Two Cortical Systems for Reaching in Central and Peripheral Vision

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Summary

Parietal lesions in humans can produce a specific disruption of visually guided hand movement, termed optic ataxia. The fact that the deficit mainly occurs in peripheral vision suggests that reaching in foveal and extrafoveal vision rely on two different neural substrates. In the present study, we have directly tested this hypothesis by event-related fMRI in healthy subjects. Brain activity was measured when participants reached toward central or peripheral visual targets. Our results confirm the existence of two systems, differently modulated by the two conditions. Reaching in central vision involved a restricted network including the medial intraparietal sulcus (mIPS) and the caudal part of the dorsal premotor cortex (PMd). Reaching in peripheral vision activated in addition the parieto-occipital junction (POJ) and a more rostral part of PMd. These results show that reaching to the peripheral visual field engages a more extensive cortical network than reaching to the central visual field.

Introduction

Reaching for an object in visual space is an effortless process that nevertheless engages complex control systems in the posterior parietal cortex. Visually guided hand movements are naturally performed in two condi-

tions. Optimal accuracy is obtained when hand movements are combined with eye movements, and subjects grasp an object after foveal capture. However, hand movements can also be made, albeit with less accuracy, without eye movements such as when one reaches for a cup of coffee while continuing to read the newspaper. One explanation for the decreased accuracy when reaching to objects in the peripheral visual field could lie in the lower spatial resolution of peripheral vision. Another possibility is that the cerebral networks engaged in central and peripheral reaching are distinct. This is suggested by the fact that a category of localized lesions in the posterior parietal cortex, centered on the parieto-occipital junction (POJ), give rise to a specific deficit of visually guided behavior referred to as optic ataxia (Karnath and Perenin, 2005). Patients with optic ataxia exhibit gross directional errors when reaching for objects located in the peripheral visual field, whereas misreaching largely disappears if the patient performs a saccadic eye movement toward the object (Karnath and Perenin, 2005; Perenin and Vighetto, 1988).

Functional imaging studies have not yet addressed the issue of the cortical networks involved in central and peripheral reaching. We have therefore looked for the existence of distinct reaching networks with an event-related fMRI paradigm on healthy subjects. Participants were scanned while reaching to a visual target. Two conditions were examined: (1) reaching to the target while making an orientation saccade and (2) reaching to the target without an orientation saccade. In condition (1) reaching movement is performed in central vision, whereas in (2) it is performed in peripheral vision.

The presence of a saccade in condition (1), but not (2), raises a problem. It is generally thought that reaching accuracy is influenced by two variables: the presence or absence of eye movements and the peripheral versus central location of the visual target. However, the contribution that either variable alone makes to reaching accuracy remains unclear. For instance, although eye-position signals are known to influence the cortical reach-related network (Andersen and Buneo, 2002; Boussaoud et al., 1998; DeSouza et al., 2000), psychophysical studies argue against the execution of a saccade playing a critical role in the control of visually guided hand movements (Prablanc et al., 1979; Prablanc et al., 1986; Vercher et al., 1994). These studies show that there is no increase in reaching accuracy in conditions where subjects had to direct the eyes toward a briefly presented target, compared to reaching without saccades. To examine if there are differences in the cortical activation patterns in central and peripheral reaching, it therefore is necessary to isolate the effects of central/peripheral location of visual target and presence/absence of accompanying eye movements. To achieve this goal, we designed a third condition consisting of a hybrid task in which subjects had to look and reach to a briefly presented target. However, because in this condition, the target was rapidly extinguished, the saccade did not lead to foveal capture, and hence the target was only seen in peripheral vision.

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The contrast of activity patterns resulting from the hybrid reaching condition with the other reaching tasks is critical for distinguishing the two hypotheses concerning the possible difference in cortical activation patterns: (1) that it depends on retinal position of the target or (2) that it depends on the occurrence of a saccade. If the retinal position of the target is the determinant parameter for the cortical activation pattern, then the posterior parietal cortex (and particularly POJ) should be similarly activated in the two peripheral-vision reaching tasks. If however saccades play a determinant role, there should be an identical involvement of the posterior parietal cortex in the two reaching with saccade tasks. Our results reveal that the determinant parameter is the foveal capture of the target. Two different cortical systems are involved in reaching in the central and peripheral visual field respectively. We show that compared to central reaching, reaching to a peripheral-located target activates significantly more the medial part of POJ and a rostral part of the dorsal premotor cortex (PMd). In contrast, a medial intraparietal area (mIPS) and the caudal part of PMd were activated irrespective of the retinal location of the target. In addition, we show that saccades are not responsible for the observed differences in cortical activation patterns in central and peripheral reaching. The determinant factor is the foveal capture of the target. If the target is not "grasped" by the fovea, then POJ shows increased levels of activation and activation of PMd is more widespread.

Results

In three experimental conditions, participants are required to reach to a target appearing in their peripheral visual field (see Figure 1). In two conditions, subjects are allowed to accompany their hand-reaching movement with an orientation saccade. In the first condition, the target remains visible throughout the whole trial and is thus captured by the fovea. We refer to this experimental (e) condition as reaching to a Visible Target after Saccade (VT/Se). In a second condition, the target disappears before the foveal capture. We refer to this condition as reaching to an Invisible Target after Saccade (IT/Se). In a third condition, the target remains visible during the whole trial, but subjects are not allowed to make a saccade. We refer to this condition as reaching to a Visible Target with No Saccade (VT/NSe). Each of these experimental reaching conditions (VT/Se, IT/Se and VT/NSe) are controlled (c) by conditions in which visual stimulation is identical, but participants are instructed to either orient their eyes toward the target (VT/Sc and IT/Sc) or to displace covert attention (VT/NSc). To ensure that each task is performed correctly, subjects undergo training, and eye movements are recorded in the scanner.

Whole-Brain Analysis

Simple main effects of reaching are shown on Figure 2 and Table 1. The reaching movement in the VT/S task (VT/Se-VT/Sc) activated the left motor and somatosensory cortex, corresponding to movement of the right hand. In the frontal lobe, the medial frontal gyrus was activated bilaterally in the supplementary motor area (SMA), and the caudal part of the precentral region (the
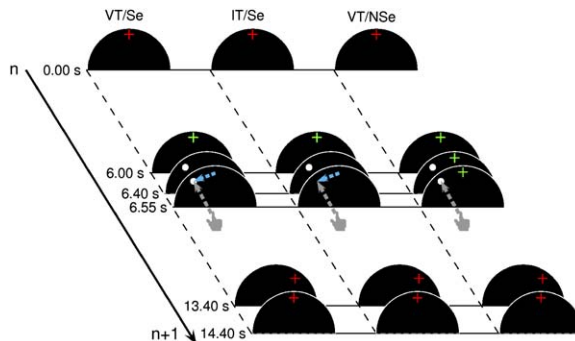

Figure 1. Overview of Each Reaching Condition

For the whole experiment, the screen in front of the subjects was a black semicircle on which red and white targets were projected at 5° or 10° on either sides of a green fixation cross. Gray and blue arrows represent, respectively, hand and eye movements. When the visual target was white, subjects had to reach at it under three different conditions, reaching to Visible Target after Saccade (VT/Se), reaching to Invisible Target after Saccade (IT/Se), and reaching to Visible Target with No Saccade (VT/NSe). When the visual target was red (not shown), subjects did not reach at target but only moved their eyes (VT/Sc and IT/Sc) or displaced covert attention (VT/NSc). FMRI events were time locked to the appearance of the visual target.

most caudal part of PMd) was activated on the left hemisphere. In the posterior parietal cortex, there was a bilateral activation of the medial bank of the intraparietal sulcus. The peak of activation of this "mIPS" region was found on Talairach's coordinates x = −30, y = −47, z = 61 (Z = 4.24) in the left hemisphere and x = 34, y = −48, z = 61 (Z = 3.71) in the right hemisphere.

The reaching movement in the IT/S task (IT/Se-IT/Sc) revealed a bilateral activation in the SMA and a unilateral activation in the left central sulcus and precentral gyrus. Activation of the precentral gyrus was larger than in the task above and extended anteriorly to a more rostral part of PMd up to the precentral sulcus. In the parietal lobe, there was a bilateral activation of the postcentral gyrus and upper part of posterior parietal cortex, with a peak in mIPS for the latter region at x = −22, y = −49, z = 61 (Z = 4.32) in the left hemisphere and x = 24, y = −53, z = 62 (Z = 3.84) in the right hemisphere. Unlike the VT/S task, another parietal region, POJ, was additionally activated. This activation was bilateral, extensive and located along the parieto-occipital junction with a local maximum at x = −18, y = −79, z = 43 (Z = 4.86) in the left hemisphere and x = 16, y = −79, z = 43 (Z = 4.08) in the right hemisphere.

The reaching movement in the VT/NS task (VT/NSe-VT/NSc) revealed a network similar to that described above. In addition to bilateral SMA and left central sulcus, activations of rostral and caudal parts of PMd were observed on both hemispheres. In the parietal lobe, mIPS and POJ were also activated bilaterally. In this task, mIPS had a local maximum at x = −22, y = −52, z = 66 (Z = 3.96) in the left hemisphere and x = 30, y = −53, z = 58 (Z = 3.42) in the right hemisphere. Coordinates of POJ were x = −16, y = −74, z = 44 (Z = 3.87) in the left hemisphere and x = 10, y = −82, z = 37 (Z = 3.74) in the right hemisphere.

Direct comparisons between these tasks enable us to test the two main hypotheses concerning cortical activation patterns (see Introduction). First, we examined
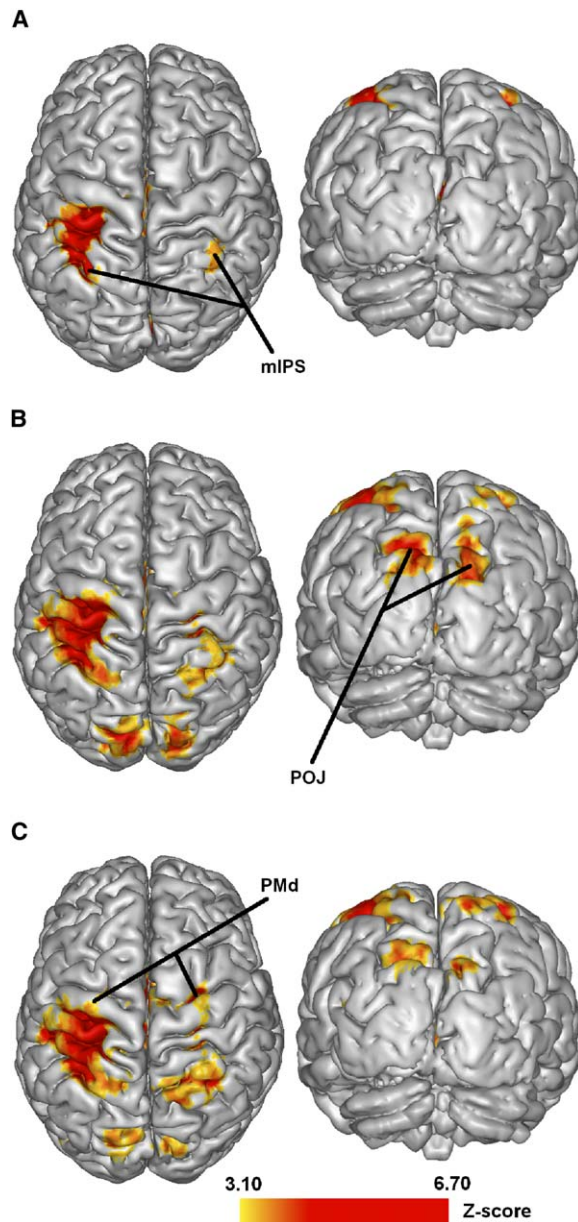
A

mIPS

B

POJ

C

PMd

3.10   6.70
Z-score

Figure 2. Reaching-Related Activations for the Three Tasks

(A) Simple main effect of reaching in the reach to Visible Target after Saccade task (VT/Se − VT/Sc).
(B) Simple main effect of reaching in the reach to Invisible Target after Saccade task (IT/Se − IT/Sc).
(C) Simple main effect of reaching in the reach to Visible Target with No Saccade task (VT/NSe − VT/NSc). The three contrasts are shown on superior and posterior views of a rendered three-dimensional brain of one of the participants (random effect analysis, voxel level p < 0.001, cluster level p < 0.05 corrected for multiple comparisons). PMd, dorsal premotor area; mIPS, medial intraparietal sulcus; POJ, parieto-occipital junction.

Table 1. Reaching-Related Regions in the Three Tasks

Contrast	Coordinates			Z Score	Region
	x	y	z		
VT/Se − VT/Sc	−38	−22	53	5.83	Left central sulcus
	−34	−24	60	5.24	Left precentral gyrus
	−4	−13	56	4.59	Left medial frontal gyrus
	−2	−67	14	3.57	Left cuneus
	0	−79	22	3.57	Right cuneus
	−48	−25	9	4.03	Left superior temporal gyrus
	−30	−47	61	4.24	Left medial intraparietal sulcus
	34	−48	61	3.71	Right medial intraparietal sulcus
	−36	−11	47	4.37	Right superior frontal gyrus
	12	−17	43	4.07	Right cingulate gyrus
IT/Se − IT/Sc	−36	−23	53	6.63	Left central sulcus
	−32	−16	66	4.18	Left precentral gyrus
	26	−22	64	5.12	Right precentral gyrus
	−32	−28	64	6.53	Left postcentral gyrus
	36	−29	40	3.81	Right postcentral gyrus
	−2	−15	49	5.81	Left medial frontal gyrus
	−46	−25	9	5.33	Left superior temporal gyrus
	−18	−79	43	4.86	Left parieto-occipital junction
	16	−79	43	4.08	Right parieto-occipital junction
	18	−72	50	4.10	Right precuneus
	−4	−78	2	3.97	Left lingual gyrus
	2	−74	−8	4.58	Right lingual gyrus
	−22	−49	61	4.32	Left medial intraparietal sulcus
	24	−53	62	3.84	Right medial intraparietal sulcus
	−49	−28	25	3.85	Left inferior parietal lobule
	36	−37	42	4.21	Right inferior parietal lobule
VT/NSe − VT/NSc	−38	−25	53	6.44	Left central sulcus
	−34	−11	43	3.88	Left precentral gyrus
	26	−14	63	4.24	Right precentral gyrus
	−32	−40	61	6.60	Left postcentral gyrus
	28	−36	55	4.73	Right postcentral gyrus
	8	−3	63	4.02	Right medial frontal gyrus
	−42	−68	8	4.59	Left middle temporal gyrus
	−16	−74	44	3.87	Left parieto-occipital junction
	10	−82	37	3.74	Right parieto-occipital junction
	−22	−52	66	3.96	Left medial intraparietal sulcus
	30	−53	58	3.42	Right medial intraparietal sulcus
	−2	−76	2	4.03	Left lingual gyrus
	14	−64	−12	4.55	Right lingual gyrus

Coordinates (x, y, z) are expressed within the Talairach coordinate system: voxel level p < 0.001, cluster level p < 0.05 corrected. VT/Se, reach to visible target after saccade; IT/Se, reach to invisible target after saccade; VT/NSe, reach to visible target with no saccade. VT/Sc, saccade to visible target; IT/Sc, saccade to invisible target; VT/NSc, attention shift to visible target.

the interaction between *reaching and peripheral* vision of the target with the simple main effects of reaching in the two tasks involving saccades, IT/S and VT/S (interaction was masked by the simple main effect of reaching [IT/Se − IT/Sc]). Modulation of reaching by removing saccade ([IT/Se − IT/Sc] − [VT/Se − VT/Sc]) revealed activation of POJ in the left (x = −10, y = −90, z = 36; Z = 3.85) and in the right hemisphere (x = 16, y = −84,

z = 37; Z = 4.18). There were also clusters of activation in the left precentral gyrus, the right inferior parietal lobule, the left middle frontal gyrus, the left precuneus, and
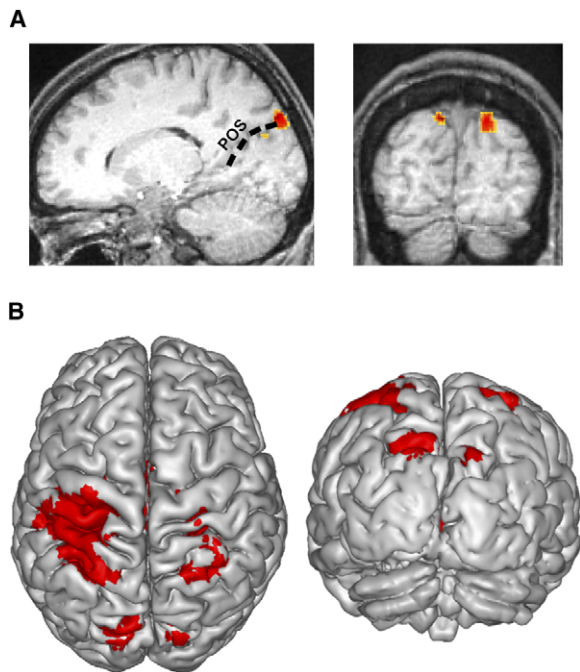
A

B

Figure 3. Direct Comparisons between Tasks

(A) Effect of the peripheral position of the target during reaching (interaction [IT/Se − IT/Sc] − [VT/Se − VT/Sc]) showing bilateral activation of the parieto-occipital junction (POJ). SPMs rendered into standard stereotaxic space and superimposed on to a sagittal and coronal MRI in standard space. For display purpose, the threshold for the whole brain was set to p < 0.005 (uncorrected). POS, parieto-occipital sulcus.

(B) Boolean intersection of the two simple main effects of reaching in peripheral vision ([IT/Se − IT/Sc] AND [VT/NSe − VT/NSc]). Each simple main effect was thresholded at p < 0.001 (voxel level) and p < 0.05 corrected (cluster level) and superimposed on superior and posterior views of a rendered three-dimensional brain of one of the participants.

the left postcentral gyrus (see Figure 3A and Table 2). The interaction between *reaching and saccade* ([IT/Se − IT/Sc] − [VT/NSe − VT/NSc]) did not lead to any significant clusters of activation (p < 0.001 uncorrected).

To determine reach-related regions common to the two peripheral-vision tasks (IT/S and VT/NS), we performed a Boolean intersection of the simple main effects

of reaching ([IT/Se − IT/Sc] AND [VT/NSe − VT/NSc]). This analysis (Figure 3B) confirmed that left PMd (rostral and caudal part), bilateral mIPS, and bilateral POJ were common to these reaching tasks (for each map: voxel level p < 0.001, cluster level p < 0.05 corrected).

Region of Interest Analysis

Whole-brain analysis revealed that mIPS and the more caudal part of PMd were activated in all tasks, whereas POJ and a rostral part of PMd were only significantly more involved when reaching was performed in peripheral vision. Hence, it suggests that it is the position of the target relative to the fovea and not the saccade that is the determinant parameter. To confirm this observation and perform direct comparisons between tasks in these regions, we used a region of interest (ROI) approach for each subject. Based on the frontal and parietal reach-related regions obtained in the VT/NS task (contrast [VT/NSe − VT/NSc]), we defined three bilateral ROIs, mIPS, POJ, and PMd (see Experimental Procedures). We measured the average β weights (as indices of effect size) for all conditions in the two tasks with saccade (VT/S and IT/S) (Figure 4).

To determine whether the position of the target (i.e., inside or outside the fovea) influenced regions involved in the control of reaching movement, we compared the two reaching conditions relative to their respective controls (i.e., [IT/Se − IT/Sc] versus [VT/Se − VT/Sc]) in each ROI. One-tailed paired t tests (with the false discovery rate procedure for multiple comparisons) revealed that only two bilateral ROIs were more active during reaching in peripheral (IT/Se − IT/Sc) compared to central visual field (VT/Se − VT/Sc), POJ (left hemisphere p = 0.015, right hemisphere p = 0.024) and PMd (left hemisphere p = 0.019, right hemisphere p = 0.004). The bilateral mIPS region was not modulated by this factor (left hemisphere p = 0.325, right hemisphere p = 0.295). Although both POJ and PMd are influenced by Task, our previous analyses had shown that PMd was activated in all tasks, whereas POJ was significantly more activated when reaching was performed in peripheral vision. In fact, the Task effect appeared to influence the extent of PMd activation. In order to confirm this observation, we calculated the number of voxels activated in the precentral gyrus for the simple main effects of reaching in the three

Table 2. Direct Comparisons between Tasks

Contrast	Coordinates			Z Score	Region
	x	y	z		
Effect of the retinal position of the target					
[IT/Se − IT/Sc] − [VT/Se − VT/Sc]	16	−84	37	4.18	Right parieto-occipital junction
	34	−37	41	3.98	Right inferior parietal lobule
	−10	−90	36	3.85	Left parieto-occipital junction
	−20	−22	67	3.79	Left precentral gyrus
	−24	−12	61	3.73	Left middle frontal gyrus
	−12	−79	45	3.54	Left precuneus
	22	−49	63	3.35	Right postcentral gyrus
Effect of the saccade					
[IT/Se − IT/Sc] − [VT/NSe − VT/NSc]				No suprathreshold clusters	

Coordinates (x, y, z) are expressed within the Talairach coordinate system: voxel level p < 0.001, extent threshold of 5 voxels. VT/Se, reach to visible target after saccade; IT/Se, reach to invisible target after saccade; VT/NSe, reach to visible target with no saccade. VT/Sc, saccade to visible target; IT/Sc, saccade to invisible target; VT/NSc, attention shift to visible target.
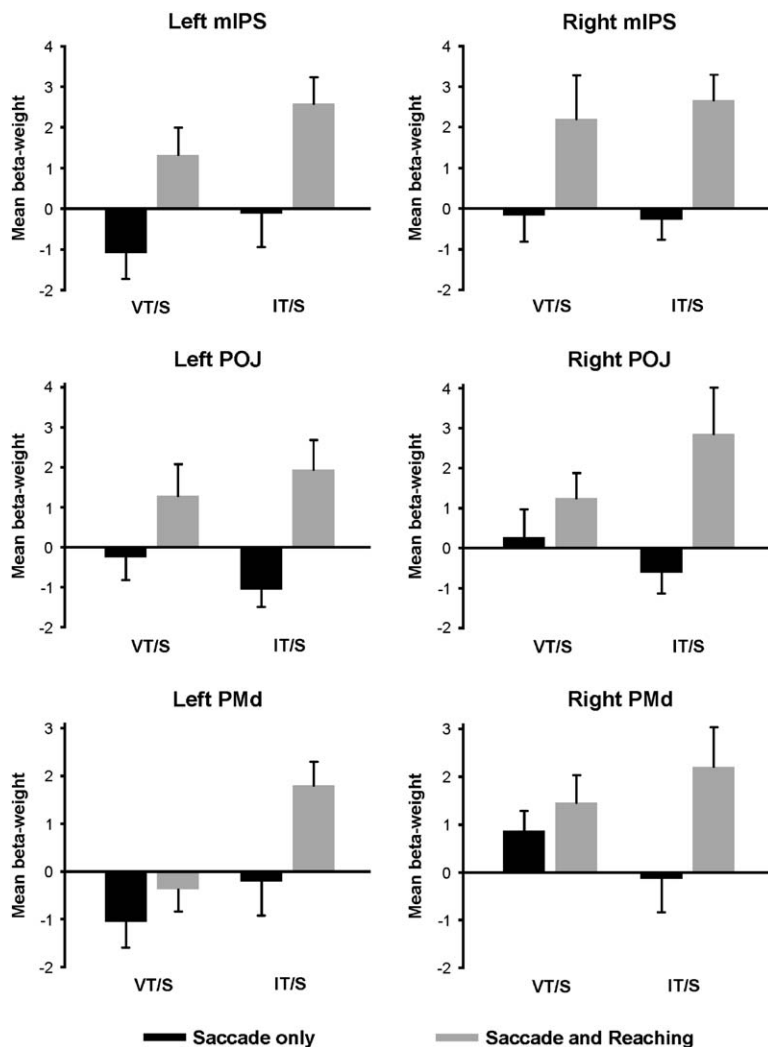
Figure 4. Region of Interest Analyses

Activity related to control (saccade) and experimental (saccade and reaching) conditions when the visual target was located in the central (VT/S task) or peripheral (IT/S task) visual field in the three bilateral regions of interest: dorsal premotor cortex (PMd), medial intraparietal sulcus (mIPS), and parieto-occipital junction (POJ). For each area, the graphs show the regionally averaged β weights averaged across participants. Error bars indicate intersubject standard error of the mean (SEM). Significant differences (p < 0.05) between reaching in central and peripheral vision relative to their respective control were observed in bilateral PMd (left, p = 0.019; right, p = 0.004) and POJ (left, p = 0.015; right, p = 0.024) but not in mIPS.

tasks (VT/S, IT/S, and VT/NS). In the left hemisphere, this analysis showed that 3560 mm³ of the precentral region (PrC) was activated during the reaching movement in the VT/S task (with saccade), 7192 mm³ during the IT/S task, and 6452 mm³ during the VT/NS task. In the right hemisphere, no activated voxel was found in the VT/S, 584 mm³ in IT/S and 448 mm³ in VT/NS (Figure 4). To describe in greater details this phenomenon subject per subject, we performed the same type of analysis in the left and right PrC for each of the twelve subjects (see Experimental Procedures). Here, we compare the volumes (Vol) activated in the IT/S and VT/S reaching tasks
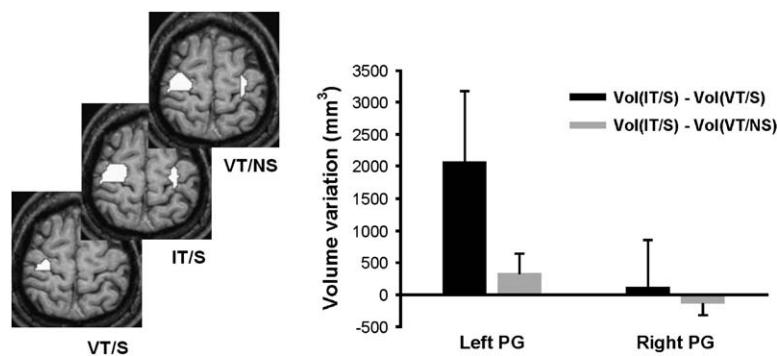

Figure 5. Extent of PMd Activity in the Precentral Region (PrC)

Left, voxels activated (p < 0.001 uncorrected; random-effect analysis) in the left and right PrC in the three tasks superimposed on the anatomical image of one participant. There were more voxels when pointing was performed in peripheral (VT/NS and IT/S tasks) than in central vision (VT/S). Right, change in volume of PMd activated in the left and right PrC averaged across participants. Bars show the volume variation because of the "peripheral-vision effect" (Vol[IT/Se − IT/Sc] − Vol[VT/Se − VT/Sc]) and to the "saccade effect" (Vol[IT/Se − IT/Sc] − Vol[VT/NSe − VT/NSc]). There was more volume variation (asterisk, p < 0.05) because of peripheral vision of the target than saccade in left PrC (p = 0.016). Error bars indicate SEM across participants.

(Vol[IT/Se − IT/Sc] − Vol[VT/Se − VT/Sc]) so as to isolate the "peripheral-vision effect" and the volumes activated in the IT/S and VT/NS tasks (Vol[IT/Se − IT/Sc] − Vol[VT/NSe − VT/NSc]) so as to isolate the "saccade effect." This shows that the "peripheral-vision effect" modulates significantly more the extent of PMd than does the "saccade effect" in the left (one-tailed Wilcoxon test, p = 0.016) but not in the right hemisphere (one-tailed Wilcoxon test, p = 0.145) (Figure 5, right).

Discussion

This is the first demonstration that the reach-related pattern of brain activity is dependent on the central versus peripheral location of the target. The present results indicate that visually guided reaching movements involve a well-defined fronto-parietal network. This network is composed of cortical areas commonly activated in all three tasks: the central sulcus, the SMA, the caudal part of PMd in the left hemisphere, and mIPS bilaterally. These results agree with previous imaging studies of visually guided reaching movements (Astafiev et al., 2003; Connolly et al., 2000, 2003; Desmurget et al., 2001; Grafton et al., 1996; Inoue et al., 1998; Kawashima et al., 1996; Medendorp et al., 2003; Simon et al., 2002).

Reaching for a visual target in the peripheral field engages a more extensive network in both hemispheres than reaching in central vision. In addition to activate areas engaged in central visual reaching, reaching in the peripheral visual field activates significantly more the area POJ located on both banks of the parieto-occipital sulcus. In the frontal cortex, the extent of PMd activity depends on the reaching condition. Activation in PMd is larger when reaching toward peripheral compared to central-located targets independently of whether the hand movement is accompanied by an eye movement.

The present results reveal two distinct reach-related parietal regions, one influenced by the central versus peripheral visual location of the target (POJ) and the other (mIPS) is activated independently of target location. These findings shed light on apparent discrepancies of published findings from imaging studies. PET studies employing free-gaze reaching movement paradigms indicate specific activation patterns in the intra-parietal sulcus and the superior parietal lobule (Desmurget et al., 2001; Grafton et al., 1996; Inoue et al., 1998; Kawashima et al., 1996). In contrast, most fMRI studies with an imposed gaze fixation paradigm suggest activity patterns in a more medial and posterior region of the parietal lobe in addition to those obtained in free-gaze conditions (Astafiev et al., 2003; Connolly et al., 2000, 2003; Medendorp et al., 2003; Simon et al., 2002) (Figure S1).

Relating our findings with monkey data is difficult because of the lack of corresponding experiments in monkey. Given the different sites and patterns of activation found in the present study, the reaching-specific regions mIPS and POJ appear as likely homologs of the macaque areas MIP (Colby and Goldberg, 1999) and V6/V6A (Galletti et al., 1999). This has been proposed by other human studies (Chapman et al., 2002; Dechent and Frahm, 2003; Grefkes et al., 2004). As monkey area V6A preferentially projects to rostral PMd (Matelli et al., 1998; Tanné-Gariepy et al., 2002) this would fit with the increase of activity in both POJ and the rostral part of PMd when reaching movements are performed in peripheral vision.

The Extra-Foveal Vision of the Target Is a Determinant Feature for POJ Activation

It is established that fixation of visual targets increases reaching-movement accuracy (Bock, 1986; Neggers and Bekkering, 1999; Prablanc et al., 1979; van Donkelaar and Staub, 2000). This increase of accuracy is not only related to the higher resolving power of the fovea. Importantly, less accurate reaching is observed not only in the peripheral visual field but also when eye and hand are aimed conjointly at a visual target in the dark (i.e., when there is no visual feedback concerning target and hand location) (Henriques and Crawford, 2000; Henriques et al., 1998; Vercher et al., 1994).

Our results show that the main factor modulating the activity of the cortical network controlling eye-hand coordination is the retinal position of the target with respect to the fovea and not the saccade per se. Psychophysical studies with identical tasks to those used in the present study showed that there is no increase in reaching accuracy in conditions in which subjects had to direct the eyes toward a briefly presented target, compared to reaching without saccades (Prablanc et al., 1979, 1986). Therefore, these studies showed that higher accuracy was only observed when the saccade led to foveal capture of the target. These earlier findings, together with the present result suggest that it is the absence of the target on the fovea at the end of the saccade that is the key factor determining (1) the increased level of activation of POJ and (2) the poor accuracy of the reaching movement.

The present results describe a specific role of POJ in exactly the reaching situation in which patients with optic ataxia show a strong impairment (namely the imposed fixation task, or VT/NSe in this study). Interestingly, POJ was recently found to be the core site of the lesions responsible for optic ataxia (Karnath and Perenin, 2005). Thus, both the anatomo-clinical and functional imaging approaches provide converging evidence of a parieto-occipital region specifically dedicated to reaching in the peripheral visual field. These results suggest a possible resolution to the controversy about the nature of the deficit after parietal lesions. Heading errors were observed in optic ataxia patients reaching at peripheral targets but not in subjects with virtual parietal lesions, pointing to foveal targets, in a free-gaze condition (Desmurget et al., 1999; Milner et al., 1999). The existence of two cortical systems for reaching in central and peripheral vision suggests a number of predictions for optic ataxia patients. One can predict that optic ataxia patients will also make errors in reaching movements in the peripheral visual field in the reach to invisible target condition (IT/Se). Furthermore, one can speculate that patients with optic ataxia that present large brain lesions including the mIPS region will not show any improvement with foveation of the target, in contrast to patients with lesions confined to the POJ that theoretically will only show deficits when reaching to peripheral targets.

Several studies have shown that reach-related spatial representations are encoded in retinocentric coordinates in the posterior parietal cortex (Bock, 1986; Henriques et al., 1998; van Donkelaar et al., 2000). In order to ensure optimal accuracy, these representations have to be remapped during each saccade. Importantly, POJ has been shown to be crucial for this function (Khan et al., 2005a; Medendorp et al., 2003; Merriam et al., 2003). The POJ activation in the present study is not due to a role in updating visual information because there is no updating in our imposed fixation task when POJ was found to be more active. These considerations are in agreement with the recent results showing that optic ataxia is not due to a problem of spatial remapping (Khan et al., 2005a; Khan et al., 2005b).

Eye-Hand Coordination
It is well known from neurophysiological and neuroimaging studies that oculomotor signals (whether related to corollary discharge or proprioception) influence the cortical network involved in hand-reaching movements (Andersen and Buneo, 2002; DeSouza et al., 2000). Hence, in the dark, subjects can point fairly accurately to their current or recent direction of gaze (Blouin et al., 1995, 2002; Bock, 1986). However, it has been shown that in the absence of foveal capture of the reaching target, oculomotor signals do not make a significant contribution to eye-hand accuracy (Prablanc et al., 1979). Foveal capture leads to optimal reaching accuracy that is influenced by oculomotor signals, and under these conditions, only a core cortical reaching network is activated. The present results show that during peripheral reaching, when oculomotor signals fail to influence eye-hand accuracy (i.e., when there is no foveal capture), an extended cortical reaching network is engaged. This suggests that the additional reaching regions lead to a relative independency of the hand from the oculomotor signals.

Both the oculomotor and hand motor systems are driven by the visual targets encoded in retinocentric coordinates. There is abundant evidence of temporal coupling between both effectors (Fisk and Goodale, 1985; Neggers and Bekkering, 1999, 2000; Prablanc et al., 1979, 1986; Sailer et al., 2000; Vercher et al., 1994). This contrasts with spatial coupling that has only been convincingly demonstrated in central vision conditions, in studies examining the relationship between terminal spatial errors of the eyes and hands (de Graaf et al., 1995; van Donkelaar, 1997; van Donkelaar and Staub, 2000). Asking subjects to make a saccade and a reaching movement toward the same target while changing the starting point of the eye revealed a strong correlation between saccade amplitude and reaching error amplitude (van Donkelaar, 1997; van Donkelaar and Staub, 2000). This close relation depends on the activity of the posterior parietal cortex (van Donkelaar et al., 2000). These experiments underline the uniqueness of the central vision condition in coordinating visuomotor behavior. It needs to be taken into consideration that reaching toward targets in the fovea is the most usually performed condition. Perfect coordination between eye and hand results from intensive learning (Henriques et al., 2003; Pelz et al., 2001). Systematic misreaching when gaze is off the target position has been interpreted

as a sign of incomplete learning (Henriques et al., 2003) and that the visuomotor system is better calibrated for the "Gaze-on-target" situation than for the "Gaze-off-target" situation. Given the broader brain activity in the two peripheral-vision conditions (with or without saccade) compared to activity in the central vision condition, we propose that the calibration is related to "Target-on-fovea" as opposed to "Gaze-on-target."

In the "Target-on-fovea" situation, both motor systems share common control strategies. The brain network is shaped by learning and the present study reveals a particularly restricted network in the central vision reaching task without involvement of POJ. When POJ is not involved in the reaching movement (namely during Target-on-fovea), then the reaching error amplitude is closely related to the saccade amplitude (van Donkelaar and Adams, 2005). Because this spatial coupling does not appear when the target is "off-fovea," this suggests that POJ does not support spatial coupling of the eye and the hand. One may further hypothesize that activation of POJ serves to decouple the spatial coordination of the eye and the hand. This latter hypothesis is supported by the fact that temporary as well as permanent lesions of the posterior parietal cortex can lead to an impossibility to decouple reach direction from gaze direction (van Donkelaar and Adams, 2005; Carey et al., 1997, 2002; Jackson et al., 2005).

Experimental Procedures

Participants
Twelve healthy right-handed volunteers (four males and eight females, aged 20–30 years, mean: 23 years) with no history of neurological or psychiatric disorders participated in the study. All subjects gave written informed consent and were paid for their participation. Procedures were approved by the local ethics committee (CCPPRB of Alsace, France).

Experimental Setup
Visual stimuli were generated with Inquisit 1.33 software (Millisecond Software, Seattle, WA) and projected onto a translucent screen with a NEC MultiSync MT1030G+ projector (fresh rate, 60 Hz). The screen was fixed on the ceiling of the magnet bore within reaching distance and in front of the subjects. For the duration of the three runs, the subjects lay supine in the magnet bore with the head tilted (25°–30°) in the cylindrical head coil, thereby enabling them to look directly at the screen on which the targets were projected. Hence, subjects had a direct view of the objects with no mirrors. Many prior studies used a mirror, which requires additional transformations. In order to minimize head motion during scanning, the subject's head was fixed by means of a decompression mold (an immobilization system) around the shoulders and the head. Moreover, the right upper arm was maintained along the body with a velcro strap in order to prevent shoulder movement. At rest, subjects had their elbow flexed, with the index finger resting on the sternum. For reaching, they were required to simply move the forearm (elbow and wrist extension) and to perform a fast and precise natural reach. Therefore, we use the term reaching (i.e., lifting the forearm to touch the target) and not pointing (i.e., angling the finger in the direction of the target without actually touching the target). The magnet room was maintained in total darkness, and the forearm placed in a black glove so as to avoid any visual feedback of arm position and eliminate activation because of visual motion of a body part (Astafiev et al., 2004; Downing et al., 2001). The electro-oculographic signals (EOG) were recorded simultaneously with fMRI, by using six shielded electrodes with an MRI-compatible electro-encephalographic (EEG) device (Schwarzer EMR, Munich, Germany). Signals were sampled at 1000 Hz with preamplification filters set from 0.1 to 300 Hz.

Task and Procedures

Subjects were required to perform three different experimental reaching conditions: reaching to a Visible Target after Saccade (VT/Se), reaching to an Invisible Target after Saccade (IT/Se), and reaching to a Visible Target with No Saccade (VT/NSe). Each of these conditions was performed in a separate block and was balanced with a condition in which participants were instructed to only move their eyes toward the target in the VT/S and IT/S blocks (VT/Sc and IT/Sc) or to displace covert attention in the VT/NS block (VT/NSc). In each block, the visual targets were projected along a semicircle at the top of the screen. Subjects maintained eye fixation on a red cross located in the top center of the screen for a 6 s rest period. Trial onset was indicated by a color change (red to green) of the fixation cross. The fixation cross was turned off after 400 ms, and a peripheral target appeared at 5° or 10° to the right or left of the fixation point. Subjects were informed on the type of next coming condition by the target color. If the target was white, they had to perform a reaching condition (VT/Se, IT/Se, or VT/NSe depending on the block); if it was red, they had to perform a control condition (VT/Sc, IT/Sc, or VT/NSc, depending on the block). The target remained on for 7 s, except in the IT/S task in which it was on for 150 ms only (i.e., less than the oculomotor reaction time). Subjects were instructed not to move their eyes after the saccade was completed.

A green fixation cross was present at top center during target presentation time in the VT/NS block. In this block, the experimental condition (VT/NSe) consisted of reaching at the target while fixating the green cross at the center of the screen, and the control condition (VT/NSc) of fixating the green cross without reaching at the target. In all the three blocks, subjects were instructed not to move anymore during a 7 s period, once their arm had reached the screen. The end of the trial was indicated by means of a distracter (a red cross at a random position). Subjects were then free to move their eyes (for 1 s). The trial order within each block was pseudorandomized to ensure a balanced number of saccade/reaching and left/right movements. Moreover, the task order was counterbalanced from subject to subject. In each block, there were 62 stimulus presentations, 31 in experimental conditions and 31 in control conditions.

Training

Prior to scanning, all subjects were trained in the different tasks for a 10–15 min period, until they were able to perform each task correctly (i.e., no saccades during the fixation periods and no error in the condition order). During training, eye movements down to ±0.03° were monitored with an infrared eye-tracker IRIS 6500 IR Light (Skalar, Delft, Netherlands).

Imaging Procedures

Images were collected by using a 2T MRI system (Bruker Medizintechnik, Ettlingen, Germany) with an event-related design (repetition time, 2.5 s). The fMRI BOLD signal was measured using a T2*-weighted echoplanar sequence (flip angle, 90°; echo time, 43 ms). 28 axial slices (4 mm thickness; field of view, 25.6 × 25.6 cm; 64 × 64 matrix) were acquired per volume, which did not include the cerebellum. After functional image acquisition, a high-resolution (1 × 1 × 1 mm) 3D MDEFT brain scan (180 sagittal slices, matrix of 256 × 256 voxels) was recorded.

Whole-Brain Analysis

fMRI data were analyzed with SPM2 software (Wellcome Department of Cognitive Neurology, London, UK, http://www.fil.ion.ucl.ac.uk/). The first three functional volumes of each block were removed to eliminate nonequilibrium effects of magnetization. The 350 remaining images were spatially realigned to the first image of each time series on a voxel-by-voxel basis so as to correct for head movements. Realignment parameters were checked to confirm that none of the twelve subjects had moved of more than 5 mm during the entire session. The realigned functional images and the anatomical scans for each subject were then normalized into a standard stereotaxic space with the Montreal Neurological Institute template. The functional images were spatially smoothed with an isotropic Gaussian filter (6 mm full width at half maximum). The event-related statistical analysis was performed according to the general linear model (Josephs et al., 1997) by using the standard hemodynamic response function (HRF) provided by SPM2. We defined two event types per block. These corresponded to the experimental (i.e., reaching) and control (i.e., saccade or attention shift) conditions of the three blocks. Events were time locked to the appearance of the visual target. Because we used saccadic-related activities as control for reaching after saccade (no low-level baseline was designed), the internal remapping related activity is therefore removed. The time series data were high-pass filtered (1/60 Hz) to remove artifacts because of slow physiological variations.

Random effect analyses were applied to individual contrasts to account for between-subject variance and to generalize to the population as a whole. The activations reported survived a voxel-level threshold of p < 0.001, uncorrected for multiple comparisons, and a cluster-level threshold of p < 0.05, corrected for multiple comparisons. An uncorrected threshold of p < 0.001 with an extent threshold of five voxels was used for interactions because they were inclusively masked by the simple main effect of reaching for IT/S. To reveal regions of overlap between the reaching movement performed in the IT/S and VT/NS tasks, we performed a Boolean intersection of their corresponding simple main effects of reaching (i.e., [IT/Se − IT/Sc] AND [VT/NSe − VT/NSc]), each at a voxelwise threshold of p < 0.001 and a corrected clusterwise threshold of p < 0.05. The SPM2 coordinates were converted from MNI coordinate space into Talairach space (http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml) and localized with Talairach Atlas (Talairach and Tournoux, 1988).

Region of Interest Analysis

Data were complementary processed with the extension of SPM MarsBaR (http://marsbar.sourceforge.net/). For each subject, three unbiased ROIs in each hemisphere were defined from the contrast corresponding to the simple main effect of reaching in the VT/NS task (VT/NSe − VT/NSc): the dorsal premotor cortex (PMd, bilateral), the parieto-occipital junction (POJ, bilateral), and the medial bank of the intraparietal sulcus (mIPS, bilateral). ROIs images included all significant voxels (p < 0.001 uncorrected) within a 10 mm radius of each maximum. Using these ROIs images, we extracted then the regression coefficients (i.e., the β weights) for all conditions in the VT/S and IT/S blocks so as to obtain indices of the effect size for all voxels included in the ROIs. Normality of the values was confirmed by the Shapiro-Wilk's W test (p = 0.11). An additional analysis was also performed for comparing the extent of PMd in the precentral gyrus (PrC) for each subject and for each task. SPM maps of each subject were thus superimposed on the canonical brain in the MNI-space, and ROI images of left and right PrC were constructed with the automated anatomic labeling template (Tzourio-Mazoyer et al., 2002). We then calculated the number of activated voxels in the left and right PrC in the three simple main effects of reaching (p < 0.001 uncorrected). We then calculated the change in activated volume between IT/S and VT/S main effects of reaching (Vol[IT/Se − IT/Sc] − Vol[VT/Se − VT/Sc]) to isolate the "peripheral-vision effect" and the change in activated volume between the IT/S and VT/NS main effects of reaching (Vol[IT/Se − IT/Sc] − Vol[VT/NSe − VT/NSc]) to isolate the "saccade effect." Because normal distribution of these values was not verified (Shapiro-Wilk's W test, p < 0.001), two nonparametric Wilcoxon tests (one tailed) were applied (p values were posthoc corrected by the false discovery rate method).

Control of Ocular Movements

The EOG recordings were filtered in order to remove the electro-ballisto-cardiography artifacts (Allen et al., 1998) and the artifacts induced by the rapid changes of the magnetic field during functional runs (Hoffmann et al., 2000). After visual control of EOG signals, we discarded trials during which the subjects failed to carry out correctly one of the tasks (i.e., ocular fixation error, or task mismatch).

Supplemental Data

The Supplemental Data for this article can be found online at http://www.neuron.org/cgi/content/full/48/5/849/DC1/.

References

Allen, P.J., Polizzi, G., Krakow, K., Fish, D.R., and Lemieux, L. (1998). Identification of EEG events in the MR scanner: the problem of pulse artifact and a method for its subtraction. Neuroimage 8, 229–239.

Andersen, R.A., and Buneo, C.A. (2002). Intentional maps in posterior parietal cortex. Annu. Rev. Neurosci. 25, 189–220.

Astafiev, S.V., Shulman, G.L., Stanley, C.M., Snyder, A.Z., Essen, D.C.V., and Corbetta, M. (2003). Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing. J. Neurosci. 23, 4689–4699.

Astafiev, S.V., Stanley, C.M., Shulman, G.L., and Corbetta, M. (2004). Extrastriate body area in human occipital cortex responds to the performance of motor actions. Nat. Neurosci. 7, 542–548.

Blouin, J., Gauthier, G.M., and Vercher, J.L. (1995). Internal representation of gaze direction with and without retinal inputs in man. Neurosci. Lett. 183, 187–189.

Blouin, J., Amade, N., and Vercher, J.L. (2002). Visual signals contribute to the coding of gaze direction. Exp. Brain Res. 144, 281–292.

Bock, O. (1986). Contribution of retinal versus extraretinal signals towards visual localization in goal-directed movements. Exp. Brain Res. 64, 476–482.

Boussaoud, D., Jouffrais, C., and Bremmer, F. (1998). Eye position effects on the neuronal activity of dorsal premotor cortex in the macaque monkey. J. Neurophysiol. 80, 1132–1150.

Carey, D.P., Coleman, R.J., and Della Sala, S. (1997). Magnetic misreaching. Cortex 33, 639–652.

Carey, D.P., Della Sala, S., and Ietswaart, M. (2002). Neuropsychological perspectives on eye-hand coordination in visually-guided reaching. Prog. Brain Res. 140, 311–327.

Chapman, H., Gavrilescu, M., Wang, H., Kean, M., Egan, G., and Castiello, U. (2002). Posterior parietal cortex control of reach-to-grasp movements in humans. Eur. J. Neurosci. 15, 2037–2042.

Colby, C.L., and Goldberg, M.E. (1999). Space and attention in parietal cortex. Annu. Rev. Neurosci. 22, 319–349.

Connolly, J.D., Goodale, M.A., Desouza, J.F., Menon, R.S., and Vilis, T. (2000). A comparison of fronto-parietal fMRI activation during anti-saccades and anti-pointing. J. Neurophysiol. 84, 1645–1655.

Connolly, J.D., Andersen, R.A., and Goodale, M.A. (2003). FMRI evidence for a 'parietal reach region' in the human brain. Exp. Brain Res. 153, 140–145.

de Graaf, J.B., Pelisson, D., Prablanc, C., and Goffart, L. (1995). Modifications in end positions of arm movements following short-term saccadic adaptation. Neuroreport 6, 1733–1736.

Dechent, P., and Frahm, J. (2003). Characterization of the human visual V6 complex by functional magnetic resonance imaging. Eur. J. Neurosci. 17, 2201–2211.

Desmurget, M., Epstein, C.M., Turner, R.S., Prablanc, C., Alexander, G.E., and Grafton, S.T. (1999). Role of the posterior parietal cortex in updating reaching movements to a visual target. Nat. Neurosci. 2, 563–567.

Desmurget, M., Gréa, H., Grethe, J.S., Prablanc, C., Alexander, G.E., and Grafton, S.T. (2001). Functional anatomy of nonvisual feedback loops during reaching: a positron emission tomography study. J. Neurosci. 21, 2919–2928.

DeSouza, J.F., Dukelow, S.P., Gati, J.S., Menon, R.S., Andersen, R.A., and Vilis, T. (2000). Eye position signal modulates a human pa-

rietal pointing region during memory-guided movements. J. Neurosci. 20, 5835–5840.

Downing, P.E., Jiang, Y., Shuman, M., and Kanwisher, N. (2001). A cortical area selective for visual processing of the human body. Science 293, 2470–2473.

Fisk, J.D., and Goodale, M.A. (1985). The organization of eye and limb movements during unrestricted reaching to targets in contralateral and ipsilateral visual space. Exp. Brain Res. 60, 159–178.

Galletti, C., Fattori, P., Kutz, D.F., and Gamberini, M. (1999). Brain location and visual topography of cortical area V6A in the macaque monkey. Eur. J. Neurosci. 11, 575–582.

Grafton, S.T., Fagg, A.H., Woods, R.P., and Arbib, M.A. (1996). Functional anatomy of pointing and grasping in humans. Cereb. Cortex 6, 226–237.

Grefkes, C., Ritzl, A., Zilles, K., and Fink, G.R. (2004). Human medial intraparietal cortex subserves visuomotor coordinate transformation. Neuroimage 23, 1494–1506.

Henriques, D.Y., and Crawford, J.D. (2000). Direction-dependent distortions of retinocentric space in the visuomotor transformation for pointing. Exp. Brain Res. 132, 179–194.

Henriques, D.Y., Klier, E.M., Smith, M.A., Lowy, D., and Crawford, J.D. (1998). Gaze-centered remapping of remembered visual space in an open-loop pointing task. J. Neurosci. 18, 1583–1594.

Henriques, D.Y., Medendorp, W.P., Gielen, C.C., and Crawford, J.D. (2003). Geometric computations underlying eye-hand coordination: orientations of the two eyes and the head. Exp. Brain Res. 152, 70–78.

Hoffmann, A., Jager, L., Werhahn, K.L., Jaschke, M., Noachtar, S., and Reiser, M. (2000). Electroencephalography during functional echo-planar imaging: detection of epileptic spikes using post-processing methods. Magn. Reson. Med. 44, 791–798.

Inoue, K., Kawashima, R., Satoh, K., Kinomura, S., Goto, R., Koyama, M., Sugiura, M., Ito, M., and Fukuda, H. (1998). A PET study of pointing with visual feedback of moving hands. J. Neurophysiol. 79, 117–125.

Jackson, S.R., Newport, R., Mort, D., and Husain, M. (2005). Where the eye looks, the hand follows; limb-dependent magnetic misreaching in optic ataxia. Curr. Biol. 15, 42–46.

Josephs, O., Turner, R., and Friston, K. (1997). Event-related fMRI. Hum. Brain Mapp. 5, 243–248.

Karnath, H.O., and Perenin, M.T. (2005). Cortical control of visually guided reaching: evidence from patients with optic ataxia. Cereb. Cortex 15, 1561–1569.

Kawashima, R., Naitoh, E., Matsumura, M., Itoh, H., Ono, S., Satoh, K., Gotoh, R., Koyama, M., Inoue, K., Yoshioka, S., and Fukuda, H. (1996). Topographic representation in human intraparietal sulcus of reaching and saccade. Neuroreport 7, 1253–1256.

Khan, A.Z., Pisella, L., Rossetti, Y., Vighetto, A., and Crawford, J.D. (2005a). Impairment of gaze-centered updating of reach targets in bilateral parietal-occipital damaged patients. Cereb. Cortex 15, 1547–1560.

Khan, A.Z., Pisella, L., Vighetto, A., Cotton, F., Luaute, J., Boisson, D., Salemme, R., Crawford, J.D., and Rossetti, Y. (2005b). Optic ataxia errors depend on remapped, not viewed, target location. Nat. Neurosci. 8, 418–420.

Matelli, M., Govoni, P., Galletti, C., Kutz, D.F., and Luppino, G. (1998). Superior area 6 afferents from the superior parietal lobule in the macaque monkey. J. Comp. Neurol. 402, 327–352.

Medendorp, W.P., Goltz, H.C., Vilis, T., and Crawford, J.D. (2003). Gaze-centered updating of visual space in human parietal cortex. J. Neurosci. 23, 6209–6214.

Merriam, E.P., Genovese, C.R., and Colby, C.L. (2003). Spatial updating in human parietal cortex. Neuron 39, 361–373.

Milner, A.D., Paulignan, Y., Dijkerman, H.C., Michel, F., and Jeanerod, M. (1999). A paradoxical improvement of misreaching in optic ataxia: new evidence for two separate neural systems for visual localization. Proc. R. Soc. Lond. B. Biol. Sci. 266, 2225–2229.

Neggers, S.F., and Bekkering, H. (1999). Integration of visual and somatosensory target information in goal-directed eye and arm movements. Exp. Brain Res. *125*, 97–107.

Neggers, S.F., and Bekkering, H. (2000). Ocular gaze is anchored to the target of an ongoing pointing movement. J. Neurophysiol. *83*, 639–651.

Pelz, J., Hayhoe, M., and Loeber, R. (2001). The coordination of eye, head, and hand movements in a natural task. Exp. Brain Res. *139*, 266–277.

Perenin, M.T., and Vighetto, A. (1988). Optic ataxia: a specific disruption in visuo-motor mechanisms. I. Different aspects of the deficit reaching for objects. Brain *111*, 643–674.

Prablanc, C., Echallier, J.F., Komilis, E., and Jeannerod, M. (1979). Optimal response of eye and hand motor systems in pointing at a visual target. I. Spatio-temporal characteristics of eye and hand movements and their relationships when varying the amount of visual information. Biol. Cybern. *35*, 113–124.

Prablanc, C., Pelisson, D., and Goodale, M.A. (1986). Visual control of reaching movements without vision of the limb. I. Role of retinal feedback of target position in guiding the hand. Exp. Brain Res. *62*, 293–302.

Sailer, U., Eggert, T., Ditterich, J., and Straube, A. (2000). Spatial and temporal aspects of eye-hand coordination across different tasks. Exp. Brain Res. *134*, 163–173.

Simon, O., Mangin, J.F., Cohen, L., Bihan, D.L., and Dehaene, S. (2002). Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. Neuron *33*, 475–487.

Talairach, J., and Tournoux, P. (1988). Co-Planar Stereotaxic Atlas of the Human Brain (New York, NY: Thieme).

Tanné-Gariepy, J., Rouiller, E.M., and Boussaoud, D. (2002). Parietal inputs to dorsal versus ventral premotor areas in the macaque monkey: evidence for largely segregated visuomotor pathways. Exp. Brain Res. *145*, 91–103.

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., and Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage *1*, 273–289.

van Donkelaar, P. (1997). Eye-hand interactions during goal-directed pointing movements. Neuroreport *8*, 2139–2142.

van Donkelaar, P., and Adams, J. (2005). Gaze-dependent deviation in pointing induced by transcranial magnetic stimulation over the human posterior parietal cortex. J. Mot. Behav. *37*, 153–163.

van Donkelaar, P., and Staub, J. (2000). Eye-hand coordination to visual versus remembered targets. Exp. Brain Res. *133*, 414–418.

van Donkelaar, P., Lee, J.H., and Drew, A.S. (2000). Transcranial magnetic stimulation disrupts eye-hand interactions in the posterior parietal cortex. J. Neurophysiol. *84*, 1677–1680.

Vercher, J.L., Magenes, G., Prablanc, C., and Gauthier, G.M. (1994). Eye-head-hand coordination in pointing at visual targets: spatial and temporal analysis. Exp. Brain Res. *99*, 507–523.