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Cross-Modal Plasticity Preserves Functional Specialization in Posterior Parietal Cortex

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In congenitally blind individuals, many regions of the brain that are typically heavily involved in visual processing are recruited for a variety of nonvisual sensory and cognitive tasks (Rauschecker 1995; Pascual-Leone et al. 2005). This phenomenon—cross-modal plasticity—has been widely documented, but the principles that determine where and how cross-modal changes occur remain poorly understood (Bavelier and Neville 2002). Here, we evaluate the hypothesis that cross-modal plasticity respects the type of computations performed by a region, even as it changes the modality of the inputs over which they are carried out (Pascual-Leone and Hamilton 2001). We compared the fMRI signal in sighted and congenitally blind participants during proprioceptively guided reaching. We show that parietooccipital reach-related regions retain their functional role—encoding of the spatial position of the reach target—even as the dominant modality in this region changes from visual to nonvisual inputs. This suggests that the computational role of a region, independently of the processing modality, codetermines its potential cross-modal recruitment. Our findings demonstrate that preservation of functional properties can serve as a guiding principle for cross-modal plasticity even in visuomotor cortical regions, i.e. beyond the early visual cortex and other traditional visual areas.

Keywords: congenital blindness, cross-modal plasticity, proprioceptively guided reaching

A large number of studies in humans have highlighted the massive potential of cross-modal plasticity to reorganize the functional architecture of the brain (Rauschecker 1995; Bavelier and Neville 2002). This has been best documented in congenitally blind individuals whose visual cortex is now known to be recruited for a wide range of sensory and cognitive tasks (Burton et al. 2002; Amedi et al. 2003; Pascual-Leone et al. 2005; Bedny et al. 2011). However, less work has been devoted to describing more general principles that determine where and how cross-modal plasticity emerges (Pascual-Leone and Hamilton 2001; Bavelier and Neville 2002), and studies testing them directly in humans have been scant (Mahon et al. 2009; Renier et al. 2010; Collignon et al. 2011; Reich et al. 2011). Here, we try to evaluate one such principle—the claim that cross-modal plasticity preserves the types of computations a brain region performs, even though many other aspects of the region's function, such as the dominant modality of the inputs it processes, are altered.

This claim, spelled out most directly in Pascual-Leone and Hamilton (2001), is motivated by several recent reports of functional homologies between different modalities within certain brain regions undergoing cross-modal plasticity (Amedi et al. 2004; Renier et al. 2010; Collignon et al. 2011; Reich et al. 2011). There is evidence, for instance, that an area in the occipitotemporal cortex that is differentially activated during visual reading in the sighted becomes recruited during tactile reading of Braille characters in congenitally blind individuals (Reich et al. 2011). Such results suggest a potentially important role of functional specialization in determining the organization of cortical regions that is to a considerable degree independent of the modality of the inputs they receive.

We test the hypothesis by comparing the patterns of activity in the posterior parietal cortex (PPC) in sighted and congenitally blind individuals executing proprioceptively guided hand reaching actions, a region that has been left largely unexplored by prior studies on cross-modal plasticity. Besides being involved in a variety of cognitive functions including attention and memory, PPC is known to play a major role in the representation of space and the guidance of actions, combining visual, eye, and arm movement-related signals (Johnson et al. 1996; Burnod et al. 1999; Battaglia-Mayer et al. 2000; 2001; Andersen and Buneo 2002). A dominant feature of organization of PPC is the fact that functional specialization of its subregions varies along the posterior–anterior axis. More posterior regions such as macaque area V6a in the dorsal part of the anterior bank of the parietooccipital sulcus (POS) contain a large proportion of visually responsive neurons (Galletti et al. 1996; 1997; Battaglia-Mayer et al. 2000; 2001). However, as one moves anteriorly to macaque areas PEc, MIP, and PEa and finally area PE the sensitivity for visual stimulation decreases while movement-related activity increases (Johnson et al. 1996; Burnod et al. 1999; Battaglia-Mayer et al. 2001; Marconi et al. 2001). A similar visual-to-motor gradient is observed in the frontal cortex, going from dorsal-rostral premotor cortex (F7) to dorsocaudal premotor cortex (F2) and primary motor cortex (M1) (Battaglia-Mayer et al. 2001; Marconi et al. 2001). These functional gradients in parietal and frontal cortex are also reflected in the reciprocal connections between V6A and F7, PEc and F2, and PE and M1, respectively (Battaglia-Mayer et al. 2001; Marconi et al. 2001), thus providing an ideal anatomical basis for eye–hand coordination during visually guided reaching.

A similar functional organization has been suggested in the human PPC (Filimon 2010). As an example, there are reports of various posterior–anterior gradients associated with visually guided versus proprioceptively guided reaching (Filimon et al. 2009), visual versus motor representations (Stark and Zohary 2008; Heed et al. 2011), sensitivity to reach errors related to encoding of target location versus errors related to motor execution (Diedrichsen et al. 2005), encoding of spatial targets of motor actions versus encoding of effector-related motor programs (Beurze et al. 2009), or integration of information about the position of the target and effector in different reference frames (Beurze et al. 2010).

We emphasize the complementary rather than competing nature of these different accounts. In particular, they seem to converge on broad specialization for maintaining spatial representations of locations relevant for performance of motor

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actions (e.g. the location of the target object) in the most posterior portions of PPC, and around the parietooccipital junction. In macaque area V6 in the ventral part of the anterior bank of the POS, the majority of neurons is visually responsive, whereas V6a, dorsal to V6 in the superior POS (sPOS), contains a large proportion of cells that do not respond to visual stimulation (Galletti et al. 1996). Visual neurons in V6A are sensitive to orientation and direction of movement of visual stimuli (Galletti et al. 1999). Nonvisual cells in V6a are modulated by hand orientation during reach-to-grasp movements (Galletti et al. 1997). The majority of neurons in V6a are modulated during arm reaching movements both in light and in darkness (Fattori et al. 2001). Neurons in V6a respond to different combinations of visual, eye, and arm-related signals (Battaglia-Mayer et al. 2000; 2001). Interestingly, the orientation of preferred directions across different epochs (signal, set, and movement related) and tasks are not distributed equally across space, but rather cluster within a limited range, called global tuning fields. Matching information from the retina, the eye, and the hand within the global tuning fields on the basis of spatial congruence might provide the physiological mechanism for the combination of signals coming from the retina, the eye, and the hand across different epochs and tasks.

In humans, Filimon et al. (2009) demonstrated that sPOS, likely the human homolog of macaque V6a, responds more strongly during reaching with visual feedback in comparison to reaching without visual feedback, whereas the anterior precuneus was equally activated by both types of reaching. In line with this view, lesions to the parietooccipital junction have been shown to lead to optic ataxia, i.e. an impairment in visually guided reaching toward peripheral target locations (Perenin and Vighetto 1988; Battaglia-Mayer and Caminiti 2002; Karnath and Perenin 2005; Pisella et al. 2009). Using left/right reversing prisms, Fernandez-Ruiz et al. (2007) reported that sPOS is more strongly driven by visual target location and visually perceived direction in comparison to actual movement direction. Taken together, these data suggest that the most posterior part of PPC in the vicinity of the sPOS plays a role in visually guided control of reaching and grasping movements. In contrast, the most anterior parts of PPC seem to be involved in mediating representations more closely tied to planning and execution of motor actions with specific effectors. The intermediate subregions of PPC exhibit a mixture of the 2.

The assumption that functional role, rather than modality, is the dominant organizing principle in PPC leads to a prediction about the potential effects of cross-modal plasticity in this region. In the current study, we use the term cross-modal plasticity to describe the effect of changing the dominant (visual) input into a multimodal area known to be strongly (though not exclusively) responsive to visual stimulation to proprioceptive. In this context, we expect the same broad posterior–anterior gradient of specialization to be observed in both sighted and congenitally blind participants. The prediction is especially interesting in the most posterior portions of PPC. In sighted individuals, encoding of spatial information and object-directed reaching typically rely heavily on visual information. For the sighted, the sensory context of proprioceptively guided reaching in our task is thus impoverished of an important source of information. At the same time, the spatial information encoded in posterior parts of PPC is not intrinsically visual. Therefore, in the measure to which cross-modal plasticity preserves function, we would expect an increased sensitivity of this region in the congenitally blind to nonvisual sources of spatial information. Consequently, the posterior part of PPC in the congenitally blind should be more heavily involved in proprioceptively guided reaching, compared with the sighted. In contrast, no differences between congenitally blind and sighted participants should be observed in more anterior regions that are more closely involved in the planning and execution of actions.

Materials and Methods

Participants

Data from 15 sighted (5 female, mean age 34 years, age range 26–60, 1 left-handed) and 15 congenitally blind (8 female, mean age 44 years, age range 26–60, 1 left-handed) participants were included in the analyses. Congenital blindness and the absence of any residual light perception were self-reported by the participants from the latter group. All participants gave a written informed consent to their participation in the experiment, and the study was approved by the Internal Review Boards of Beijing Normal University Imaging Center for Brain Research, Harvard University Psychology Department, and the University of Trento.

Behavioral Task

During the fMRI scan, participants performed proprioceptively guided motor actions with their right hand in a task based on experiments by Fabbri et al. (2010; 2012). Participants lay in the scanner with a custom-made response device (depicted in Fig. 1*a*) strapped to the lower part of their torso. In every trial, participants reached to 1

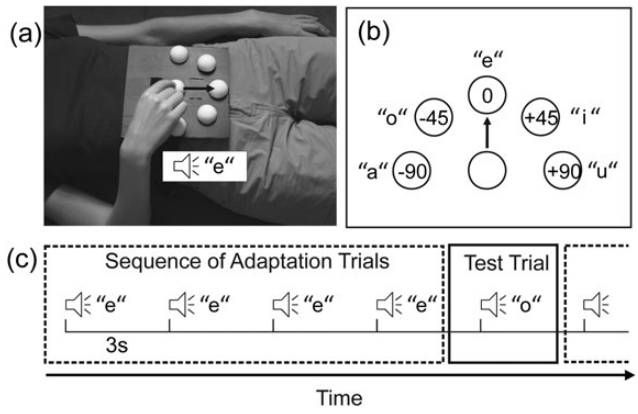

Figure 1. Experimental setup and behavioral task. (*a*) The response device used in the experiment. The device consists of a board with target locations and the starting location marked with plastic half-spheres. The response device was strapped to the lower torso of the subject. During the experiment, participants lay on their back in the fMRI scanner, and could not see their hand while performing the required reaching actions at the target locations. At the beginning of each trial, participants had the index finger of their right hand resting at the target location. The target location and the Type of Motor Act to be performed were indicated by an auditory cue. The cue consisted of a vowel pronounced by a male or a female speaker. The gender of the speaker indicated the Type of Motor Act (Point, Grasp), and each vowel corresponded to one of the 5 different reach directions. (*b*) A schematic layout of the target locations on the response device. Reach directions during test trials represented different angular deviations from the adapted direction (−90, −45, 0, +45, +90°). Note that the vowels used as instructions followed the Chinese alphabetical order from the left-most to the right-most (i.e. a, o, e, i, and u) target location. (*c*) Participants performed a variable number of adaptation trials (pointing, Reach Direction 0°), which were followed by a single test trial that differed in the Reach Direction, the Type of Motor Act, or both. Note that for data analysis, only test trials were considered.

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of 5 possible locations (marked −90, −45, 0, 45, and 90 according to the angular degree of deviation from one of them; see Fig. 1*b*), and either pressed or grasped a plastic half-sphere attached at the target location. The particular combination of "Reach Direction" and "Type of Motor Act" was indicated by a sound stimulus presented at the beginning of each trial (see Fig. 1*c*). The sound stimulus consisted of a vowel pronounced by either a male or a female speaker. Each target location had a single vowel associated with it, and the Type of Motor Act was conveyed by the gender of the speaker. The vowels, "a," "o," "e," "i," and "u," (arranged in Chinese alphabetical order) corresponded to directions −90, −45, 0, 45, and 90°, respectively. Female voice denoted pressing the target sphere with the index finger, male voice denoted grasping the target sphere with a whole-hand grasp. Participants were instructed to perform the desired reaching action, and after its completion, return with their index finger to the central half-sphere to wait for the onset of the next trial. Trial repetition time was 3 s. Participants received extensive training outside the scanner prior to the start of the experiment.

Experimental Design

We used an fMRI rebound design (Piazza et al. 2004; Fabbri et al. 2010) for ordering of trials during the scans. In this design, participants perform a variable number (between 3 and 8) of adaptation trials of a single type (Reach Direction: 0°, Type of Motor Act: Point), followed by a single test trial that may differ from the adaptation trial in the Reach Direction, the Type of Motor Act, or both. The same type of adaptation trial was used for all participants. As Fabbri et al. (2010) demonstrate, different adaptation directions do not change the qualitative character of the results obtained with the rebound paradigm.

For each participant, we collected data from 12 scanning runs. A single run lasted 490 s, and included 12 test trials. There were 10 (2 types of motor act × 5 directions) types of test trials. Each type of test trial was presented once during a run, with the exception of test trials in direction 0, which appeared twice per run because we intended to collapse test trials with positive (+90, +45) and negative (−90, −45) sign. As a result, there were 12 test trials per run.

Data Acquisition

Anatomical and functional magnetic resonance images were acquired on a 3T Siemens Trio scanner at Beijing Normal University. Functional images were collected using the following parameters: TR 2000 ms, TE 33 ms, flip angle 73°, matrix size 64 × 64, voxel resolution 3.125 × 3.125 × 4 mm, 32 slices with interleaved axial acquisition, gap thickness 0.8 mm. Structural images were collected with TR 2530 ms, TE 3.39 ms, flip angle 7°, matrix size 256 × 256, voxel resolution 1 × 1 × 1 mm, 128 sagittal slices.

fMRI Data Processing

Data analysis was performed using AFNI (Cox 1996) and Freesurfer (Dale et al. 1999; Fischl et al. 1999) software packages, and custom-written software in Python and R. For each subject, a high-resolution anatomical image was aligned with the first volume of the first functional run. The raw time series in each voxel of the functional volumes was time-shifted to account for the temporal order of acquisition of the individual slices. The functional volumes were then motion-corrected, masked so as to exclude any nonbrain voxels, and the time series in each voxel contained within the brain mask was scaled to a common mean. No smoothing was applied at this stage.

For each participant, we estimated a general linear model (GLM) of the fMRI time series. The model included a single regressor modeling the adaptor trial, and 1 regressor for every type of test trial, for 11 regressors (adaptation trial; test trial motor act "point," Reach Direction ±90, ±45°; test trial motor act "grasp," Reach Direction ±90, ±45°). The trial regressors were created by convolving a boxcar function indicating when the participant was performing trials of a given type with a canonical double-gamma hemodynamic response function. The model further included constant, linear, and quadratic dummy regressors for each scanning session to account for signal baseline shifts between sessions as well as slow signal drifts within sessions, 6 regressors containing the estimated motion-correction parameters to reduce any residual motion-induced signal changes, and, finally, the temporal derivatives of the trial-type regressors.

Using Freesurfer, we created a model of the cortical surface from the high-resolution anatomical image of every participant. Individual surfaces were then remapped to a standard space with AFNI' program MapIcosahedron. The estimated coefficients (β's) of the 11 trial type regressors from the single-subject GLMs were then interpolated from each voxel onto the nodes of the subject's standardized surface model. On the surface, the interpolated parameter estimates were then iteratively smoothed with AFNI' program SurfSmooth until their estimated smoothness reached the equivalent of a gaussian with an 8-mm full-width half-maximum (Saad et al. 2006).

Group analyses were subsequently performed by evaluating a random effects model at every surface node in the standard space. Results of the group analyses are visualized on the fsaverage template brain shipped with Freesurfer (Fischl et al. 1999).

Whole-Brain Analysis

We ran a random effects (RFX) GLM analysis, including the factors Reach Direction (0°, ±45°,±90°), Type of Motor Act (adapted, nonadapted), and Subject Group (normal sighted, congenitally blind). This analysis was carried out on the surface, FDR corrected ($P < 0.001$) for multiple comparisons (Genovese et al. 2002). To identify areas involved in proprioceptively guided reaching, we computed the contrast Reach Direction versus baseline, collapsed over Type of Motor Act, and Group. To test whether visual experience modulates the sensitivity to proprioceptively guided reach direction across different types of motor acts, we computed the contrast "Reach Direction × Type of Motor Act × Group."

Analysis of Anatomy/T value Overlay

We aimed to investigate how the *T* values from the random effects model of the whole-brain contrast nonadapted motor act, Reach Direction ±90, ±45° >nonadapted motor act, Reach Direction 0° vary as a function of position on the anterior–posterior axis in the parietal cortex. For this analysis, we used the anatomical parcellation of the cortical surface into major gyri and sulci provided with the fsaverage template brain (Fischl et al. 2004). Using this parcellation scheme, we selected 2 elongated regions ranging from the superior occipital to the anterior parietal cortices in each hemisphere. In particular, 1 of these regions spanned the superior occipital gyrus (SOG), and the superior parietal gyrus (SPG) as labeled on fsaverage. The other spanned the superior occipital sulcus and intraparietal sulcus (IPS). Each of these elongated regions was subsequently manually subdivided into 13 cells (see Fig. 3*a*, ~30 voxels per cell), with cuts going roughly perpendicularly to the IPS. The cells thus divide the regions along the anterior–posterior axis in roughly even steps. For each cell, we then computed the average *T* values from the random effects models of the contrast, and plotted the average *T* values against the position of the corresponding cells in each region.

Results

In our analyses, we aimed to characterize cortical networks in which the direction of a reaching action is encoded in the 2 groups. Moreover, we aimed to investigate the degree to which direction encoding generalizes over lower level aspects of the movement such as the type of motor act, and how this more abstract representation is affected by visual experience. We reasoned that voxels containing neuronal populations sensitive to Reach Direction should maximally adapt when the direction during test trials and adapted trials are identical. Moreover, the BOLD signal should show a rebound from adaptation proportional to the angular difference between the adapted and the tested direction (Fabbri et al. 2010, 2012). Neuronal populations that code reach direction irrespective of

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the type of motor act should show a transfer of adaptation from the adapted to the nonadapted motor act, whereas neuronal populations that are sensitive to type of motor act should show no such transfer.

We pursued 3 strategies to characterize the encoding of reach direction in the sighted and in the congenitally blind. First, we identified the network of areas involved in proprioceptively guided reaching. Second, to examine if the generalization of adaptation to reach direction from the adapted to the nonadapted motor act differs between groups, we performed a whole-brain analysis for the interaction Reach Direction × Type of Motor Act × Group. Third, we focused on direction encoding in regions in the parietal and superior occipital cortices, and investigated how such encoding depends on the anatomical localization of each region on the anterior–posterior axis.

Whole-Brain Analysis

To identify areas involved in the decoding of reach direction, we first carried out a whole-brain RFX GLM analysis with the factors Reach Direction versus Baseline (see Fig. 2*a*). This analysis revealed an extensive frontoparietal network, including dorsal and ventral premotor areas, primary motor cortex (M1), postcentral gyrus, inferior parietal lobe (IPL), IPS, SPG, precuneus, cuneus, POS, SOG, and inferior occipital sulcus (IOS), in line with previous studies (Fiehler et al. 2009; Filimon et al. 2009; Cavina-Pratesi et al. 2010; Fabbri et al. 2010, 2012). Next, to identify areas showing a transfer of adaptation for reach direction from the adapted to the nonadapted motor act that differs between groups, we carried out a whole-brain RFX GLM contrast for the interaction Reach Direction × Type of Motor Act × Group (see Fig. 2*b*). This contrast revealed a bilateral network extending from the anterior IPS and the parietooccipital junction to occipital regions, including the SOG, intraoccipital sulcus, inferior occipital gyrus, and the cuneus. In the left hemisphere, the regions revealed by this contrast extend more anteriorly than in the right hemisphere.

Analysis of Anatomy/T-value Overlay

Having established an interaction between Reach Direction, Type of Motor Act, and Group, we then sought to clarify the nature of this interaction using post hoc contrasts and testing for simple main effects. We chose to do this by examining the effect of Reach Direction for each Group separately, for the nonadapted motor act. Furthermore, instead of presenting the results as a whole-brain analysis, we restricted the focus of the investigation to an analysis of the average *T* values within small cortical parcels along the anterior–posterior axis through parietal and occipital cortices. To do so, we divided the parietal and parietooccipital cortices in each hemisphere into 2 elongated regions that were, in turn, subdivided into smaller cells along the anterior–posterior axis (Fig. 3*a*, see Materials and Methods section for details). Next, we computed the random effects *T* value of the contrast nonadapted Motor Act, Reach Direction ±90, ±45° >nonadapted Motor Act, Reach Direction 0° as an index of involvement of an area in the encoding of hand reach direction irrespective of changes in the type of motor act. To assess how this involvement varies in different parts of the parietal cortex with their anatomical location, we plotted the mean *T* value in each cell as a function of the cell's position on the anterior–posterior axis (Fig. 3*b*).

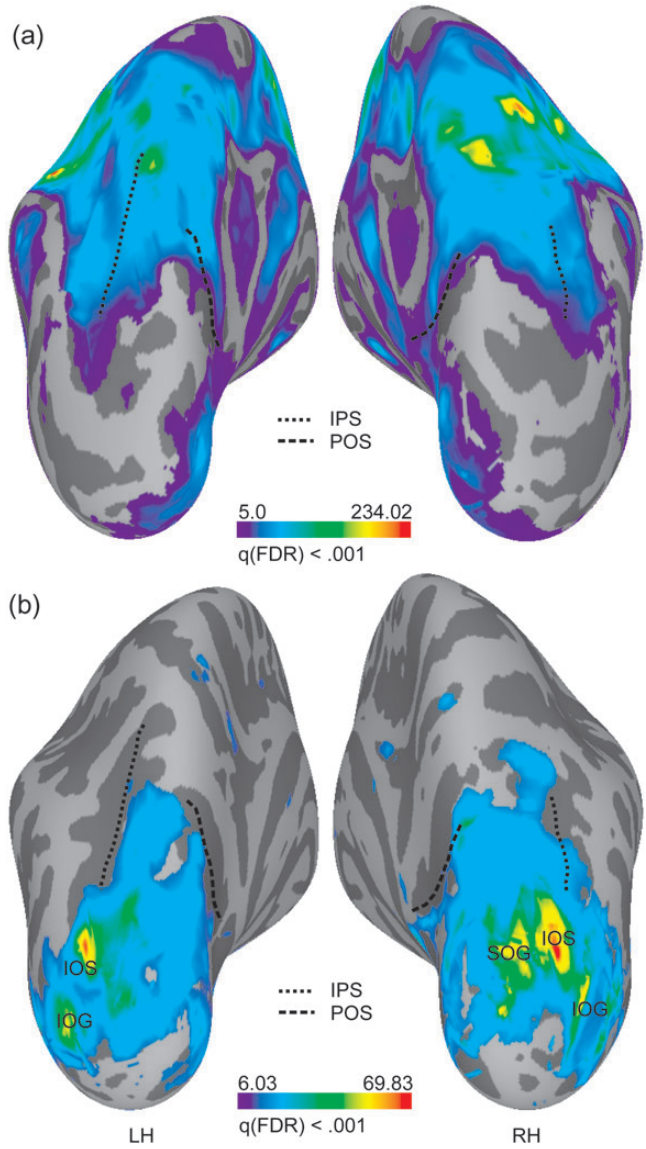

Figure 2. (*a*) Whole-brain RFX GLM contrast for the factor Reach Direction (thresholded at FDR < 0.001), collapsed over Type of Motor Act and Group. IPS, intraparietal sulcus; POS, parietooccipital sulcus. (*b*) Whole-brain RFX GLM contrast for the interaction "Reach Direction × Type of Motor Act × Group," thresholded at FDR < 0.001. IOS, inferior occipital sulcus; IOG, inferior occipital gyrus; SOG, superior occipital gyrus.

The 4 regions that we tested exhibit a similar pattern of dependence of the mean *T* values on anatomical location. The congenitally blind exhibit consistently higher *T* values in the superior occipital cortex and at the interface of the occipital and parietal cortices. This difference progressively diminishes throughout the subregions in the posterior parietal cortex. In the most anterior parts of the parietal cortex, the sighted tend to exhibit higher *T* values compared to the congenitally blind, although this group difference is not as pronounced as the one around the parietooccipital junction. Similar to the results shown in Figure 2*b*, Figure 3*b* suggests some hemispheric differences in the patterns of changes of the mean *T* values along the anterior–posterior axis. In particular, in the left

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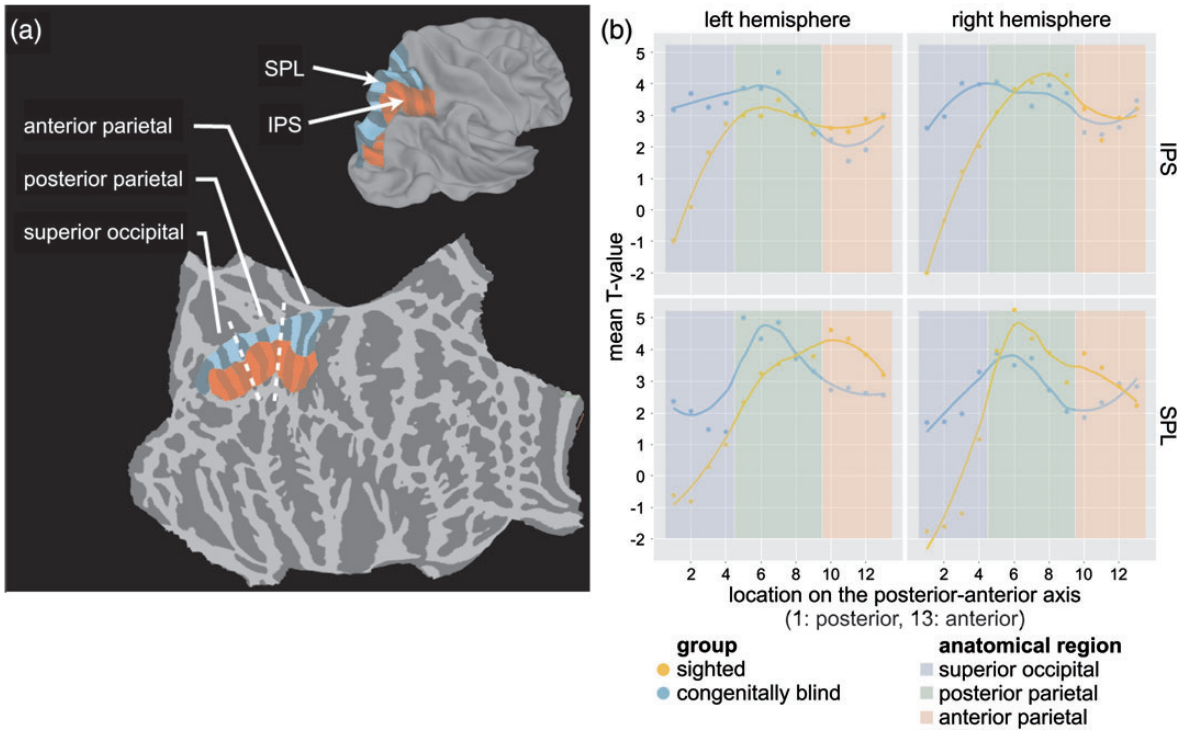

Figure 3. Sensitivity to reach direction as a function of anatomical location in PPC. To investigate the spatial patterns of sensitivity to reach direction (independent of the type of motor act) in PPC, we plot the *T* values from the random effects model of the contrast nonadapted motor act, Reach Direction ±90, ±45° >nonadapted motor act, Reach Direction 0° for each group as a function of anatomical location. (*a*) We divide PPC and a portion of the superior occipital cortex into 2 large regions, labeled SPL (marked in blue) and IPS (marked in red). Each of these regions is further subdivided into 13 smaller cells along the anterior–posterior axis, indicated by the shading on the color patches in the figure. (*b*) We computed the mean *T* value from the above random effects model of all of the surface nodes included in each cell. For each cell, we then plotted the mean *T* value as a function of the cell's position along the posterior–anterior axis. The congenitally blind exhibit systematically higher *T* values in posterior parietal and superior occipital areas. This effect is particularly pronounced in the left hemisphere.

hemisphere, greater *T* values for the congenitally blind persist more anteriorly along the parietal cortex. In the right hemisphere, the congenitally blind only maintain greater mean *T* values at the parietooccipital junction and more posteriorly in the superior occipital cortex.

Taken together, these observations provide further evidence for the existence of an anterior–posterior gradient of differential involvement of subregions of the parietal cortex in the encoding of reach direction in the sighted and in the congenitally blind.

Discussion

In this study, we examined the relationship between functional specialization and dominant input modality of sensory-motor cortical systems. Our starting point was the hypothesis that within many of these systems, functional specialization takes on the role of the dominant organizing principle, and is to a large extent independent of sensory experience. Specifically, functional specialization in these brain regions should be resilient to changes in the nature of sensory inputs due to cross-modal plasticity resulting from profound sensory deprivation.

We tested this claim by comparing the patterns of activity in PPC of sighted and congenitally blind participants. PPC is a region with a well-documented functional architecture that varies primarily along the anterior–posterior axis. As many of its parts are normally strongly driven by visual stimuli, we would expect a substantial degree of cross-modal plasticity to occur. At the same time, however, if function really were the dominant organizing principle in PPC, we would also predict that the broad anterior–posterior gradient of specialization should be preserved in both groups.

The results we report bear out these predictions: the whole-brain interaction analyses (Fig. 2*b*) and *T*-value plots along the anterior–posterior axis in PPC (Fig. 3) indicate consistently higher sensitivity to reach direction in posterior portions of PPC and superior occipital cortex in the congenitally blind in comparison to sighted participants. This finding supports the notion that functional specialization—namely integration of information about the spatial location of a reach target—is preserved in the posterior portions of PPC and superior occipital cortex, even as the dominant input modality changes from visual to nonvisual through cross-modal plasticity. We measured the involvement of different regions in our proprioceptively guided reaching task using an fMRI index of rebound from adaptation to a particular type of reaching action. A similar index has been previously used to characterize directional tuning properties within an extensive fronto-parietal network activated during production of reaching actions (Fabbri et al. 2010, 2012). The index does not explicitly distinguish between the encoding of reach direction per se, and the location of the target—whenever target location changes on a test trial, so does the reach direction. As noted above, PPC appears to contain a gradient from predominately motor-related representations in the more anterior subregions, to predominately spatial representations located more posteriorly. In line with that, our index is likely more

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influenced by directional tuning and encoding of location in the more anterior and more posterior parts of PPC and superior occipital cortex, respectively. Independently of these provisions, however, the index suggests that the congenitally blind individuals consistently recruit more posterior portions of PPC and the superior occipital cortex to encode parameters of reaching actions, compared to the sighted.

Our findings build on previous work suggesting a degree of functional preservation both through unimodal and through cross-modal changes. Lesions or altered experiences lead to reorganization in auditory, somatosensory (Merzenich et al. 1983), visual (Kaas et al. 1990; Heinen and Skavenski 1991; Gilbert and Wiesel 1992), and motor cortices. In unimodal areas, one of the principles guiding reorganization is that representations that are affected by the lesion or impaired input can be taken over by neighboring representations, a mechanism that has been described as "representational plasticity." A well-known example in the visual modality is the observation that permanent retinal lesions result in lesion projection zones that soon start responding to stimulation to neighboring locations (Kaas et al. 1990; Heinen and Skavenski 1991; Gilbert and Wiesel 1992). Likewise, deafferentation of single digits in monkeys is accompanied be an enlargement of neighboring regions in area 3b and 1 that represent neighboring digits (Merzenich et al. 1983). It has been suggested that rewiring of intercortical connections underlies this ability of the brain to adapt to an altered environment (Darian-Smith and Gilbert 1995; Das and Gilbert 1995).

In multimodal areas, deprivation within one modality leads to an enlargement of neighboring areas, resulting in enhanced representation of the remaining modalities (Rauschecker 1995). As an example, visual deprivation has been described to lead to changes in the anterior ectosylvian cortex (AEC), an area that receives input from different sensory modalities. In binocularly deprived cats, a purely visual region within the AEC has been shown to be driven by auditory and somatosensory input (Rauschecker and Korte 1993).

Several recent studies of congenitally blind individuals have demonstrated that some unimodal visual brain regions have the capacity to start responding to nonvisual stimuli while retaining aspects of their original computational roles. Renier et al. (2010), for instance, focused on middle occipital gyrus (MOG), which is involved in visuo-spatial processing in the sighted. They found that in congenitally blind individuals, MOG is also involved in spatial processing, but for auditory and haptic inputs. Along similar lines, Collignon et al. (2011) reported involvement of several subregions of the occipital cortex, normally characterized as visuo-spatial, in an auditory-spatial task in the congenitally blind. Reich et al. (2011) demonstrated that an area in the ventral stream selective for visual word processing in the sighted is recruited during Braille reading in the congenitally blind. In another study involving sighted and congenitally blind participants, Wolbers et al. (2011) presented evidence for experience-independent encoding of spatial layout in the ventral stream of the visual cortex. Moreover, it has been shown that multimodal parietal areas are more strongly involved in auditory localization in blind in comparison to normal sighted participants (Weeks et al. 2000). Finally, Lomber et al. (2010) recently demonstrated that by selectively cooling either posterior or dorsal auditory cortex in deaf cats, superior performance in visual localization or motion detection was reversibly eliminated. This latter finding supports the view that compensatory plasticity is mediated by cross-modal reorganization.

Taken together, these studies provide converging evidence for the potential of many sensory regions to retain some of their functional characteristics even as the modality of the inputs driving them changes dramatically. The expansion of auditory and somatosensory representations into visual areas within the AEC shows that plastic changes also take place in multimodal areas. Until now it was unclear, however, if reorganization in regions in which vision is still the dominant but not sole modality of inputs, is following the same principles as those observed in unimodal areas.

PPC is an example of such a region, and our data provide evidence that function-preserving cross-modal plasticity is not restricted to strictly unimodal areas. Therefore, our findings suggest that preservation of function may be a pervasive principle guiding neural plasticity throughout the brain.

It has been demonstrated that after rewiring retinal ganglion cells to project to the somatosensory rather than the visual pathway, somatosensory cortex shows visual response properties such as orientation tuning and receptive fields (Metin and Frost 1989). Similar results were observed for the auditory pathway (Sharma et al. 2000). In an elegant experimental paradigm, Von Melchner et al. (2000) furthermore reported that ferrets seem to perceive such visual stimuli projected to auditory cortex as visual. These results demonstrate that thalamic nuclei play an important role in the development of functional regionalization, but they do not answer the question of whether functional specialization is preserved if the dominant input into a multimodal region changes.

What might be the neural basis for the observed group difference in the recruitment of PPC and neighboring visual areas during proprioceptively guided reaching? A lack of visual input during the first couple of months of life dramatically reduces the visual responsiveness of neurons in parietal area 7 in monkeys, while responsiveness during active movements increased substantially (Hyvarinen et al. 1981). In humans, studies examining both the anatomical and functional connectivity using diffusion tensor imaging and resting state analysis generally report a decreased gray matter volume in the occipital cortex as well as decreased connectivity between occipital cortex and parietal and frontal areas in congenitally blind in comparison to late-blind and sighted participants (Noppeney et al. 2005; Yu et al. 2008; Shu, Li et al. 2009; Li et al. 2012). Increased connectivity was observed within primary sensory and motor cortices (Noppeney et al. 2005; Yu et al. 2008; Shu, Liu et al. 2009), which might be due to the greater effort required to acquire motor skills in congenital blindness.

In summary, to our knowledge so far no study reported changes in the functional or anatomical connectivity of the PPC in congenital blindness. We therefore consider it unlikely that our results reflect a difference in connectivity of PPC in congenitally blind in comparison to normal sighted participants. Instead, we hypothesize that the observed group difference in the PPC and adjacent visual cortex might be due to a change in the weighting of the sensitivity to proprioceptive and visual input. The combinatorial power of neurons in area V6a, bringing together visual information as well as information about eye and hand position across different epochs and tasks within a limited sector of space, the global tuning

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field (Battaglia-Mayer et al. 2000; Battaglia-Mayer et al. 2001), might make such flexible reweighting of different sources of sensory input possible. In line with this view, Battaglia-Mayer et al. (2000) suggested that in the absence of visual input, a control mechanism based on both proprioception and vision might shift to a control mechanism that is mainly based on proprioception. Likewise, Sober and Sabes (2005) demonstrated that the sensory modality of the target (visual, proprioceptive) could modulate the relative weighting of these 2 sources of information.

Gaunet and Rossetti (2006) reported that in immediate reaching to memorized proprioceptive targets, normal sighted, and late-blind participants represent reach targets in an internal (body centered, egocentric) reference frame, whereas they shift toward an external (environmentally centered) reference frame during delayed reaching. Their data also show that, by contrast, congenitally blind participants represent reach targets in an egocentric reference frame both during immediate and delayed reaching. Likewise, it has been demonstrated that sighted and late-blind participants use an external, predominantly visually defined reference frame to represent spatial information required for tactile or auditory localization, whereas early blind participants use an internal, body-centered reference frame (Roder et al. 2004; 2007). Taken together, these findings are in line with the view that the relative weighting of proprioceptive relative to visual information, and thus the stronger reliance on body centered in comparison to external, environmentally centered reference frames, underlies the observed stronger sensitivity of the most posterior part of PPC and adjacent visual areas in the congenitally blind in comparison to the normal sighted participants in proprioceptively guided reaching.

It should be noted that there are also well-documented cases of cross-modal plasticity where the original function does not appear to be preserved. The most prominent example of this is the recruitment of the early visual cortex for language processing (Sadato et al. 1996; Burton et al. 2002; Bedny et al. 2011) and verbal memory (Amedi et al. 2003) in the congenitally blind. Furthermore, the early visual cortex of the congenitally blind has been causally linked to behavioral performance in such tasks (Cohen et al. 1997; Amedi et al. 2004). These results are compatible with our claim that the functional role in the "canonical" modality is one of the codeterminants of a region's potential for cross-modal plasticity, and stress that there are other constraints that help shape the precise nature of its cross-modal recruitment. Factors that influence whether or not a region preserves its computational role through cross-modal plasticity have not been systematically explored. However, it is interesting to point out that the cases of cross-modal recruitment that does not respect the original function of a region have largely been limited to the early visual cortex. Therefore, an area's place in the processing hierarchy of the visual cortex could plausibly be another factor guiding cross-modal plasticity.

The key theoretical implications of this study concern the relationship between the effects of neural plasticity and the innate functional architecture of the brain. We have shown that the computational role of PPC and superior occipital cortex is preserved even as the dominant inputs to this area change from visual to nonvisual through cross-modal plasticity in the congenitally blind. The functional specialization of the subregions is thus experience independent, whereas the dominant modality of the information over which the computations in the subregion are performed may change as a function of sensory experience. Given the other converging evidence discussed above, it seems that in many cases, neural plasticity acts within a relatively rigid framework of predetermined functional specialization. Taken together, these findings thus help to delimit the aspects of brain function that emerge through the workings of neural plasticity and those aspects that are invariant to it.

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