Parietal modules for reaching

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Abstract

Optic ataxia (OA) is classically defined as a deficit of visually guided movements that follows lesions of the posterior part of the posterior parietal cortex (PPC). Since the formalisation of the double stream of visual information processing [Milner, A. D., & Goodale, M. A. (1995). The visual brain in action. Oxford: Oxford University Press] and the use of OA as an argument in favour of the involvement of the posterior parietal cortex (dorsal stream) in visually guided movements, many studies have looked at the visuomotor deficits of these patients. In parallel, the development of neuroimaging methods have led to increasing information about the role of the posterior parietal cortex in visually guided actions. In this article, we discuss the similarities and differences in the results that emerged from these two complementary viewpoints by combining a meta-analysis of neuroimaging data on reaching with lesion studies from OA patients and results of our own fMRI study on reaching in the ipsi- and contra-lateral visual field. We identified four bilateral parietal foci from the meta-analysis and found that the more posterior foci showed greater lateralisation for contralateral visual stimulation than more anterior ones. Additionally, the more anterior foci showed greater lateralisation for the use of the contralateral hand than the more posterior ones. Therefore, we can demonstrate that they are organised along a postero-anterio- gradient of visual-to-somatic information integration. Furthermore, from the combination of imaging and lesion data it can be inferred that a lesion of the three most posterior foci would interfere with the target-hand integration and could explain the hand and field effect revealed in OA reaching behaviour.

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1. Introduction

Bálint (1909) described a patient with a large bilateral lesion in the posterior parietal cortex (PPC) who exhibited a particular pattern of deficits (the Bálint syndrome), including reaching inaccuracy (Hecaen & De Ajuriaguerra, 1954). One of the first studies that isolated optic ataxia (OA) (ataxie optique) from the Bálint syndrome was from Garcia, Rondot and de Recondo (1967). He described pure cases of unilateral lesion patients showing reaching deficits only in peripheral vision and without any other primary sensory or motor deficit, neglect or apraxia. The interpretation of OA as a specific visuomotor deficit has been reinforced by the careful study of Vighetto in the 80s (Perenin & Vighetto, 1983, 1988). He notably showed that reaching errors of unilateral patients depended both on the use of the contralesional hand in both visual fields (hand effect) and on the presentation of the target in the contralesional field (field effect). This combination of sensory and motor influences, as well as the location of the PPC lying between the visual and the motor cortices support the idea that the OA deficit affects the visuomotor interface. This interpretation of OA was one of the arguments used by Milner and Goodale (1995) to change the interpretation of the function of the dorsal stream from “where” to “how”. Their model of the double stream of visual information processing has been one of the most influential in modern cognitive sciences and therefore has increased interest in OA. In parallel, the development of neuroimaging techniques, especially functional magnetic resonance imaging (fMRI), has been applied in the field of visually guided movement despite difficult technical matters.

Neuroimaging investigates the neuronal correlates of a function in the normal brain. New methods are now beginning to emerge for more comprehensive analysis of fMRI data. However, it is often difficult to assess the specific role of each region from the usually obtained patterns of activation and to identify the necessary anatomical component(s) and connections that sustain the studied function. Neuropsychology on the other hand, allows the identification of deficits related to a damaged brain region but with
no precise anatomical definition. Also, the consequences of the recovery mechanisms are difficult to assess. Therefore, the cross-comparison of these methods may allow us to validate findings concerning characteristics of the sensorimotor function. After first reviewing the main paradigm differences between neuroimaging and neuropsychology, we will identify the main parietal foci activated during a reaching task in fMRI or PET studies by means of a meta-analysis. Then, we will present fMRI data from a study suitably designed to further test the emerging foci for their role as an interface of vision and motor integration. Finally, we will review the main results coming from OA patient studies and compare these results with what has been found in fMRI experiments. The main focus of our polymodal approach is to provide further evidence for a fronto-parietal gradient of visuomotor information processing and to identify parietal regions involved in the processing of hand effect and field effect in analogy to OA.

2. Paradigm differences between neuroimaging and patient studies

Due to the technical limits imposed by the MRI machine, most fMRI studies claiming to investigate brain activity related to reaching have not used proper reaching movement. Instead, the subjects were asked to orient their wrist in order to point with their index finger in direction of the target (e.g. Astafiev et al., 2003; Connolly, Goodale, DeSouza, Menon, & Vilis, 2000; Connolly, Andersen, & Goodale, 2003; Simon, Mangin, Cohen, Le Bihan, & Dehaene, 2002). In this case, only the direction of the target has to be computed but not its exact spatial position. Some studies have even used a joystick to get spatially oriented movements (e.g. Oreja-Guevara et al., 2004). We can question the degree to which the results of studies which use such ecologically invalid movements are able to reveal neural structures involved in reaching.

In the same vein, in fMRI, because the subjects are lying supine in the scanner, the target presentation is a real problem. Most of the time, it is resolved by using a mirror fixed to the head coil that reflects the image of the visual target (e.g. Astafiev et al., 2003). However, this induces a dissociation between the space in which the movement is performed and where the target is presented. Some recent studies have chosen to tilt the subjects head in the MRI coil (Prado et al., 2005) or to tilt the head and the torso (Beurze, de Lange, Toni, & Medendorp, 2007) in order to have a direct view of the target and to be able to fit the movement direction to the actual target position. The matter of the mirror is important because it induces extra spatial transformations that also cause activation in the PPC. In a PET study, Binkofski et al. (2003) directly compared the brain activation induced by reaching to a visual target while directly viewing the scene or by looking at the target through a mirror. They showed that pre-motor and posterior parietal areas are additionally activated in the mirror condition. These areas are the ones primary activated in any reaching task. Furthermore, Binkofski, Buccino, Dohle, Seitz, and Freund (1999) and Binkofski et al. (2003) have isolated a specific neurological disorder called mirror ataxia. This pathology is characterised by pronounced mis-reaching towards objects that are presented through a mirror (Binkofski et al., 1999). Such patients are unable to operate in the mirrored space, and need considerable corrections to be able to grasp the object. Interestingly, most of these patients do not present OA. Mirror ataxia seems to rely on a different lesion site, the anterior part of the IPL. These observations raise a fundamental question about the use of a mirror to present targets in fMRI studies.

Another striking example of differences between paradigms used in fMRI and in behavioural patient studies is linked to one of the most counter-intuitive results of OA experiments. It is the effect of a delay between the target presentation and the movement execution. Whereas control subjects’ behaviour in such condition is worse than in immediate pointing, patients with OA are more accurate when they reach toward a memorised target (Milner, Paulignan, Dijkerman, Michel, & Jeannerod, 1999; Milner et al., 2001; Rossetti et al., 2005). The authors explain this phenomenon by the existence of an additional pathway for visually guided action based on memorised position which could be the ventral pathway instead of the dorsal one used for immediate pointing. This idea has been reinforced by studies of a visual agnosia patient (DF) who showed the reverse pattern of behaviour, i.e. her reaching capacities which are not impaired in the normal condition are drastically low in the delayed condition (Milner et al., 1999). However, to minimise the effect of the movement that causes artefacts in the scanner, and to concentrate on the planning part of the action, many fMRI experiments have added a delay between the target presentation and the movement execution (e.g. Medendorp, Goltz, Crawford, & Vilis, 2004; Connolly et al., 2003). Interestingly, neuroimaging experiments do not show a shift from the involvement of the dorsal stream to the ventral stream in the delayed condition but still show activation in the parietal areas. But no study has directly asked any of these questions; therefore we still cannot determine the effect of these paradigm differences based on previous studies.

3. Reaching: a meta-analysis of neuroimaging studies

As highlighted above, the neuroimaging studies investigating reaching are using different paradigms. Furthermore, depending on the chosen contrasts and control conditions, the results obtained can differ considerably. For example, a large number of different parietal activation coordinates have been reported in the literature (Fig. 1A), thus it could be interesting to know if these represent different foci or if they can be grouped into clusters to isolate the main areas. A way to get the pertinent network involved in a specific function while ignoring the inherent experimental differences is to realise a function-location meta-analysis. A popular method to realise statistically relevant meta-analysis is activation likelihood estimation (ALE). This method was initially developed by Turkeltaub, Eden, Jones, and Zeffiro (2002) and was integrated, after some modifications (Laird et al., 2005), to an application called GingerALE (http://www.brainmap.org/ale/index.html), which is part of the Brainmap software. We used this method to investigate the reaching network that is the most reliable independent of inter-study differences (Fig. 1B). The meta-analysis is based on 12 papers studying reaching as well as recent data of our own (Table 1). We excluded studies of other type of movements (like grasping) and only included studies that published the whole brain activations and not only the region of interests’ coordinates. There are five PET and eight fMRI studies. Most of the peak activations were in Talairach coordinates, which is the reference used by the Gin-
gerALE software, so the activations given in MNI coordinates were spatially renormalized into Talairach space using the icbm2tal function developed by Lancaster et al. (2007). We extracted 366 cortical activation foci (Fig. 1A), each focus was modelled by a 3D Gaussian distribution, defined by a 10-mm full-width half-maximum (FWHM) to give for the ALE analysis. The ALE is calculated for each voxel of the brain. To assess the significance of the results, a non-parametric permutation test with 5000 repetitions was used to test the null hypothesis that the foci are spread uniformly throughout the brain. The ALE algorithm includes a correction for multiple comparisons during the permutation test. The voxels were thresholded at $p < 0.001$ before performing the cluster analysis (Fig. 1B). We used a minimum cluster size of 100 mm$^3$. As a result, we obtained 17 clusters, in the frontal and parietal lobe (Table 2), which constitute the parieto-frontal reference network for reaching. Few more clusters appeared in the results of the meta-analysis (primary motor, somatosensory and visual areas, cerebellum, insula and cingulate) but we choose to concentrate on the parietal and frontal areas.

4. Different parietal foci

The meta-analysis allowed us to extract different parietal regions involved in reaching. We found four bilateral foci located at different points along the antero-posterior axis. The most posterior one (Talairach coordinates; left: $x = -14, y = -86, z = 28$; right: $x = 12, y = -78, z = 34$) seems to correspond to what authors have labelled as the parieto-occipital junction (POJ) or sulcus (POS).

The second pair of foci, more superior and more anterior (Talairach coordinates; left: $x = -16, y = -76, z = 46$; right: $x = 16, y = -66, z = 50$) corresponds to the posterior part of the IPS (pIPS) also called precuneus when the activation is more medial. Connolly et al. (2003) have proposed that this region is the human parietal reach region (PRR as it is more activated for hand movement than for saccades (see also Astafiev et al., 2003). Moreover, this region seems more implied in reaching in peripheral vision (Prado et al., 2005) than in central vision.

Since pIPS and POJ are on each side (superior or inferior) of the POS, this global area is the most probable candidate as the
human homologue of the monkey V6 complex. Possibly the inferior part is homologue to the purely visual monkey area V6 whilst the superior portion V6A is a visuo-motor area, although they are often considered as the same functional region. Culham, Gallivan, Cavina-Pratesi and Quinlan (2008) have called these two regions upper and lower POJ based on the anatomical separation through the parieto-occipital junction.

The third pair of foci, more anterior within the IPS (Talairach coordinates: left: x = −26, y = −56, z = 56; right: x = 18, y = −60, z = 54) corresponds to the middle part of the IPS (mIPS). This region is closely involved in the processing of visually guided movements (e.g. Grafton, Fagg, Woods, & Arbib, 1996; Kertzman, Schwarz, Zeffiro, & Hallett, 1997; Prado et al., 2005).

The last bilateral parietal foci, the most anterior ones (Talairach coordinates; left: x = −32, y = −40, z = 52; right: x = 30, y = −38, z = 56) correspond to the anterior part of the IPS (aIPS). This region is very close to the area that has been identified as specialised in grasping (Frey, Vinton, Norlund, & Grafton, 2005; Culham et al., 2003; Binkofski et al., 1998). However, even if this region is more activated in grasping than reaching, it is still activated during reaching (Culham et al., 2003).

We can wonder if different sub-functions can be assessed to these different regions. As these regions stem from anatomically defined clusters, it is more than appropriate to scrutinise the functional differences and similarities within these modules of the dorsal stream.

5. Target and hand positions integration

A possible function to attribute to these different occipito-parietal modules can be related to the hand and target positions integration. In order to plan a reaching movement toward a visual target, it is necessary to integrate both target and hand positions in the same reference frame. By its location between the visual and the somatosensory cortices, the PPC is considered to sustain this integration by combining visual and proprioceptive information. Buxton et al. (1999) proposed a model of sensorimotor transformation in which the visual-to-somatic information integration occurs along the postero-anterior axis inside the parietal cortex.

We therefore designed an fMRI experiment with a task that included reaching in peripheral vision to investigate the visual-to-somatic gradient and tested nine healthy subjects with normal vision inside a 3-T Siemens Trio Machine. Subjects lay supine in the scanner with their heads tilted forward by a 30°-angled coil position. Subjects were able to directly see the fixation point, target and their hand throughout the whole movement. There were 18 different random target positions that were grouped in far left, near left, central, near right and far right visual field. We had 16 repetitions of target presentation for each group of target eccentricity and for each hand. Additionally, 10 null events per hand were included. The movements were made by the left hand and the right hand in blocked sessions. 34 transversal slices (192 mm FOV, 64 × 64 matrix, 2 mm thickness, 1 mm spacing), parallel to the AC-PC plane and covering the whole brain were acquired using an EPI sequence (TR 2000 ms, TE 25 ms, 70° flip angle). Data analysis was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.63, part of FSL (FMRIb’s Software Library, www.fmrib.ox.ac.uk/fsf). Functional data were motion-corrected using MCFLIRT (Jenkinson, Bannister, Brady, & Smith, 2002). To correct for the temporal offset between the slices acquired in one scan, a fourier-space time-series phase-shifting was applied. Non-brain voxels were removed using BET (Smith, 2002). To correct for large drifts, a temporal high-pass filter (Gaussian-weighted least-squares straight line fitting) was used for baseline correction of the signal. A spatial smoothing using a Gaussian kernel of 5 mm FWHM as well as mean-based intensity normalisation of all volumes by the same factor was applied to the functional data. To align the individual functional data slices onto the corresponding 3D stereotactic coordinate reference system (MNI), a rigid linear registration with six degrees of freedom (three rotational, three translational) was carried out using FLIRT (Jenkinson & Smith, 2001). We used the coordinates of cluster centres isolated from the meta-analysis, namely the four bilateral parietal foci as well as premotor areas and IPL, to compare the activation (betas estimates from condition-null event) between all our conditions (hands and visual fields) (Fig. 2). Since FSL is operating in MNI space, the coordinates analysed (Fig. 2) are in MNI space.

Fig. 2 shows that depending on the parietal foci, the difference in activation between the two hands increases as one moves away from the POJ. At the POJ, the two curves are practically superimposed, whereas there is an increasing difference between them in pIPS, mIPS, aIPS and PMd as illustrated by the histograms. Moreover, the difference of activation between the two hands is significant for PMd, aIPS and mIPS (all nLeft = 4, nRight = 4; Mann–Whitney U = 0; adjusted Z = 2.309; p < 0.05) but not for POJ and pIPS (all nLeft = 4, nRight = 4; Mann–Whitney U ≥ 3; adjusted Z = 1.4; p > 0.05). That is to say that the degree of lateralisation for the contralateral hand is increasing from posterior to anterior areas. This seems to reflect the presence of an antero-posterior gradient in the importance of the hand used for the function for the level of brain activation. Additionally, the slope of the curves, reflecting the influence of the visual field, is decreasing from pIPS to aIPS, indicating that the importance of the target position for the level of activation decreases from pIPS to aIPS and PMd. Indeed, the difference of activation between the two visual fields is significant for pIPS bilaterally and for right POJ (all nLeft = 4, nRight = 4; Mann–Whitney U = 1; adjusted Z = 2.5; p < 0.05) but not for the other foci (all nLeft = 4, nRight = 4; Mann–Whitney U ≥ 3; adjusted Z = 3; p < 0.05). Thus, the parametric analysis for the contralateral visual stimulation is therefore much stronger in anterior areas than in posterior ones.

The results of our fMRI study underpin the different representation of the hand and the field effect in the parietal lobe. Some other neuroimaging studies have asked this question of the target-hand positions integration (Kertzman et al., 1997; Medendorp et al., 2004; Beurze et al., 2007) and also showed that the parietal areas are more activated by a contralateral stimulus and when the contralateral hand makes the movement compared to ipsilateral stimulation. But the novel finding of our study is that we can demonstrate the existence of an increasing activation difference between contralateral and ipsilateral hand from posterior to anterior areas and a reverse effect for the difference between con-
Fig. 2. Illustration of the location of the voxels of interest that have been selected from the meta-analysis (the four bilateral parietal clusters, bilateral premotor, IPL and SMA) on a template. For each voxel of interest, we extracted the bold activation (beta estimate) from our reaching fMRI study for each hand (blue line: left hand, green line: right hand) and for each target eccentricity: FL: far left; NL: near left; C: central; NR: near right; FR: far right. The histograms represent the mean and standard deviation of the beta estimate for each hand (dark blue, left hand; dark green, right hand) and each field (light blue, left field; light green, right field). The significance of the hand and field differences were estimated using non-parametric Mann–Whitney U-test. The asterisks indicate that the difference is significant ($p < 0.05$) and NS (not significant) that it is not.
tralateral and ipsilateral visual stimulation. We clearly show results that are in line with the gradient model, i.e., a stronger influence of the hand in anterior part of the parietal cortex and a stronger influence of the visual field in the posterior part (Burnod et al., 1999).

The integration of both pieces of information about the arm and the visual field has to be linked to the hand and field effect in OA.

6. Hand effect and field effect in OA

The most famous OA patient population study is presented in the Perenin and Vighetto (1988) paper. They studied visually directed arm movement in 10 stroke patients with unilateral OA, three with right hemisphere lesions and seven with left hemisphere lesions. They tested both hands in both hemifields and revealed that patients produce pointing errors in their contralateral field, which is called the field effect, as well as when they reach with their contralateral hand, which constitutes the hand effect. The existence of these two effects can be related to the activity found in the parietal cortex depending on the visual field and the hand used. In order to be able to compare these results with behavioural data from OA patients, we need to know which parts of the parietal cortex are lesioned in OA.

The lesion site responsible for OA was classically attributed to the superior lobule of the posterior parietal cortex (SPL) and/or the intraparietal sulcus (IPS) (Ratcliff & Davies-Jones, 1972; Perenin & Vighetto, 1988; Jeannerod and Rossetti, 1993). Perenin and Vighetto (1988) overlaid the lesions of two right and six left brain-damaged patients and found that the IPS was involved in 100% of the patient cases and that the SPL (mainly the pre-cuneus) was involved in six patients out of eight. They concluded that the main site responsible for OA includes the IPS and the SPL (pre-cuneus area). In a recent study from Karnath and Perenin (2005), the comparison of the lesions of 10 left and 6 right brain-damaged patients implicated the SPL (60% of the left lesions and 50% of the right lesions), the inferior parietal lobule (IPL) (70% of the left lesions and 100% of the right lesions), the pre-cuneus (63.5% of the cases) and the parietal white matter (86.5% of the cases). After subtracting the lesion sites of control patients with unilateral lesion without OA, they showed an overlap region involving the IPL, the pre-cuneus and the parieto-occipital junction (POJ). They concluded that the centre of the lesions overlap involves damage of the POJ at the level of the IPL, with an extension to the pre-cuneus close to the POJ via the underlying white matter.

Rossetti and collaborators (this issue) overlaid the lesions of 11 pure OA patients (5 left, 4 right unilateral and two bilateral PPC lesions) after drawing them on the MNI template and showed that the lesions are centred in the parieto-occipital regions. The centre of the maximum overlap zone is situated just in front of the POJ (left hemisphere: x = −24, y = −66, z = 44; right hemisphere: x = 30, y = −68, z = 46; MNI space). Fig. 3 shows the overlap of the main area lesioned in OA with the clusters isolated from the meta-analysis.

The centre of the maximum OA patient’s lesion overlap is located between the two most posterior clusters that we isolated from the meta-analysis and corresponds to the area revealed by Prado et al. (2005) as being specific to reaching a target in peripheral vision. In their recent fMRI study they asked their subjects to look at and reach for a visual target or simply reach for the target while keeping central fixation. In addition to the classical parieto-frontal network involved in pointing to a central vision target (mainly PMd and mIPs), they found that the parieto-occipital junction was activated specifically in the peripheral vision condition. This result has to be related to the fact that pure OA patients, even with a bilateral lesion, are not impaired when they reach for a target that they fooveate, whereas they are very inaccurate in peripheral vision (for a discussion of this aspect see Rossetti et al., this issue). Moreover, the reaching errors of the patient increase drastically with the target eccentricity from gaze fixation (Rossetti et al., 2005; Blangero et al., in press). This increased inaccuracy could be explained by the increased brain activity in this region with target eccentricity (Fig. 2), which would mean an increasing contribution of the pIPs/POJ to reaching accuracy when target eccentricity increases.

The pIPs region is also close to the region isolated by Medendorp et al. (2004), which represents, initially or after updating, the position of the target to be reached for, in eye-centred coordinates. The authors called this region retinal IPS (retIPS) and they showed an inter-hemispheric transfer of target activation in case of a trans-saccadic remapping (Medendorp et al., 2003), anti-saccade (Medendorp et al., 2005a) or even memory-guided double saccade (Medendorp et al., 2005b). Khan et al. (2005) showed in unilateral OA patients, during a trans-saccadic remapping task, that what is important for the field effect is the hemisphere in which the target is represented after the remapping, and not the visual field in which the target has been initially presented. It was also one of the first studies to clearly demonstrate that the reaching impairment of pure OA patients depends on the eye position. Other studies have confirmed this finding (Dijkerman et al., 2005; Blangero et al., in press). A disruption of the eye-centred representation of the contralateral visual target to be reached for that would correspond to the most posterior parietal foci could therefore account for the field effect of OA patients’ misreaching.

It is also important to note that in the area damaged in OA, there is a clear influence of which hand is reaching (ipsilateral or contralateral). This indicates that information about the hand is integrated in the mIPs and the pIPs (Fig. 2). A recent study involving proprioceptive pointing in unilateral OA patients showed that they are severely impaired when asked to localise their contralateral hand, despite normal primary proprioceptive and tactile sensations (Blangero, Ota, Rossetti, & Pisella, 2007). In agreement, an fMRI study conducted by Pelljieff, Bonilha, Morgan, McKenzie and Jackson (2006) showed that a change in the posture of the upper limb is associated with a significant increase in BOLD activation in the PPC, mostly around the mIPs (stronger z score at talairach coordinates: x = −8, y = −62, z = −56). This study clearly demonstrates the presence of proprioceptive information about the hand position in the areas that represent the target position. A disruption of this region could therefore explain the deficit in localising the contralateral hand and could account for the hand effect found in OA patients. There is an ongoing debate concerning the lateralisation of the hand effect. In their study, Perenin and Vighetto (1988) reported that lesions of the right hemisphere resulted in a field effect only whereas lesions of the left hemisphere induced an additional hand effect. However, Maeshima, Komai, Shigeno, Nakai and Dohi (1991) showed that five right and four left brain damage patients showed reaching errors in the ipsilesional visual field with the contralateral hand (hand effect). In Fig. 2, we can observe that the difference between the hands is slightly stronger in the right hemisphere, which would be consistent with a relative dominance of the left hemisphere for the hand position integration. However, more pieces of evidence are needed to draw conclusion on this point.

From Fig. 3, we can see that three of the four bilateral parietal foci isolated from the meta-analysis are involved in the OA lesion, but the most anterior (aIPs) is spared. This anterior parietal area corresponds to the area isolated by Binkofski et al. (1998) as responsible, when damaged, for the grasping deficit of parietal patients. Therefore, there can be a dissociation between pure OA and grasping deficit in central vision, depending on whether aIPs is involved in the parietal lesion or not. In an elegant fMRI study from (Culham et al., experiment 1, 2008) and Cavina-Pratesi et al. (2006), the authors compared the activation related to grasping versus the
activation due to the transport of the hand. Subjects were asked to grasp an object that was close to the hand, or far from it (involving a reach for the object). The aIPS was activated due to the grasping component, but the subtraction of these conditions, revealing the transport component, activated the POJ.

7. Conclusion

The hand and field effect revealed in OA reaching behaviour can be explained by the disruption of the parietal target-hand integration areas. These areas are organised along a postero-anterior gradient of visual-to-somatic information integration.

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References


Fig. 3. Overlay of the main regions damaged in three (dark blue) to eight (light blue) OA patients. The squares represent the clusters identified in the meta-analysis (in red: the three posterior parietal foci that are included in the lesion overlap; in orange: the fourth posterior parietal foci spared by the lesion overlap; in yellow the other foci). Adapted from Rossetti et al. (this issue).


