neurons of macaque V6 are very sensitive to the direction of motion of visual stimuli and act as real-motion detectors. It has been reported that patients with cortical damages which include the cortical region where human V6 is located are unable to recognize the direction of motion of visual stimuli, or to detect the visual motion *per se*. According to these data, we suggest that V6 is involved in the 'recognition' of movement in the visual field.

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### 1. Introduction

The neocortex is subdivided in cortical areas, each participating in a distinct set of functions as a result of different pattern of inputs, outputs, and intrinsic circuitry (see Finger, 1994; Gross, 1997 for review). It is nowadays accepted that in primates, the so called "visual cortex", which occupies a large part of the neocortex, is not a unitary region, but is composed by a mosaic of different areas (Felleman and Van Essen, 1991; Lewis and Van Essen, 2000). First evidence of this parcellation of the visual cortex came from seminal studies of the macaque brain where 30 or more anatomically and/or functionally distinct visual areas have been described (for a review see Van Essen, 2004). In the last decade, neuroimaging methods using functional magnetic resonance (fMRI) allowed to chart several visual areas in humans, and homologies between humans and macaque monkeys have been intensively searched for. The kinds of evidence used to infer homology include similarities in functional properties, retinotopic organization, patterns of intra-cortical connections, architectonics, and neighbour relationships (Lewis and Van Essen, 2000). Based on

these criteria a number of cortical areas are now widely accepted as homologous across species (see Sereno and Tootell, 2005 for a recent review). The striate visual cortex, or area V1, has been identified in the occipital pole of the macaque cortex and also in that of the human cortex. Similarly, homologies have been found for other visual areas, called "extrastriate visual areas": V2, V3, VP, V3A, V4v, and MT/V5 (Watson et al., 1993; Sereno et al., 1995; Tootell et al., 1995, 1997; De Yoe et al., 1996; McKeefry and Zeki, 1997; Tootell and Hadjikhani, 2001). Beyond these areas, differences between human and monkey functional organization are increasingly evident and most of higher-tier areas lack of a general agreement about name, positions and retinotopic/functional organization (Orban et al., 2004).

Making comparisons across species raises several challenges as primate groups have evolved independently from each other for at least 30 million years. The difference is not simply a matter of size, but instead likely involves divergences in the number of visual areas and in how they are functionally specialized. In light of all these considerations we are aware that any assertion of homology between two candidate cortical areas is ultimately inferential. Nevertheless, a comparative approach remains important to provide a basis for extending the results of invasive animal experiments to human (Kaas, 1995; Krubitzer, 1995; Northcutt and Kaas, 1995; Sereno, 1998; Sereno and Tootell, 2005).

\* Corresponding author. Tel.: +39 051 2091749; fax: +39 051 2091737.  
E-mail address: [patrizia.fattori@unibo.it](mailto:patrizia.fattori@unibo.it) (P. Fattori).

## 2. Area V6 in the macaque brain

Several years ago we started to record single cell activity from an unknown region of the parieto-occipital sulcus (POs) where anatomical (Zeki, 1986) and functional studies on anaesthetized monkeys (Colby et al., 1988) had described visual activity.

As shown in Fig. 1, we reached the anterior bank of POs passing through the occipital pole. As the electrode entered in the anterior bank of POs, the size of visual receptive fields suddenly increased in an unexpected way, pointing out to the presence of a new visual area that we decided to call V6. This name was used to continue the classical nomenclature of extrastriate visual areas from V2 to V5, as this new visual area in the parieto-occipital sulcus was the sixth visual area that had been discovered (Zeki, 1986).

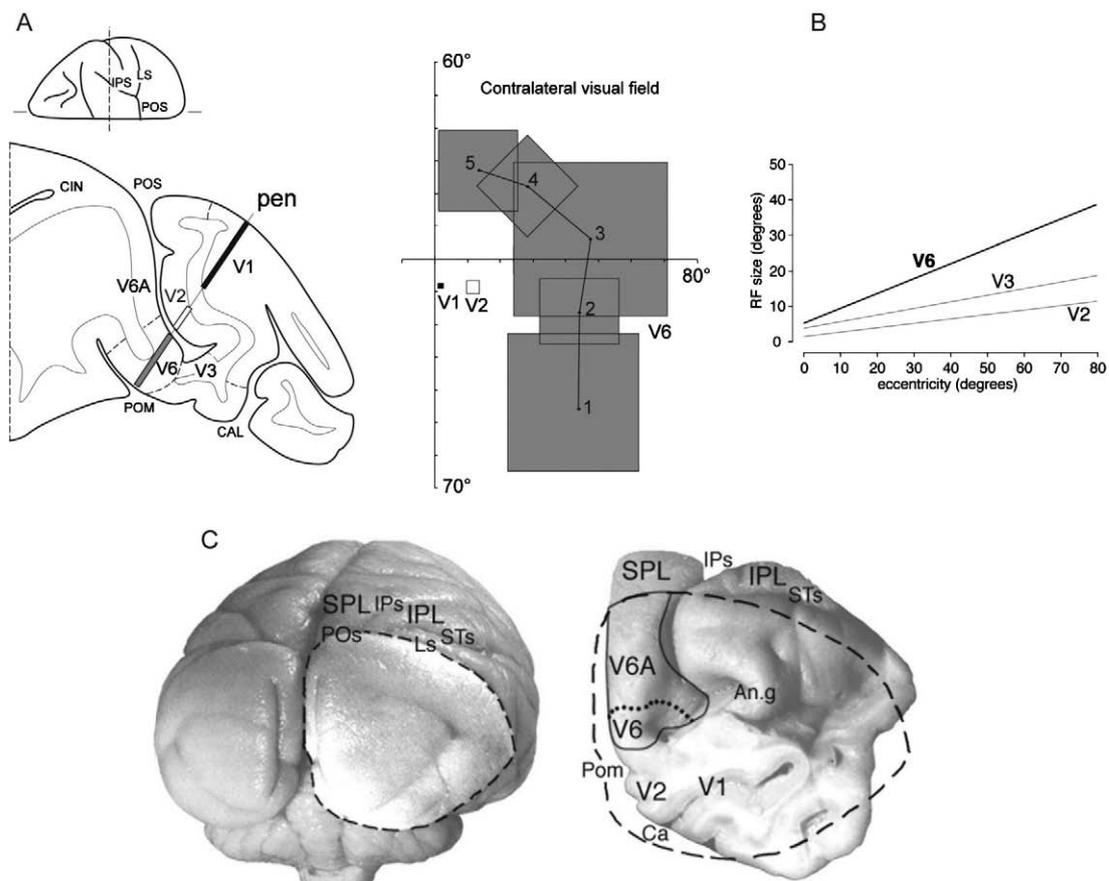
All cells encountered in area V6 were responsive to visual stimulation and the sequence of receptive fields ‘moved’ coherently along the penetration, with a physiological scatter between one cell and another. In the example of Fig. 1 we started recording V6 receptive fields in the inferior contralateral quadrant near the vertical meridian (number 1 in Fig. 1). Then receptive fields “moved” towards the horizontal meridian (number 3 in Fig. 1) and they ended in the superior contralateral quadrant (number 5 in Fig. 1).

In area V6, receptive fields were much larger than in areas V1, V2 and V3, as shown in the example of Fig. 1A as well as in the plot in Fig. 1B. The plot shows that receptive-field size in area V6 increases with eccentricity, as in all other extrastriate areas, remaining on average larger than in V2 and V3 at any given eccentricity value (Galletti et al., 1999a).

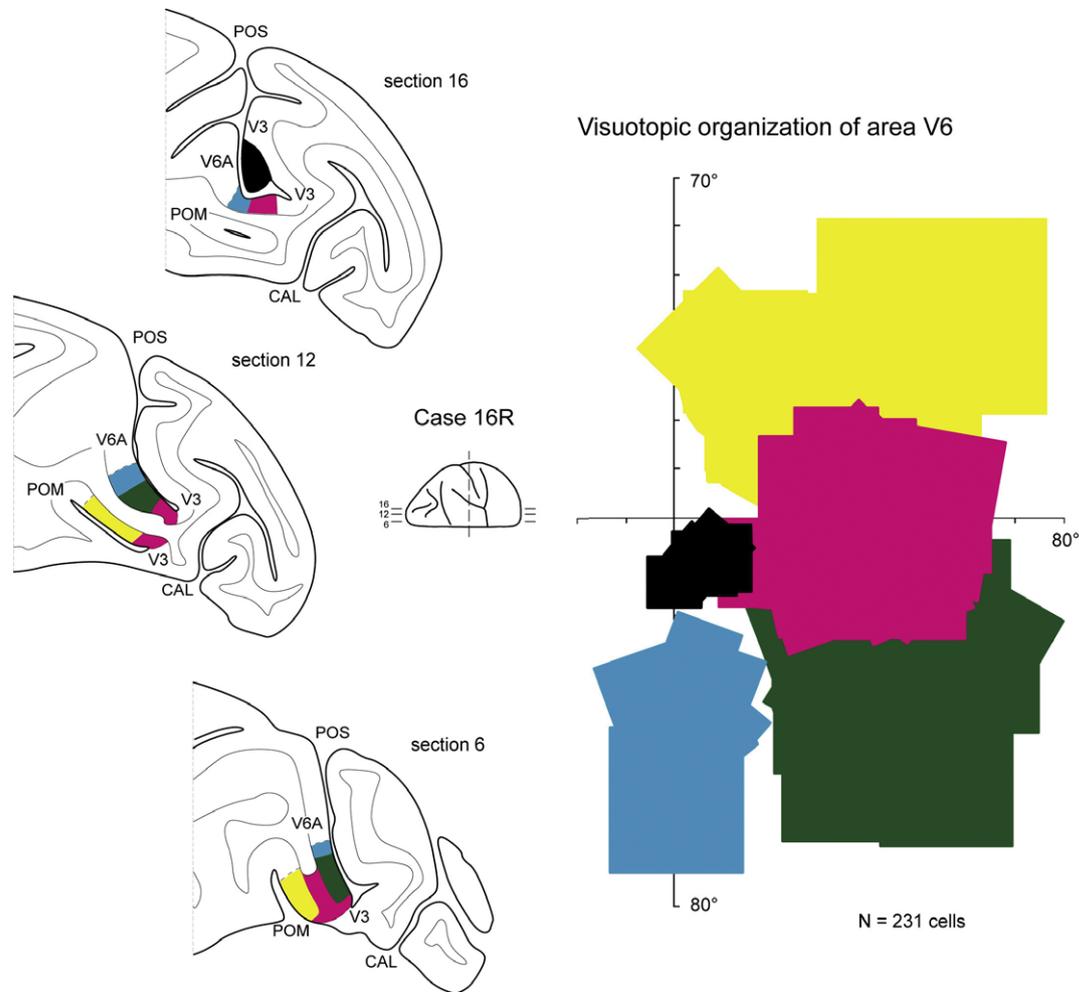
Area V6 occupies only the ventral part of the anterior bank of POs (see Fig. 1C), the dorsal part of the anterior bank of POs being occupied by the visuomotor area V6A (Galletti et al., 1999b) whose neurons show different functional properties with respect to those of V6 (Galletti et al., 2003). After the recognition of V6 as a new extrastriate area (Galletti et al., 1996), we characterized its visual topography (Galletti et al., 1999a) as well as its pattern of cortico-cortical connections (Galletti et al., 1999a, 2001, 2005).

### 2.1. Visual topography of macaque area V6

Area V6 contains a point-to-point representation of the retinal surface (Galletti et al., 1999a). To reach this conclusion, we carried out hundreds of microelectrode penetrations, on several animals, and analyzed the receptive-field sequences of V6 cells recorded along the same as well as nearby penetrations, reconstructed on



**Fig. 1.** Brain location of macaque area V6 and its relationship with neighbouring areas. (A) Parasagittal section of the posterior part of the brain taken at the level indicated above in the dorsal view of the right hemisphere. On the section, a typical penetration passing through the occipital pole (areas V1, black, and V2, white), and reaching in the depth area V6 (grey) is shown. The receptive-field sequence found along the penetration is shown to the right of the section. Thick lines join V6 receptive field centres. Numbers along these lines, indicate the centres of receptive fields of some V6 cells recorded along the penetration on the left. Modified from Galletti et al. (1999a). (B) Regression plots of receptive-field size (square root of area) against eccentricity for cells recorded in areas V2, V3, and V6. Receptive-field size increases with eccentricity in all visual areas. In area V6, receptive fields are larger than in V2 and V3 at any eccentricity. Modified from Galletti et al. (1999a). (C) Brain location of area V6. *Left*: posterior view of macaque brain. The right occipital pole is shown lightened. *Right*: posterior view of the right hemisphere after occipital pole dissection. The occipital pole has been cut away (dashed line) to show the anterior banks of POs medially and of lunate sulcus laterally. The anterior bank of POs has been bordered by a continuous line. A dotted line indicates the border between areas V6 and V6A, as detected functionally. An.g: angular gyrus; Ca, CAL: calcarine fissure; CIN: cingulate sulcus; IPL: inferior parietal lobule; IPs: intraparietal sulcus; Ls: lunate sulcus; POM, Pom: medial parieto-occipital sulcus; POS: parieto-occipital sulcus; SPL: superior parietal lobule; STs: superior temporal sulcus. Modified from Galletti et al. (1999b).



**Fig. 2.** Visual field representation in the macaque area V6. *Left:* three parasagittal sections of the brain taken at the levels shown on the brain silhouette reported at the centre of the figure. On the sections, different portions of area V6 are shown with different colors, according to the position of the receptive fields of neurons encountered there. The same colors are used in the right part of the figure to represent the part of visual field occupied by the receptive fields found in different parts of V6. It is evident the complete representation of contralateral hemifield and the emphasis in the representation of peripheral visual field. Other details and abbreviations as in Fig. 1. Modified from Galletti et al. (1999a).

the same and on nearby brain sections. This allowed us to identify sub-regions of cortex in V6 where all the receptive fields belong to the same region of visual field, as depicted in Fig. 2.

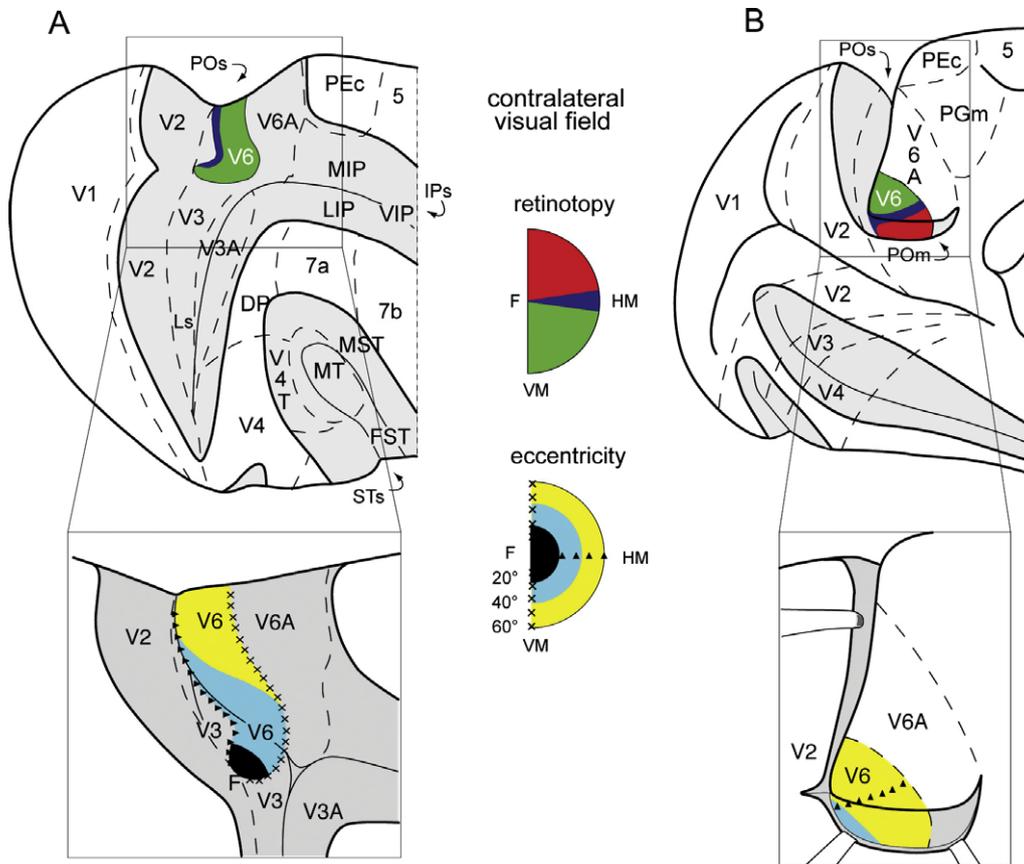
In the most lateral part of area V6 (Section 16 in Fig. 2) we found a representation of the centralmost part of contralateral visual field in the cortex of the posterior bank of POs (black in Fig. 2). In the fundus of POs, receptive fields were more eccentric and were located on, or near, the horizontal meridian (magenta<sup>1</sup> in Fig. 2), whereas in the anterior bank of POs, at the border with the visuomotor area V6A (Galletti et al., 1999b), receptive fields approached the vertical meridian (cyan in Fig. 2).

Moving medially along the POs (Section 12), the horizontal meridian representation remained located in the fundus and the vertical meridian in the anterior bank of POs, the cortex in between containing neurons with receptive fields located in the inferior contralateral quadrant (green in Fig. 2). In the medial parieto-occipital sulcus there was a horizontal meridian representation in the fundus. Adjacent to it, dorsally, there were neurons with receptive fields located in the superior contralateral quadrant (yellow in Fig. 2).

In the medialmost portion of area V6 (Section 6 in Fig. 2), the same magenta–cyan trend observed laterally was present in the anterior bank of POs, and the same magenta–yellow pattern was observed in the medial parieto-occipital sulcus.

(Fig. 3) summarizes the retinotopic organization of area V6. The upper part of the figure shows the trend of quadrant representation, the lower part the trend of eccentricity representation within area V6. V6 represents the lower visual field (green) in the POs and the upper one in the medial parieto-occipital sulcus (red). V6 has also a regular trend in the organization of receptive field eccentricity. The medial part of V6, on the mesial surface of the hemisphere, has more peripheral receptive fields (yellow) and then proceeding laterally more and more central visual field representation (from blue to black). The disproportion between black and yellow (that is between central 20° and periphery) highlights the small emphasis of central field representation with respect to the periphery, while the contrary is typical for striate as well as most of extrastriate visual areas. To summarize, the critical points in V6 visual topography are: (i) V6 represents the whole contralateral visual field; (ii) the lower visual field representation is located in POS and the upper one in the medial parieto-occipital sulcus; (iii) the vertical meridian representation is located at the border with area V6A and the horizontal one at the border with areas V2–V3; (iv) the central representation is located in the most lateral part of

<sup>1</sup> For interpretation of color in Figs. 2, 3, 4 and 6, the reader is referred to the web version of this article.



**Fig. 3.** Brain location and visual topography of area V6 in the macaque brain. (A) Dorsal view of caudal half of an hemisphere (and, below, enlargement of the parieto-occipital region) with the parieto-occipital, lunate and intraparietal sulci shown opened to reveal the cortex buried within them (dark grey area). (B) Medial view of the caudal half of an hemisphere (and, below, enlargement of the parieto-occipital region), with the medial parieto-occipital sulcus open. Area V6 is shown in color, according to the part of visual field it represents (conventions reported in the centre). Note that it represents point-to-point the entire contralateral visual field, with an emphasis in the representation of the peripheral visual field. Triangles and crosses indicate the representation of the horizontal (HM) and vertical (VM) meridians of area V6, respectively; the F, the centre of gaze. Dashed lines are the borders between different cortical areas. PEc, 5, MIP, LIP, VIP, 7a, 7b, MT, MST V4, V4T, FST, PGm: areas functionally or anatomically identified in the posterior part of the cerebral hemisphere. Other details as in Fig. 1. Modified from Pitzalis et al. (2006).

the posterior bank of POS and the far periphery on the mesial surface of the hemisphere; (v) area V6 borders with areas V2–V3, V3A, V6A.

The peculiarity of area V6 is its lack of a ‘magnification factor’, that is of an overrepresentation of the central part of the visual field which is typical of the other extrastriate areas (note in Fig. 3 the small amount of cortex devoted to the central 20° representation). To this regard, V6 is similar to the owl monkey area M (Allman and Kaas, 1976). A similar behaviour was also described for the macaque area PO (Colby et al., 1988), located as V6 in the anterior bank of POs. However, in contrast to both areas M and V6, PO was reported not to represent the central 20° of the visual field and to have an hemifield representation broken into several discontinuous parts (Gattass et al., 1986). Recent reports have suggested that PO refers to a cortical region which includes parts of areas V6 and V6A (Galletti et al., 2005), the former being point-to-point retinotopically organized and the latter lacking of a clear retinotopic organization.

### 3. Area V6 in the human brain

Retinotopic mapping combined with functional magnetic resonance imaging (fMRI) allows the visual cortex to be charted with a precision unmatched elsewhere in the human brain, and not far short of that achievable in animals using invasive techniques. As summarized in Section 1, using these brain mapping methods, a

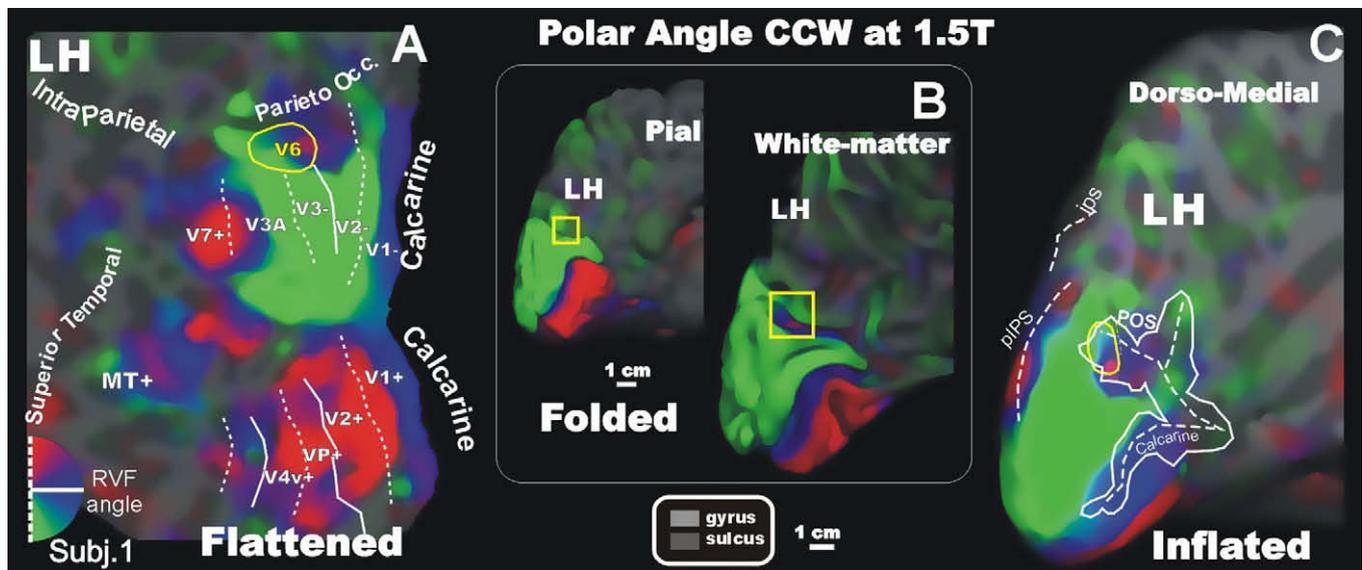
list of visual areas in the human brain have been identified. Until recently, one prominent omission in this list was the human homologue of macaque area V6.

#### 3.1. Visual topography of human area V6

Given the great emphasis for the periphery of this area in the macaque, previous fMRI studies failed to find area V6 as they typically stimulated the central 8–12° of the visual field. Consequently, these stimuli do not directly activate much of the periphery in many cortical visual areas and thus failed to activate area V6 (e.g., Sereno et al., 1995, 2001; Tootell et al., 1997, 1998). Thus, despite some attempts, the discovery of this area in the human brain was still lacking up to very recently.

We approached the delicate issue of finding the homologue of a monkey extrastriate visual area which emphasizes the periphery (and deemphasizes the centre of the visual field) implementing an innovative set-up able to stimulate the entire visual field up to 110° in total visual extent, simulating for the first time in the fMRI scanner the conditions used in the study of monkey area V6 (Pitzalis et al., 2006).

To strengthen our method we combined wide-field retinotopic stimulation with high field fMRI and phase-encoded retinotopic stimuli similar to those used so far (Sereno et al., 1995; Tootell et al., 1997) but slightly adjusted to respect the distinctive characteristics of macaque V6 (for details see Pitzalis et al., 2006).



**Fig. 4.** Brain location and retinotopy of polar angle representation of human area V6. Flattened (A), folded (B), and inflated (C) reconstructions of the left hemisphere of one participant are shown as appeared in Pitzalis et al. (2006). Folded cortex (inside the white box and with its own scale bar) is shown in two versions: pial and white matter. Red, blue, and green areas represent preference for upper, middle, and lower parts of the contralateral visual field, respectively (pseudocolour scale is sketched in bottom left part). Here and throughout this paper, yellow outlines indicate location (in folded) or borders (in flattened/inflated) of the human area V6. The flattened map shows also the boundaries of the early visual areas as defined by mapping visual field sign (dotted and solid white lines indicate vertical and horizontal meridians; [39,49], and the location of MT/MST complex (labelled 'MT+'). On the inflated, the borders (closed lines) and fundi (dashed lines) of calcarine, intraparietal (IPS) and parieto-occipital (POS) sulci are indicated. The calibration bar (1 cm) on the bottom refers to the cortical surface of the panels A and C.

Another refinement was the use of either standard flashing checkerboard rotating wedge or video wedge stimuli (Sereno et al., 2004). The use of video-retinotopy was implemented in the Sereno's lab (Sereno and Huang, 2006) and turned out to be a powerful method especially in terms of mapping new areas in the parietal and temporal cortices. Compared to checkerboards, the video attracts more attention, has spatiotemporal statistics closer to real world stimulation, and have been found to elicit stronger signal in both lower and higher visual areas in humans than standard checkerboards.

Thanks to the wide-field retinotopic stimulation combined with this innovative set-up, we mapped in a large sample of subjects the organization of human visual area V6. This newly identified retinotopic map is located in the dorsalmost part of the human parieto-occipital sulcus (POS) and represents the entire contralateral hemifield.

The results obtained from one exemplary subject are reported in Fig. 4. Here the periphery was stimulated the most completely (up to 110° total visual angle) and the signal obtained was strong and consistent in all visual areas. The greatly enlarged mapping stimuli used here revealed the presence of a previously unidentified upper-field representation unusually located in dorsal extrastriate cortex, where the other visual areas represent the peripheral lower visual field. As indicated by the yellow square over the folded surfaces in Fig. 4B, this upper-field representation is not visible on a reconstruction of the pial surface of the brain because it is completely buried within the POs on the medial wall of the hemisphere. It is visible on the white-matter reconstruction of the brain and, even better, in flattened and inflated formats (Fig. 4A and C, respectively).

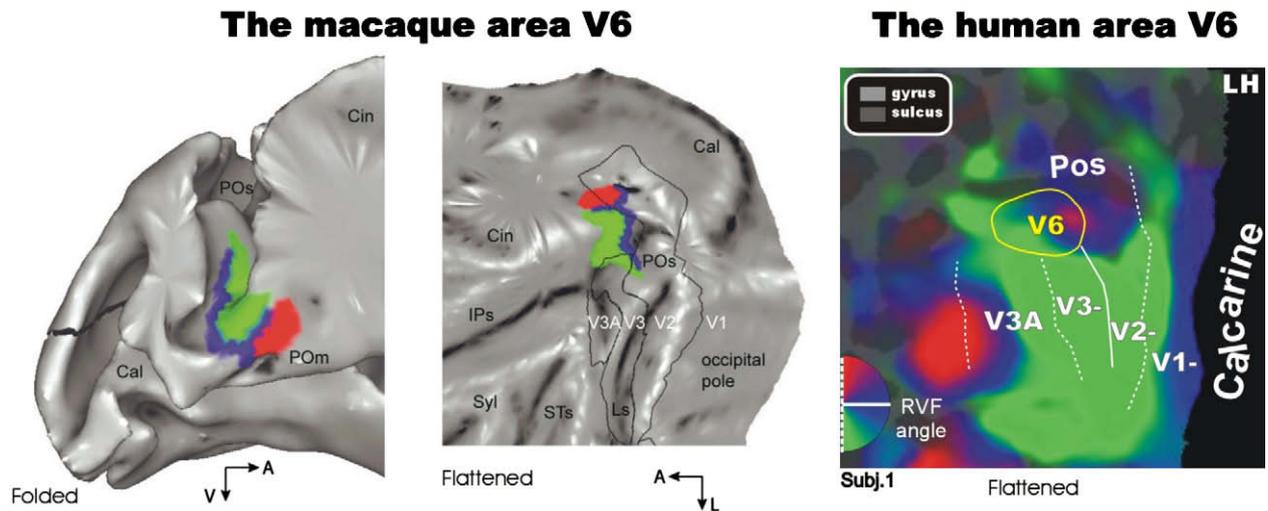
The detailed analysis (frame-to-frame) of the phase direction movements in the polar angle data shown in Pitzalis et al. (2006) demonstrates the presence of a retinotopic map of the contralateral visual hemifield with a characteristic medially-located upper-field representation distinct from the ones in dorsal areas V3A and V7 (this latter is an unlabeled region anterior to V3A and originally described as representing just the contralateral upper visual field; see Fig. 4A) which are located more laterally

(Tootell et al., 1997, 1998). This previously unidentified upper-field representation is located just anterior to peripheral V2/V3 lower representations. The V6 lower field is superior to its upper field on the unfolded cortex, anteromedial to peripheral V3/V3A.

We verified the reliability of the retinotopic organization of human V6 by (i) reversing the direction of rotation of the polar angle stimulus, (ii) combining counterclockwise with clockwise data (in different times and different scanners) to correct residual phase delay differences, and (iii) performing a group analysis of phase-encoded polar angle data (Pitzalis et al., 2006). The map consistently survived across the various experimental verifications supporting the view that the orientation of the polar angle map inside area V6 is systematic also when finely tested with respect to the position of horizontal and vertical meridians.

The organization and neighbour relations of this human area closely resemble those reported for macaque V6 (Galletti et al., 1999a). As (Fig. 4) points out, (see for comparison the top part of Fig. 3) both macaque and human areas share a quite similar retinotopic organization, with the upper field (red) located medially, just above area V3 and in front of dorsal area V2 in the flattened map, and the lower field (green) located medially, above areas V3/V3A in the flattened map, with the horizontal meridian (blue) located in between.

The similar relative position between area V6 and its neighbouring visual areas in human and macaques is highlighted in Fig. 5. In the left part of the figure, the monkey area V6 has been reported on a 3D reconstruction of the brain. The lower visual field (green) is located dorsally and the upper one ventrally in the ventral part of POs. On the flattened map (second inset), the full extent of V6 (Galletti et al., 2005) and of neighbouring areas (Lewis and Van Essen, 2000) are reported. The right inset of Fig. 5 shows the flattened reconstruction of a portion of the human brain containing area V6 as well as neighbouring visual areas (Pitzalis et al., 2006). Note that the retinotopic organization and the relative position of V6 with respect to neighbouring visual areas is the same in monkey and human. About relationships with neighbouring visual areas, for instance, note that the upper visual field adjoins the lower field representation of V2 in both primates, and the lower field



**Fig. 5.** Retinotopy of polar angle representation in macaque and human area V6. *Left:* medial view of the caudal half of a left hemisphere of macaque monkey and, to the right, flattened map of the same brain region. Location and extent of area V6 are reported in both reconstructions according to the color code of visual field representation sketched in bottom left part of the right inset. Location and extent of the visual areas V1, V2, V3, and V3A according to Van Essen (2002) are reported on the flattened map. *Right:* close-up of left flattened hemisphere of one participant representing polar angle map in the superior row of cortical areas. The panel shows the representations of the contralateral lower quarter field in superior V1, then superior V2, then V3, then V3A. Over (anterior to) V3 is the distinctive dorsally-located upper-field representation of V6 (red area inside the yellow outline). The newly identified dorsal area has a clear map of the contralateral hemifield. Details about borders of visual areas and color code of visual field representation are as in Fig. 4. Modified from Pitzalis et al. (2006).

representation is adjacent to peripheral visual fields of V3 and V3A in monkey as well as in human.

Not only does the visual field representation in V6 of macaques and humans follow a common organization, but the same is true also for the eccentricity profile of area V6. This aspect is shown in Fig. 6 (left inset) representing a colorplot of the response to a wide-field ring stimulus expanding at a constant slow speed (about 1°/s), displayed on the right hemisphere of one participant. Eccentricity increases as one moves medially toward the mesial surface (red-to-blue-to-green trend). The human area V6 contains

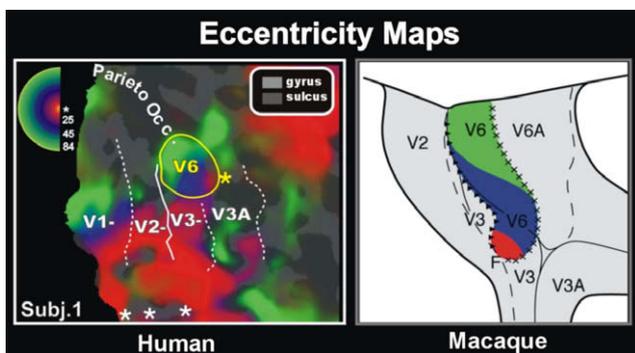
a central representation of the visual field laterally and a peripheral representation of the visual field medially. This is in line with the macaque data (see right part of Fig. 6), where the representation of the central 20° of the visual field (red) is located at the lateral end of POS, and the most peripheral representation (green) is at the medial end of POS. Eccentricity plots suggest that central and peripheral visual field representations have similar extents, as in macaque V6 but in contrast with all other known visual areas (Galletti et al., 1999a). The analysis of isoeccentricity contours shown in Pitzalis et al. (2006) reveals the presence of a foveal representation in the most lateral part of V6 (indicated with an asterisk in the figure) which stands apart from the foveal representations of areas V2 and V3, and also from the foveal representation of V3A, previously shown to be separated from foveal V2 and V3 (Tootell et al., 1997). Finally, visual field sign calculations (Sereni et al., 1995) show that V6 has a mirror-image representation, like V1 and V3 (Pitzalis et al., 2006).

Overall, because of the similarity to macaque area V6 in terms of position, internal organization and neighbouring relations with V2, V3 and V3A we labelled this area ‘human V6’.

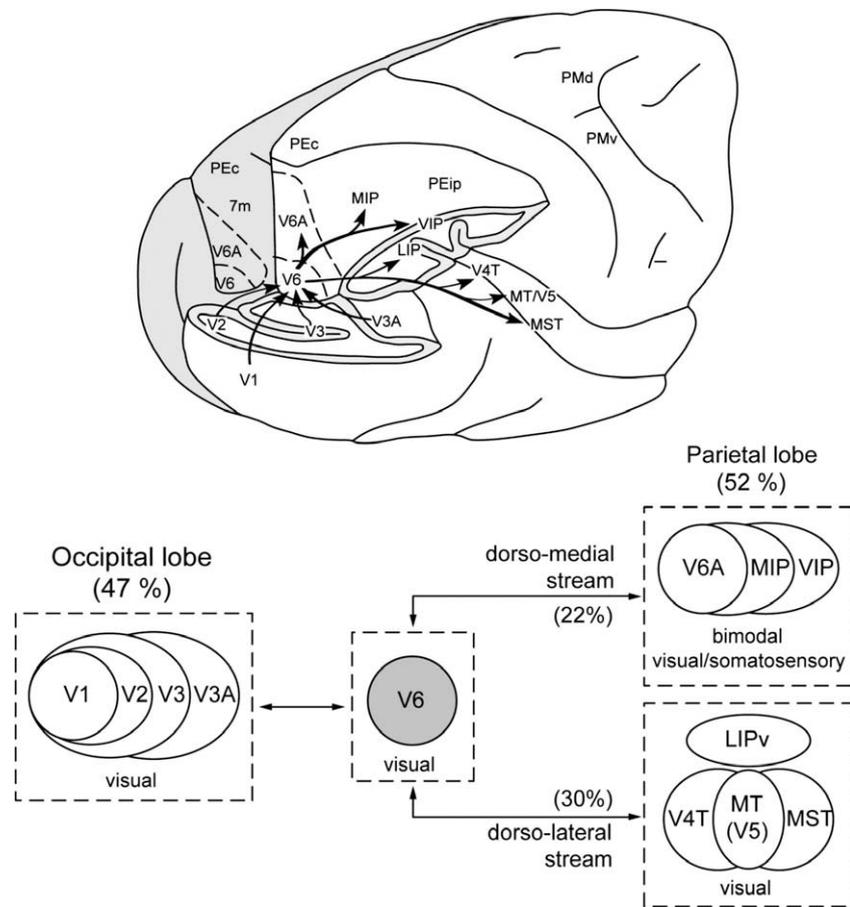
#### 4. Functional role of area V6

A way to study the functional role of a brain area is that of analyzing the pattern of its connections. We did this for macaque area V6 and found that its major connections are with visual areas of the occipital pole and with several areas within superior and inferior parietal lobules (Galletti et al., 2001). It has a direct connection with the primary visual cortex, as well as with the other extrastriate areas of the occipital lobe, as summarized in Fig. 7. In addition, macaque area V6 is connected with visual and bimodal visual and somatosensory areas, all belonging to the dorsal visual stream (see bottom part of Fig. 7).

The dorsal visual stream is a network of areas of the monkey and human brain that process sensory information for the purpose of organizing actions (Mishkin et al., 1983; Goodale and Milner, 1992). This network is mainly involved in capturing the sensory



**Fig. 6.** Eccentricity profile in human and macaque area V6. Here, the color codes the eccentricity of the local visual field representation (as sketched on the top left part of the left inset). *Left:* flattened map of the dorsal, caudal part of the human brain showing the retinotopy of eccentricity representation of area V6 by fMRI mapping. Phase-encoded eccentricity map is rendered on close-up of the right flattened hemisphere in one participant. The representation of central-through-more-peripheral eccentricities is coded using red–blue–green, respectively (as sketched in the leftmost pseudocolor inset). The pseudocolor inset indicates also the maximal periphery we were able to reach in that subject. The representation of the centre of gaze is indicated with an asterisk. Area V6 clearly has its own representation of the fovea, distinct from the foveal representation of the other dorsal visual areas. Modified from Pitzalis et al. (2006). Details about borders of visual areas are as in Fig. 4. *Right:* eccentricity profile of area V6 of the macaque with the same colors used for human V6: enlarged, dorsal view of the parieto-occipital region of the brain, with the sulci opened to show the cortex buried within them (see Fig. 3).



**Fig. 7.** Cortical connections of area V6 *Top*: summary of the cortical connections (arrows) of area V6. In the right hemisphere, the occipital pole and a part of the inferior parietal lobule have been dissected to show the cortex hidden in the anterior banks of parieto-occipital and intraparietal sulci. The left hemisphere, in grey, shows the areas located in the precuneate cortex of the mesial surface of the hemisphere. MIP, 7 m, PEip, VIP, MT/V5, PMd, PMv: cortical areas functionally or anatomically identified in the macaque brain. *Bottom*: connectivity diagram showing the weight of V6 cortical connections (Galletti et al., 2001).

properties of objects useful to guide our actions to interact with them. It is not involved in fine analysis of visual properties for identifying and classifying objects or for storing their images in long-term memory, a role which is typical of the ventral visual stream (Milner and Goodale, 1993; Milner et al., 2001; Steeves et al., 2004). Visual areas of the dorsal stream mainly elaborate “transient” visual information and do it fast because of their role in visuo-motor transformations. Indeed, on-line guidance of movements needs to elaborate these sensory properties quickly, in order to transform these properties in patterns of muscular contractions (Goodale et al., 1991; Gréa et al., 2002).

In light of all these considerations it seems reasonable to ask: what is the role of an area like V6, that receives input from basic visual areas and is connected only to a neural pathway (the dorsal visual stream) devoted to action execution and control? In this respect, hints come from the analysis of the visual properties of V6 neurons.

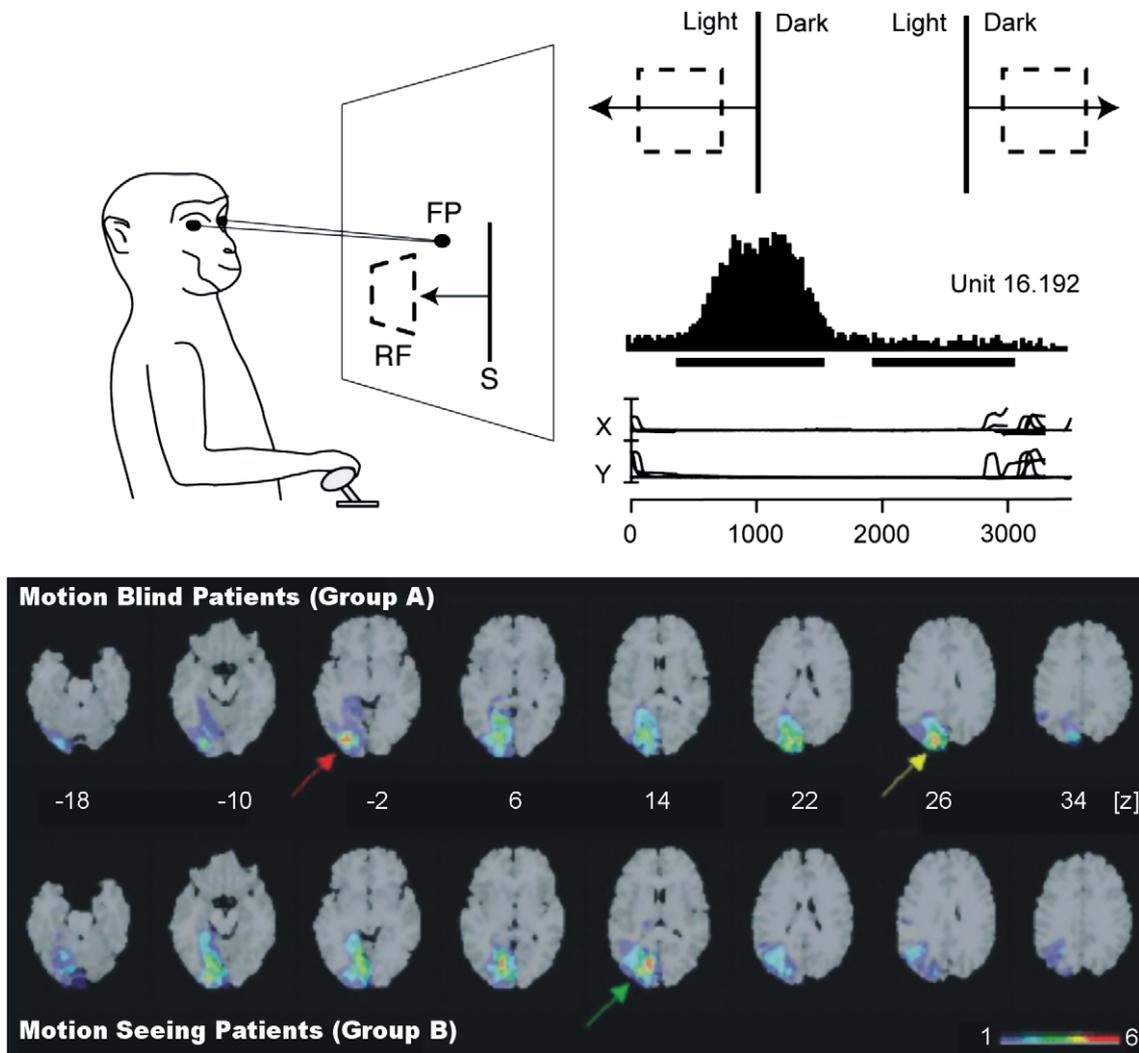
In macaque V6, the best visual stimulus was an oriented light/dark border moving across the neuronal receptive field. A typical experimental situation is sketched in the top left part of Fig. 8. Here, the border (S) is moved horizontally across the receptive field (RF) of a V6 cell, while the monkey is keeping its eyes fixed on a point (FP) in the centre of the screen. The neural response to this visual stimulation is shown in the right part of Fig. 8. This V6 cell strongly discharged for the stimulus moving in a certain direction (from right to left), but did not discharge at all for stimulus movement in the opposite direction (from left to right) This is typical of

V6 neurons: they are very sensitive to the movement of visual stimuli and are direction selective.

This functional property could be fed to V6 by its direct projections from area V1 (see Fig. 7), and more precisely from layer IVB of the primary visual cortex (Galletti et al., 2001). Layer IVB of V1 is rich of neurons receiving directly from the magnocellular layers of the lateral geniculate nucleus, which elaborate visual information of high temporal and low spatial frequency and therefore are particularly suitable to detect visual objects moving in the visual field.

About the *human* V6, preliminary data show that it is selectively activated by coherent motion of random dot fields (Pitzalis et al., 2005), similarly to macaque V6 (Galletti unpublished data), and to owl monkey area M (Baker et al., 1981). Moreover, some previous functional imaging studies reported a general activation around the medial parieto-occipital cortex for visual motion perception, (e.g., Cheng et al., 1995; Brandt et al., 1998; Previc et al., 2000; Kleinschmidt et al., 2002) a finding which is in line with the view that human V6 is involved in the analysis of motion in the visual field.

Human clinical studies also reported that lesions or electrical stimulation of the cortex of human POs produce motion-related visual disturbance (e.g., Heide et al., 1990; Richer et al., 1991). In particular, Blanke and co-workers reported that cortical lesions in the dorsal part of human POs, approximately around the location of human area V6 (Pitzalis et al., 2006), cause motion recognition deficits (Blanke et al., 2003). The bottom part of Fig. 8 reports the data



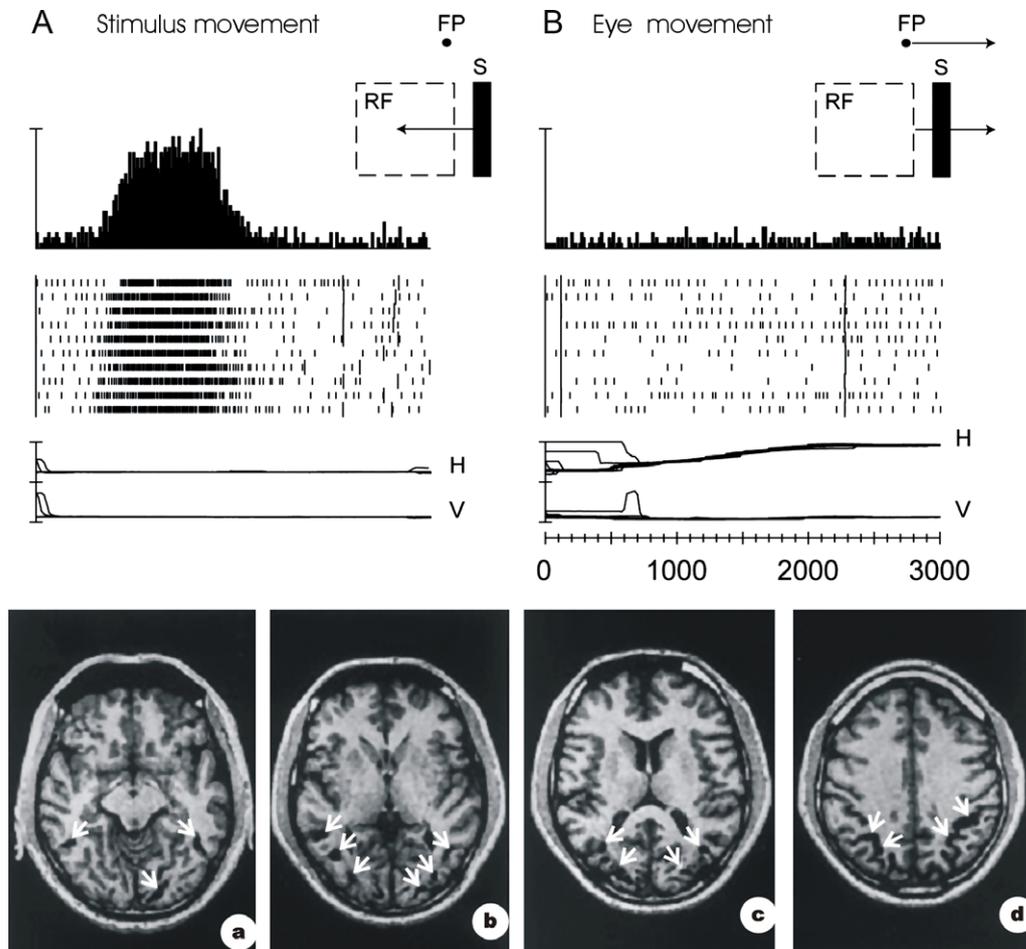
**Fig. 8.** Direction selectivity in macaque and human brain. *Top:* direction-selective cell in monkey area V6. *Left:* experimental set-up used to visually stimulate V6 cells. FP: fixation point; RF: visual receptive field; S: visual stimulus; arrow: direction of motion. *Right:* neural response of a direction-selective V6 cell. From top to bottom: schematic representation of the receptive field (dashed line) and of the stimulus (light/dark border) moved across the receptive field in the direction indicated by the arrow, peri-event time histogram of the neural responses, bars indicating the durations of visual stimulations, recordings of horizontal (X) and vertical (Y) components of eye positions. *Bottom:* loss of the ability to detect motion direction in human patients lesioned in the parieto-occipital sulcus. Figure shows the lesion analysis (overlap plots) of patients with (group A, top) and without (group B, bottom) direction-selective motion blindness as reported in Blanke et al. (2003). The number of overlapping lesions is indicated by color, from blue ( $n = 1$ ) to red ( $n = 6$ ). The centre of overlap is indicated in red for both group patients. The Talairach coordinates of the transverse sections are given in the middle of the figure (z-coordinates). In motion-blind patients two centres of overlap were found, one at the temporo-occipital junction (red arrow) and the other in the posterior parietal cortex (yellow arrow). Both overlap areas were anatomically distinct from the centre of overlap in patients from group B localized on the cuneus and lingual gyrus (green arrow) and able to see motion. Lesions inducing motion blindness are centered on two cortical regions located in or near the brain location of area MT/V5 and in or near the brain location of V6. Modified from Blanke et al. (2003).

of this study on patients with parieto-occipital lesions (Blanke et al., 2003). The study reported that patients whose lesions were focused around the POs showed *motion blindness*, that is a selective disturbance of visual motion perception despite intact perception of other features of the visual scene. These patients were completely unable to discriminate the direction of motion of visual stimuli and the authors speculated that a loss of direction selective neurons could be the reason of that deficit (Blanke et al., 2003). Since monkey area V6 is rich in direction selective cells, it is likely that human V6 is rich too in this type of cells, and that motion recognition is a common role for monkey and human area V6.

In monkey area V6 we found a consistent number of cells that behave as “*real motion detectors*” (Galletti and Fattori, 2003). These cells strongly discharged if a visual stimulus moved in the visual field, but their activity was not modulated if the same retinal motion was produced by the movement of the eyes while the stimulus remained stationary. In other words, real-motion cells are not de-

ceived by signals of image motion on the retina; they detect whether or not a visual stimulus is really moving in the visual field (Galletti and Fattori, 2003). A typical example of such a behaviour is shown in the top part of Fig. 9. The same retinal movement, with the same velocity and same direction of motion, does evoke two completely different activations. In the first case (Fig. 9A), the cell discharges strongly, because the visual stimulus is actually moving in the external world. In the second (Fig. 9B), the cell does not change its baseline activity despite identical retinal stimulation because the stimulus is motionless in space.

A parallel neural behaviour can be hypothesized for human V6 after a single case study reporting of a patient showing *false perception of motion* after lesions in the region of POs (Haarmeier et al., 1997). The patient had a correct perception of visual motion while maintaining steady fixation, but showed impairments in detecting motion while moving the eyes. The patient interpreted any retinal image motion as object motion, even when it resulted from his



**Fig. 9.** Detection of real motion in macaque and human. *Top:* behaviour of a real-motion cell recorded in area V6. (A) Neural responses (peri-event time histogram and raster displays of action potential sequences) evoked by sweeping an optimal visual stimulus (S) across the receptive field (RF) while the animal looked at a stationary fixation point (FP). H and V indicate the horizontal and vertical components, respectively, of the eye movements. (B) Neural activity evoked by sweeping the receptive field across the stationary visual stimulus thanks to the pursuit eye movement evoked by the movement of the fixation spot. Modified from Galletti and Fattori (2003). *Bottom:* a case report showing loss of the ability to disambiguate real motion from self-evoked motion after lesions of the parieto-occipital cortex, as appeared in Haarmeier et al. (1997). Selected MRI axial slices (0.9-mm thick) show bilateral cyst-like local widenings (indicated by white arrows) of the sulci of the occipital lobe mainly affecting parts of areas 18,19 and possibly 37 on the lateral aspect of the hemispheres and areas 18 and 19 on the inferior aspect (a–c). In addition, cortex in and around the intraparietal sulcus of the parietal lobes is involved (d). Subcortical white matter and basal ganglia are intact. Lesions likely included the human homologues of monkey areas V3A, V6, and MT/MST. Modified from Haarmeier et al. (1997).

pursuit eye movements. As shown by the arrows in the bottom part of Fig. 9, MRI analysis revealed that the lesion involved the parieto-occipital cortex, affecting parts of dorsal areas (Goodale and Milner, 1992; Goodale et al., 1991) and the cortex in and around the intraparietal sulcus. The lesion involved a number of occipital areas where real-motion cells were found (Galletti and Fattori, 2003), including the dorsal part of POs where area V6 is located.

Combining parallel observations on the functional properties of V6 neurons with preliminary fMRI evidences of motion-related signal in human V6 and deficits arising after lesions of a brain region involving human area V6, we conclude that this extrastriate visual area has a role in recognizing object motion in natural conditions, where many retinal image movements elicited by self-motion may confound the visual system.

## 5. Conclusions

The studies reviewed here add area V6 to the list of the extrastriate visual areas in both monkey and human brains. V6 is a simple, retinotopically-organized visual area that represents point-to-point the entire contralateral visual field, like the other extrastriate areas known so far. It lacks the typical magnification

factor shown by the other extrastriate visual areas, and represents the visual field in a quite uniform way. With respect to the other extrastriate areas, V6 has an emphasis in the representation of the peripheral visual field and its role is likely that of detecting motion, especially in the periphery of the visual field. In the macaque, V6 cells are selective for the direction of motion of moving objects and are sensitive to the real motion of them in the visual field. In the human, area V6 seems to have a role in recognition of motion in the visual field.

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## References

- Allman, J.M., Kaas, J.H., 1976. Representation of the visual field on the medial wall of occipital-parietal cortex in the owl monkey. *Science* 191, 572–575.
- Baker, J.F., Petersen, S.E., Newsome, W.T., Allman, J.M., 1981. Visual response properties of neurons in four extrastriate visual areas of the owl monkey (*aotus*

- trvirgatus): a quantitative comparison of medial, dorsomedial, dorsolateral, and middle temporal areas. *J. Neurophysiol.* 45, 397–416.
- Blanke, O., Landis, T., Mermoud, C., Spinelli, L., Safran, A.B., 2003. Direction-selective motion blindness after unilateral posterior brain damage. *Eur. J. Neurosci.* 18, 709–722.
- Brandt, T., Bartenstein, P., Janek, A., Dieterich, M., 1998. Reciprocal inhibitory visual-vestibular interaction. Visual motion stimulation deactivates the parieto-insular vestibular cortex. *Brain* 121, 1749–1758.
- Cheng, K., Fujita, H., Kanno, I., Miura, S., Tanaka, K., 1995. Human cortical regions activated by wide-field visual motion: an (H<sub>2</sub>O)-O-15 PET study (Review). *J. Neurophysiol.* 74, 413.
- Colby, C.L., Gattass, R., Olson, C.R., Gross, C.G., 1988. Topographical organization of cortical afferents to extrastriate visual area PO in the macaque: a dual tracer study. *J. Comp. Neurol.* 269, 392–413.
- De Yoe, E.A., Carman, G., Bandettini, P., Glickman, S., Weiser, J., Cox, R., Miller, D., Neitz, J., 1996. Mapping striate and extrastriate visual areas in human cerebral cortex. *Proc. Natl. Acad. Sci. USA* 93, 2382–2386.
- Felleman, D.J., Van Essen, D.C., 1991. Distributed hierarchical processing in the primate cerebral cortex. *Cereb. Cortex* 1, 1–47.
- Finger, S., 1994. *Origins of Neuroscience*. Oxford University Press, New York.
- Galletti, C., Fattori, P., 2003. Neuronal mechanisms for detection of motion in the field of view. *Neuropsychologia* 41, 1717–1727.
- Galletti, C., Fattori, P., Battaglini, P.P., Shipp, S., Zeki, S., 1996. Functional demarcation of a border between areas V6 and V6A in the superior parietal gyrus of the macaque monkey. *Eur. J. Neurosci.* 8, 30–52.
- Galletti, C., Fattori, P., Gamberini, M., Kutz, D.F., 1999a. The cortical visual area V6: brain location and visual topography. *Eur. J. Neurosci.* 11, 3922–3936.
- Galletti, C., Fattori, P., Kutz, D.F., Gamberini, M., Breviglieri, R., Fattori, P., 2003. Role of the medial parieto-occipital cortex in the control of reaching and grasping movements. *Exp. Brain Res.* 153, 158–170.
- Galletti, C., Gamberini, M., Kutz, D.F., Baldinotti, I., Fattori, P., 2005. The relationship between V6 and PO in macaque extrastriate cortex. *Eur. J. Neurosci.* 21, 959–970.
- Gattass, R., Sousa, A.P.B., Covey, E., 1986. Cortical visual areas of the macaque: possible substrates for pattern recognition mechanisms. *Exp. Brain Res.* 11 (Suppl.), 1–20.
- Goodale, M.A., Milner, A.D., 1992. Separate visual pathways for perception and action (review). *Trends Neurosci.* 15, 20–25.
- Goodale, M.A., Milner, A.D., Jakobson, L.S., Carey, D.P., 1991. A neurological dissociation between perceiving objects and grasping them. *Nature* 349, 154–156.
- Gréa, H., Pisella, L., Rossetti, Y., Prablanc, C., Desmurget, M., Tiliakete, C., Grafton, S., Vighetto, A., 2002. A lesion of the posterior parietal cortex disrupts on-line adjustments during aiming movements. *Neuropsychologia* 40, 2471–2480.
- Gross, C.G., 1997. From Imhotep to Hubel and Wiesel: the story of visual cortex. In: Rockland, K.S., Kaas, J.H., Peters, A. (Eds.), *Extrastriate Cortex in Primates*, Cerebral Cortex, vol. 12. Plenum Press, New York, pp. 1–58.
- Haarmeier, T., Thier, P., Repnow, M.P.D., 1997. False perception of motion in a patient who cannot compensate for eye movements. *Nature* 389, 849–852.
- Heide, W., Koenig, E., Dichgans, J., 1990. Optokinetic nystagmus, self-motion sensation and their after effects in patients with occipito-parietal lesions. *Clin. Vision. Sci.* 5, 145–156.
- Kaas, J.H., 1995. Human visual cortex – progress and puzzles. *Curr. Biol.* 5, 1126.
- Kleinschmidt, A., Thilo, K.V., Buchel, C., Gresty, M.A., Bronstein, A.M., Frackowiak, R.S., 2002. Neural correlates of visual-motion perception as object- or self-motion. *Neuroimage* 16, 873–882.
- Krubitzer, L., 1995. The organization of neocortex in mammals: are species differences really so different? *Trends Neurosci.* 18, 408–417.
- Lewis, J.W., Van Essen, D.C., 2000. Mapping of architectonic subdivisions in the macaque monkey, with emphasis on parieto-occipital cortex. *J. Comp. Neurol.* 428, 79–111.
- McKeefry, D.J., Zeki, S., 1997. The position and topography of the human colour centre as revealed by functional magnetic resonance imaging. *Brain* 120, 2229–2242.
- Milner, A.D., Goodale, M.A., 1993. Visual pathways to perception and action. In: Hicks, T.P., Ono, S.M.T. (Eds.), *Progress in Brain Research*. Elsevier, Amsterdam.
- Milner, A.D., Dijkerman, H.C., Pisella, L., McIntosh, R.D., Tiliakete, C., Vighetto, A., Rossetti, Y., 2001. Grasping the past delay can improve visuomotor performance. *Curr. Biol.* 11, 1896–1901.
- Mishkin, M., Ungerleider, L.G., Macko, K.A., 1983. Object vision and spatial vision: two cortical pathways. *Trends Neurosci.* 6, 414–417.
- Northcutt, R.G., Kaas, J.H., 1995. The emergence and evolution of mammalian neocortex. *Trends Neurosci.* 18, 373–379.
- Orban, G.A., Van Essen, D., Vanduffel, W., 2004. Comparative mapping of higher visual areas in monkeys and humans. *Trends Cogn. Sci.* 8, 315–324.
- Pitzalis, S., Galletti, C., Patria, F., Committeri, G., Galati, G., Fattori, P., Sereno, M.I., 2005. Functional properties of human visual area V6. *Neuroimage* 120, S23.
- Pitzalis, S., Galletti, C., Huang, R.S., Patria, F., Committeri, G., Galati, G., Fattori, P., Sereno, M.I., 2006. Wide-field retinotopy defines human cortical visual area V6. *J. Neurosci.* 26, 7962–7973.
- Previc, F.H., Liotti, M., Blakemore, C., Beer, J., Fox, P., 2000. Functional imaging of brain areas involved in the processing of coherent and incoherent wide field-of-view visual motion. *Exp. Brain Res.* 131, 393–405.
- Richer, F., Martinez, M., Cohen, H., Sthilaire, J.M., 1991. Visual motion perception from stimulation of the human medial parieto-occipital cortex. *Exp. Brain Res.* 87, 649.
- Sereno, M.I., Huang, R.S., 2006. A human parietal face area contains aligned head-centered visual and tactile maps. *Nat. Neurosci.* 9, 1337–1343.
- Sereno, M.I., Tootell, R.B., 2005. From monkeys to humans: what do we now know about brain homologies? *Curr. Opin. Neurobiol.* 15, 135–144.
- Sereno, M.I., Dale, A.M., Reppas, J.B., Kwong, K.K., Belliveau, J.W., Brady, T.J., Rosen, B.R., Tootell, R.B.H., 1995. Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science* 268, 889–893.
- Sereno, M.I., Pitzalis, S., Martinez, A., 2001. Mapping of contralateral space in retinotopic coordinates by a parietal cortical area in humans. *Science* 294, 1350–1354.
- Sereno, M.I., Huang, R.S., Saygin, A., Filimon, F., Hagler, D., Retinotopy of human cortex using phase-encoded video. In: *The 34th Annual Meeting of Society for Neuroscience*, San Diego, CA, 2004.
- Sereno, M.I., 1998. Brain mapping in animals and humans. *Curr. Opin. Neurobiol.* 8, 188–194.
- Steeves, J.K., Humphrey, G.K., Culham, J.C., Menon, R.S., Milner, A.D., Goodale, M.A., 2004. Behavioral and neuroimaging evidence for a contribution of color and texture information to scene classification in a patient with visual form agnosia. *J. Cogn. Neurosci.* 16, 955–965.
- Tootell, R.B., Hadjikhani, N., 2001. Where is ‘dorsal V4’ in human visual cortex? Retinotopic, topographic and functional evidence. *Cereb. Cortex* 11, 298–311.
- Tootell, R.B.H., Reppas, J.B., Kwong, K.K., Malach, R., Born, R.T., Brady, T.J., Rosen, B.R., Belliveau, J.W., 1995. Functional analysis of human MT and related visual cortical areas using magnetic resonance imaging (review). *J. Neurosci.* 15, 3215.
- Tootell, R.B.H., Mendola, J.D., Hadjikhani, N.K., Ledden, P.J., Liu, A.K., Reppas, J.B., Sereno, M.I., Dale, A.M., 1997. Functional analysis of V3A and related areas in human visual cortex. *J. Neurosci.* 17, 7060–7078.
- Tootell, R.B., Hadjikhani, N., Hall, E.K., Marrett, S., Vanduffel, W., Vaughan, J.T., Dale, A.M., 1998. The retinotopy of visual spatial attention. *Neuron* 21, 1409–1422.
- Van Essen, D.C., 2002. Windows on the brain: the emerging role of atlases and databases in neuroscience. *Curr. Opin. Neurobiol.* 12, 574–579.
- Van Essen, D.C., 2004. Organization of visual areas in macaque and human cerebral cortex. *Visual Neurosci.*
- Watson, J.D.G., Myers, R., Frakowiak, R.S.J., Hajnal, J.V., Woods, R.P., Mazziotta, J.C., Shipp, S., Zeki, S., 1993. Area-V5 of the human brain – evidence from a combined study using positron emission tomography and magnetic resonance imaging. *Cereb. Cortex* 3, 79–94.
- Zeki, S., 1986. The anatomy and physiology of area V6 of macaque monkey visual cortex. *J. Physiol.* 381, 62P.