# Detailed Exploration of Face-related Processing in Congenital Prosopagnosia: 2. Functional Neuroimaging Findings

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## Abstract

■ Specific regions of the human occipito-temporal cortex are consistently activated in functional imaging studies of face processing. To understand the contribution of these regions to face processing, we examined the pattern of fMRI activation in four congenital prosopagnosic (CP) individuals who are markedly impaired at face processing despite normal vision and intelligence, and with no evidence of brain damage. These individuals evinced a normal pattern of fMRI activation in the fusiform gyrus (FFA) and in other ventral occipito-temporal areas, in response to faces, buildings, and other objects, shown both as line drawings in detection and discrimination tasks and under more naturalistic testing conditions when no task was required. CP individuals also showed normal adaptation levels in a block-design adaptation experiment and, like control subjects, exhibited evidence of global face representation in the FFA. The absence of a BOLD–behavioral correlation (profound behavioral deficit, normal face-related activation in the ventral occipito-temporal cortex) challenges existing accounts of face representation, and suggests that activation in these cortical regions per se is not sufficient to ensure intact face processing. ■

## INTRODUCTION

Findings from neuropsychology (Wada & Yamamoto, 2001; De Renzi, 1997; Farah, 2004; Sergent & Signoret, 1992; Damasio, Tranel, & Damasio, 1990), event-related potential (ERP) studies (McCarthy, Puce, Belger, & Allison, 1999; Bentin, Allison, Puce, Perez, & McCarthy, 1996), and single-unit recording studies in monkeys (Gross, Rocha-Miranda, & Bender, 1972) implicate specific regions within the occipito-temporal cortex in the processing of faces. Consistent with this, functional imaging studies in humans (Halgren et al., 1999; Kanwisher, McDermott, & Chun, 1997; McCarthy, Puce, Gore, & Allison, 1997; Clark et al., 1996) have documented face-selective activation in a core set of regions (Rossion, Caldara, et al., 2003; Haxby, Hoffman, & Gobbini, 2000), including the fusiform gyrus (Levy, Hasson, Avidan, Hendler, & Malach, 2001; Kanwisher, McDermott, et al., 1997; McCarthy, Puce, et al., 1997), the lateral occipital region in the vicinity of the lateral occipital sulcus and inferior occipital gyrus (Hasson, Harel, Levy, & Malach, 2003; Gauthier et al., 2000; Hoffman & Haxby, 2000), and the superior temporal sulcus (STS) (Hoffman & Haxby, 2000; Puce, Allison, Bentin, Gore, & McCarthy, 1998). Because face-related activation in the fusiform gyrus is the most robust (Haxby, Hoffman, et al., 2000), this region is termed ''the fusiform face area'' (FFA) (Kanwisher, McDermott, et al., 1997) in recognition of its putative modular, face-dedicated property (Kanwisher, 2000; McCarthy, Puce et al., 1997).

Although there is general consensus that the FFA is involved in face processing, its precise role remains controversial. One possibility is that it mediates face detection, giving rise to a signal that differentiates between faces and all other visual objects. Such a role is consistent with findings showing that this region responds equally well to a range of face stimuli, including human faces and cat and cartoon faces (Tong, Nakayama, Moscovitch, Weinrib, & Kanwisher, 2000). Additionally, face detection (but not face identification) is unaffected by the orientation of the face and, likewise, the FFA response is minimally affected by face inversion (Aguirre, Singh, & D'Esposito, 1999; Haxby, Ungerleider, et al., 1999; Kanwisher, Tong, & Nakayama, 1998).

However, such a minimal detection role for the FFA is inconsistent with the fact that individuals with acquired prosopagnosia, an impairment in face processing following a lesion to the occipito-temporal cortex, perform well in face detection tasks (Bruyer et al., 1983) and, rather, are impaired at discriminating between and/or identifying faces (Mundel et al., 2003; Wada & Yamamoto, 2001). Moreover, electrical stimula-

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tion of face-specific ERP sites located in the fusiform gyrus most commonly results in a transient failure to identify, rather than detect, faces (Mundel et al., 2003; Puce, Allison, & McCarthy, 1999). Finally, a recent fMRI study showed that although a major component of the FFA BOLD activation was correlated with successful face detection, a significant, additional signal increase was correlated with successful face identification (Grill-Spector, Knouf, & Kanwisher, 2004). Note, however, that direct evidence supporting the contribution of the FFA to face identification is not clear-cut either. Thus, although some studies do not find a differential response to familiar versus unfamiliar faces (Leveroni et al., 2000; Nakamura et al., 2000), as might be expected of an area mediating identification, others do report such differences (Henson, Shallice, & Dolan, 2000; Rossion, Schiltz, Robaye, Pirenne, & Crommelinck, 2001).

To address the ongoing controversy concerning the role of the FFA in face processing, we adopted a different approach in which we examined the extent to which there is face-selective activation in the FFA in a group of unusual individuals who are impaired at face recognition despite normal visual acuity and intelligence, a deficit termed ''congenital prosopagnosia'' (CP). In contrast with acquired prosopagnosic patients in whom the ventral occipito-temporal cortex has been damaged, CP individuals exhibit an impairment in face recognition that is present from early childhood, in the absence of any discernible cortical lesion or neurological disease. As such, these individuals provide us with a window onto the function of the fusiform gyrus and enable us to examine the neural mechanisms mediating face recognition using fMRI, unaffected by damage that might disrupt normal blood flow or neurovascularization (D'Esposito et al., 2003).

To date, there have been relatively few studies of CP individuals (e.g., Behrmann & Avidan, 2005; Duchaine & Nakayuma, 2005; Grueter et al., in press; Kress & Daum, 2003a; Duchaine, 2000; De Haan & Campbell, 1991; McConachie, 1976), only two of which include ERP recordings (Kress & Daum, 2003b; Bentin, Deouell, & Soroker, 1999) and two of which include functional imaging findings (Hasson, Avidan, Deouell, Bentin, & Malach, 2003; Hadjikhani & De Gelder, 2002). The present study, however, is the first to provide both detailed and concurrent functional imaging and behavioral findings in a group of four CP individuals. To derive brain–behavior correlations fully, we first assessed the behavioral performance of CP individuals on faces, common objects, and novel objects in a variety of tasks (see Behrmann, Avidan, Marotta, & Kimchi, 2005). Having definitively established that all CP subjects were markedly impaired, relative to control subjects, we then carried out an extensive set of four different imaging experiments, two of which have been used previously (Hasson, Avidan, et al., 2003) and two of which involve new paradigms. We used whole-brain scanning to explore the differences between CP individuals and their controls across the entire cortex and not only in occipito-temporal regions, as was done previously. Finally and critically, behavioral responses collected during the scanning session enabled us to show directly that even when CP subjects performed poorly in a face-discrimination task, their face-related activation in the FFA was not differentiable from that of the normal control subjects. The dissociation between the apparently normal FFA BOLD activation and the impairment in face processing in CP challenges existing accounts of face processing and forces us to reconceptualize the role of the FFA in the representation of faces.

## RESULTS

### Behavioral Profile of CP Subjects

To document the extent and specificity of the behavioral impairment, CP subjects and 12 normal controls first completed a set of behavioral experiments with faces and nonface objects (for a detailed description of the different experiments and their results, see Behrmann et al., 2005). In brief, relative to their controls, all CP subjects were significantly poorer in recognizing familiar faces and in making same/different discrimination judgments on unfamiliar faces. CP subjects were also impaired, although to a lesser extent and with greater variability, on tasks involving nonface stimuli. All CP subjects performed within the normal range on various low-level visual processing tasks. Taken together, the behavioral data establish a clear deficit in face processing for all CP subjects.

### Imaging Experiments

#### *Conventional Face and Object Mapping Experiment*

fMRI responses for line drawings of faces, buildings, objects, and patterns were first mapped for the CP subjects and 10 control subjects. Stimuli were presented in a short block design and subjects performed a one-back memory task while fixating on a central dot (Figure 1A). Note that this one-back task is equivalent to a sequential face-discrimination task (''are consecutive images the same or different?''). We also mapped out the meridian borders of visual areas for each subject to assess the location of face- and object-related activation in relation to an objective definition of the visual retinotopic regions (Levy et al., 2001).

Importantly, even though the one-back memory task performed in the scanner was relatively easy, as evident from the high accuracy of the control subjects (Figure 1B), the CP group exhibited a significant and specific behavioral impairment for faces, reflected both in accuracy and RT (Figure 1B) (ANOVA for accuracy: significant stimulus type × group interaction, $p < .05$; no significant main effect of stimulus type, $p = .09$ nor of group $p = .24$; ANOVA for RT: significant stimulus

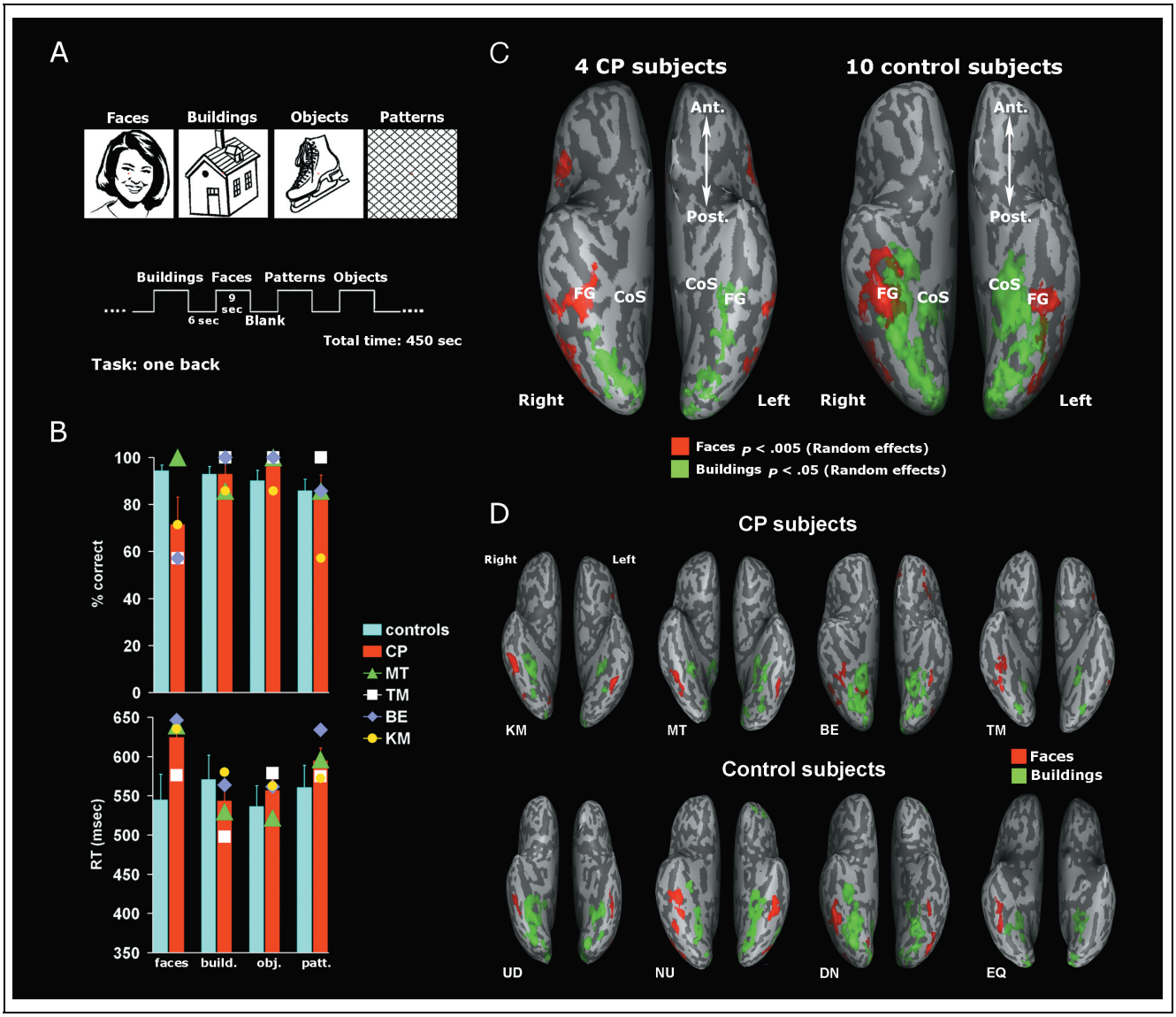


**Figure 1.** Behavioral performance and functional maps of the conventional face and object mapping experiment. (A) Examples of stimuli and experimental design. Subjects viewed short epochs containing line drawings of faces, buildings, common objects, or geometrical patterns while maintaining fixation and performing a one-back memory task. (B) Accuracy (top graph) and reaction time on the one-back memory task performed in the scanner for the CP (red) and control subjects (light blue); error bars indicate standard error of the mean (*SEM*) across subjects in each group. The graphs also show the behavioral data for individual CP subjects. (C) Averaged face (red) and building (green) activation maps of the CP subjects and control subjects projected on an inflated brain representation shown from a ventral view. The activation is projected on the same brain and is shown in the same statistical threshold (multisubjects GLM statistics, faces: $p < .005$; buildings: $p < .05$, random effects) to enable direct comparison between the two groups. (D) Face and building activation maps are shown for each of the CP subjects (top row) and for four representative control subjects (bottom row). Note that all CP subjects exhibit similar activation patterns to the control groups. Abbreviations: FG = fusiform gyrus; CoS = collateral sulcus; Ant. = anterior; Post. = posterior.

type × group interaction, $p < .05$; significant main effect of stimulus type, $p < .05$, no significant main effect of group, $p = .55$). As evident from the figure, however, there was some variability within the CP group with some subjects trading off speed for accuracy or vice versa (compare subject MT with TM).

For each subject, we first localized face-related activation by searching for voxels that were selectively activated by faces compared to buildings and objects. Similar to the control group and in agreement with previous studies (Hasson, Harel, et al., 2003; Gauthier et al., 2000; Halgren et al., 1999; Levy et al., 2001), face-related activation in CP subjects was located anterior to the retinotopic regions within the fusiform gyrus in regions corresponding to the previously defined FFA (Kanwisher, McDermott, et al., 1997) and in the lateral occipital region in the vicinity of the lateral occipital sulcus and the inferior occipital gyrus. The average face-related activation maps of the 4 CP subjects and 10 controls are shown in Figure 1C (red patches). The maps are

projected on an inflated brain of one individual subject and shown from a ventral view. To enable direct comparisons between CP and control subjects, both maps are shown using the same statistical threshold ($p < .005$ for faces, $p < .05$ for buildings, General Linear Model [GLM] multisubjects, random-effects analysis). Note the similarity between the maps of the two groups in the location and extent of the face-related activation. Similar maps are also shown in Figure 1D for each of the four CP subjects and four representative controls. Note that despite the variability between subjects, all CP subjects still clearly exhibited face related activation similar to the control subjects.

In order to assess further the activation in the fusiform gyrus, we analyzed the spatial extent of the activation in this region by counting the number of activated voxels in the left and right hemispheres for each subject in each group. A repeated-measures ANOVA with group (CP/controls), hemisphere (left, right) as the repeated measure, and the number of voxels as the dependent measure did not reveal any significant effect ($p > .1$), thus suggesting that the spatial extent of the activation in the fusiform gyrus did not differ between the two groups. The similarity between the groups is also evident from the Talairach coordinates (Talairach & Tournoux, 1988) of the face-related activation in the fusiform gyrus presented in Table 2 (Part 1).

Figure 1C also shows the average building-related activation (building vs. faces and objects) in the two groups (green patches). Building-related activation is typically located outside the retinotopic borders in the parahippocampal gyrus and collateral sulcus, medial to the face-related activation in the FFA (Levy et al., 2001; Epstein & Kanwisher, 1998), and thus, serves as an important indicator for the reliability of the anatomical location of the face-related activation. The control group shows the same loci of activation as depicted in previous studies, as do the CP subjects. Again, this same pattern is also evident for each individual CP subject as shown in Figure 1D.

To assess the selectivity for the different object categories within the face-related regions, the activation profile from the fusiform gyrus and lateral occipital region was extracted for each subject using the ''internal localizer'' approach (see Methods). Figure 2A shows the percent signal change averaged across all the repetitions of each condition and collapsed across both hemispheres for the face-related regions for both CP (left column) and control subjects (right column) (see Table 2, Part 2, for the left and right activation foci for each group). A repeated-measures ANOVA was performed separately for the activation in the fusiform region and lateral occipital region, with group (CP/controls), stimulus type (faces, buildings, objects, patterns), and percent signal change as the dependent measure. Only a main effect of stimulus type ($p < .0001$) was found in both face-related regions. Note that the activation profiles were obtained using the internal localizer approach, and thus, were not biased in any way, confirming the clear face selectivity. There was no main effect of group nor a significant interaction between group and stimulus type, however, the interaction effect in the fusiform gyrus was close to significant ($p < .06$: activation for faces was slightly increased for CP compared with controls, whereas activation for patterns was decreased). Note that although not statistically significant, the face selectivity in the lateral occipital focus was somewhat reduced in the CP subjects compared to their controls (percent signal change for faces compared to buildings and patterns).

Face-related regions are part of a large distributed occipito-temporal network of object representation (Hasson, Harel, et al., 2003; Avidan, Hasson, Hendler, Zohary, & Malach, 2002; Haxby, Gobbini, et al., 2001) in which multiple regions, even if not selective for faces, still carry substantial information about faces (Haxby, Gobbini, et al., 2001). It is therefore possible, that the source of the behavioral deficit in CP might arise from a dysfunction in such regions. To explore this possibility, we assessed the stimulus selectivity in regions that were preferentially activated by the nonface stimuli used in the experiment by applying the same procedure described above for faces (Figure 2B and C). This analysis was first performed for the building-related activation in the collateral sulcus and, importantly, the activation profile was only sampled from the anterior nonretinotopic part of this region. Three CP and all control subjects exhibited building-related activation bilaterally and one CP subject (TM) showed right-lateralized activation. As in the face-related regions, only a main effect of stimulus type ($p < .0001$) was observed, with no main effect of group nor an interaction between these factors.

Using the same procedure, we delineated foci with object-specific activation (compared with faces and buildings) in the lateral occipital sulcus, the medial bank of the fusiform gyrus, and the inferior temporal sulcus (ITS). However, these activations were less consistent across both groups and were mostly found in the left hemisphere. The most consistent activation was found in the ITS in both groups (Figure 2C). Two CP subjects exhibited bilateral activation and two others exhibited left-lateralized activation. In the control group, six subjects exhibited left-lateralized activation and two exhibited right-lateralized activation, whereas two others exhibited bilateral activation. Again, only the main effect of condition was significant ($p < .001$), the group effect was close to significant ($p < .06$, higher percent signal change in the control group for all conditions compared to CP) and the interaction between the factors was not significant.

The absence of group differences cannot be attributable to reduced statistical power; although the patterns of activation were largely similar in occipito-temporal regions across the groups, clear differences emerged in

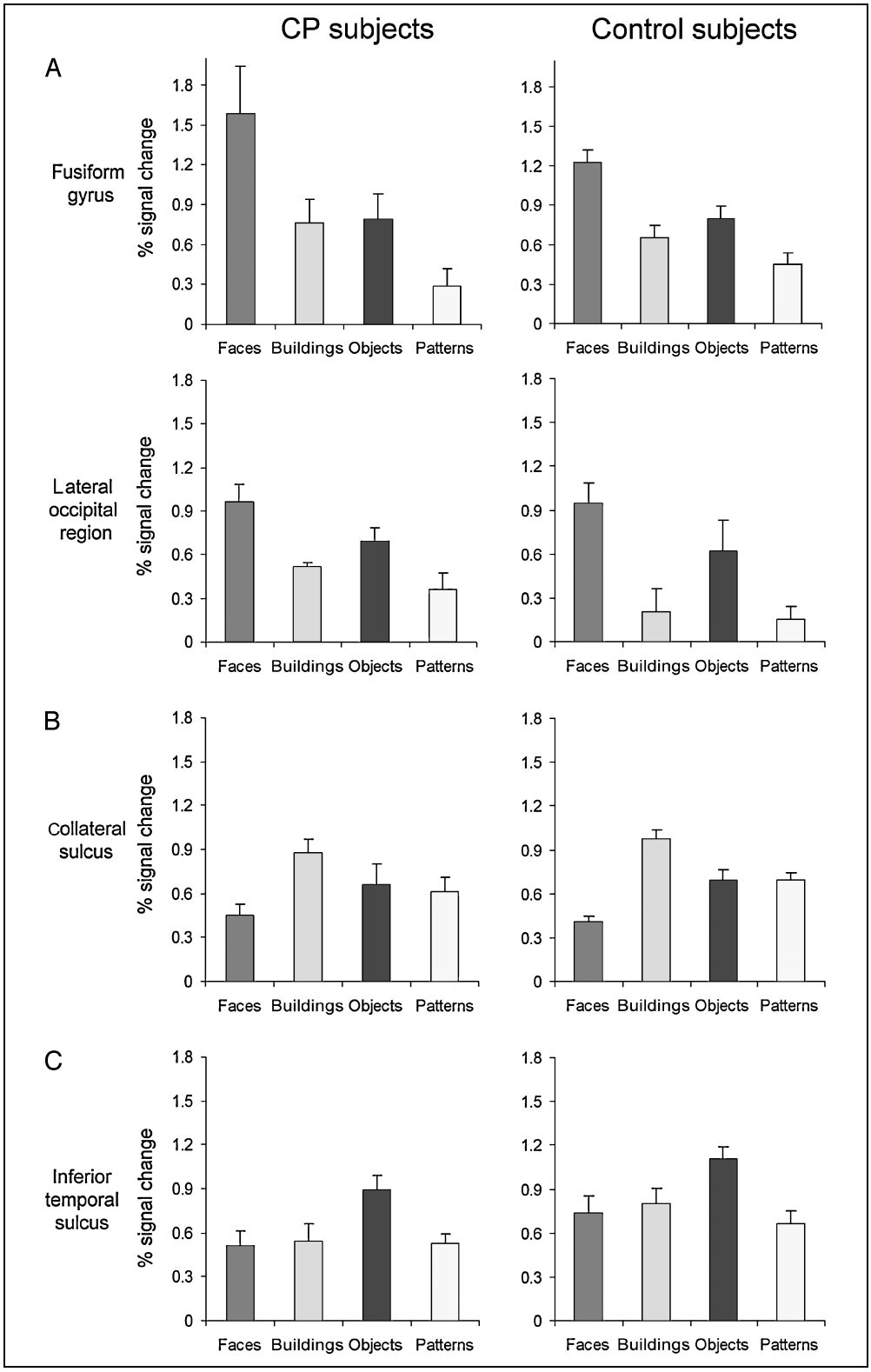


**Figure 2.** Activation profiles in ROIs in the conventional face and object mapping experiment. (A) Averaged activation profiles of face-related voxels in the fusiform gyrus and lateral occipital region of CP and control subjects. Activation profiles were obtained using the ''internal localizer'' approach (see Methods) and the graphs show the averaged percent signal change for each experimental condition (faces, buildings, objects, patterns). Error bars indicate *SEM* across subjects in each group. (B) Averaged activation profiles in building-related voxels in the collateral sulcus. (C) Averaged activation profiles in object-related voxels in the inferior temporal sulcus.

prefrontal regions. As is evident from Figure 3, the CP group exhibited strong face-related activation (faces vs. building and objects, $p < .005$, GLM multisubjects, random-effects analysis) in the precentral sulcus, the inferior frontal sulcus, and the anterior part of the lateral sulcus in both hemispheres. The control group exhibited some activation in the precentral sulcus, but to a much lesser extent and only in the right hemisphere (Figure 3). Face-selective activation in prefrontal regions has been previously reported when normal subjects

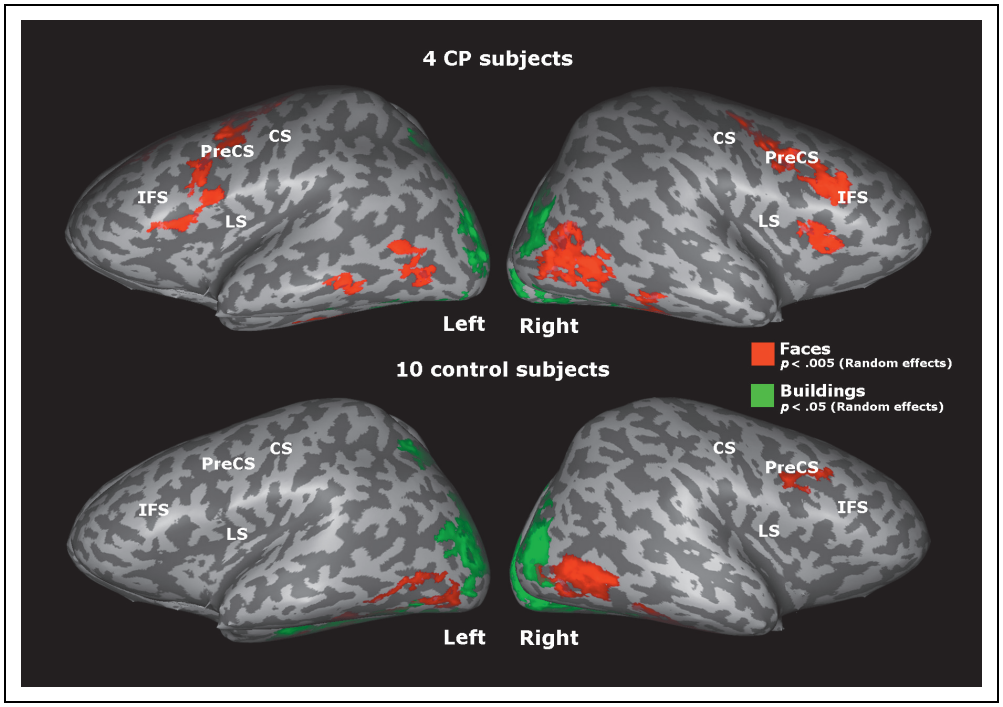


**Figure 3.** Activation maps in prefrontal regions in the conventional face and object mapping experiment. Same activation maps as in Figure 1C but here the brain is shown in a lateral view in order to reveal the activation in prefrontal regions. CP subjects are shown in the upper panel and controls in the lower one. Abbreviations: LS = lateral sulcus; CS = central sulcus; PreCS = precentral sulcus; IFS = inferior frontal sulcus.

perform working memory tasks using face stimuli (Druzgal & D'Esposito, 2003; Sala, Rama, & Courtney, 2003; Haxby, Petit, Ungerleider, & Courtney, 2000). The prefrontal face-related activation in the current study might then reflect the increased difficulty for the CP subjects in the one-back memory task for faces, relative to the other conditions and to the control subjects, and the consequent recruitment of prefrontal regions to maintain face representations (see Figure 1B).

The results from the conventional face and object mapping experiment indicate that individuals with CP reveal normal face-related activation in the ventral occipito-temporal cortex, and close-to-normal selectivity in the lateral occipital region, in terms of the anatomical location of face-selective activation and its spatial extent, the signal strength, and the stimulus selective response. Crucially, this normal profile of activation is apparent despite the significant face processing impairment exhibited at the very same time. Of note also is that the CP subjects also exhibited normal object-related activation (common objects and buildings) in the occipito-temporal cortex. That group differences between the CP subjects and their controls can be detected (in prefrontal regions) attests to the sufficiency of the statistical power of the current paradigm to detect differences, when they exist, and therefore lends further weight to the conclusion that there are no detectable group differences in the posterior areas of cortex.

These results reveal a dissociation of a BOLD–behavior correlation in the ventral occipito-temporal cortex, and particularly in the FFA. To further confirm this result, we utilized additional paradigms that could assist in exploring the mechanisms giving rise to the abnormal behavior.

## Motion Pictures Experiment

Although serving as a powerful tool for studying object selectivity in the human visual cortex, the conventional face and object mapping experiment exploits viewing conditions and stimuli that are rather contrived. Furthermore, as evident from Figure 1B, the one-back memory task performed during this experiment was significantly more difficult for the CP subjects compared to their controls particularly for the face stimuli. It has previously been shown that activity in the FFA can increase as a function of working memory load in tasks involving faces (Druzgal & D'Esposito, 2001). Thus, the seemingly normal activation found in the conventional mapping experiment in the CP subjects could actually reflect additional computation taking place due to the relative difficulty of the behavioral task for these individuals.

To address these issues, in this next experiment, we used a motion picture paradigm first to test whether the face and object-related activation similarities observed in the conventional mapping experiment are replicable with more natural stimuli and under more natural viewing conditions, and second, to determine whether normal face-related activation can be found regardless of the behavioral task performed in the scanner. In this experiment, subjects freely viewed a sequence of short video clips, each containing stimuli

of faces and people, buildings, navigation, or miscellaneous objects (Hasson, Nir, Levy, Fuhrmann, & Malach, 2004). Importantly, no specific task was required, making this experiment more akin to naturally surveying one's visual environment. Figure 4A shows the activation maps of a single representative CP and control subject, projected on an inflated and unfolded brain representation. The white lines on the posterior part of the unfolded representation show the retinotopic borders mapped for each subject. The face and building activation maps obtained in this experiment largely replicate the results from the conventional mapping experiment (compare Figure 4A and Figure 1C), except that the activation seems to be more widespread in the motion pictures experiment; selective activation for faces was found in the fusiform gyrus and the lateral occipital region, when contrasting faces with buildings and navigation scenes (red patches) and selective activation for buildings and navigation scenes were found in the collateral sulcus when applying the opposite contrast (green patches). Interestingly, face-related activation was also found within the STS in regions typically activated in response to facial movements (Hoffman & Haxby, 2000; Puce, Allison, et al., 1998) and biological motion (Puce and Perrett, 2003). That these regions are activated here is consistent with the richness of the faces and motions in the displays.

To assess the spatial extent of the face-related activation obtained in this experiment in both CP and controls, the number of face-related voxels within the lateral occipital region, fusiform gyrus, and STS was counted for each subject in each group. To allow direct comparisons, all face-related foci for all subjects were selected using the same statistical threshold ($p < .0005$) (see Figure 4A for two representative subjects). A repeated-measures ANOVA with group (CP/controls) hemisphere (left, right) and face-related region as the repeated-measures within-subject factors, and the number of voxels as the dependent measure, was used. There were infrequent instances of control subjects for whom not all face-related foci could be identified in the selected statistical threshold and these were excluded from the ANOVA. Critically, all face-related regions were detected for the CP subjects using that threshold. This analysis revealed a significant main effect of hemisphere ($p < .001$), confirming that overall there were more face-related voxels in the right compared with the left hemisphere. In addition, there was a significant main effect of face-related region ($p < .005$), with more activated voxels in the lateral occipital region than in the fusiform gyrus or STS. Importantly, however, this analysis did not reveal a main effect of group or any two- or three-way interactions, thus suggesting that there were no differences in the spatial extent of the activation between the CP and control group in any of the face-related regions.

To further quantify the similarity between the CP and control groups, we sampled the activation profile of three regions of interest (ROIs) (fusiform gyrus, lateral occipital region, and collateral sulcus), defined independently for each subject on the basis of the conventional face and object mapping experiment (see Methods). Percent signal change, averaged across the entire experiment and collapsed across the left and right hemispheres for each group, is shown in Figure 4B. As above, all ROIs exhibited clear stimulus selectivity but, of even greater importance, is the striking similarity between the activation profiles of the two groups (CP = black line; controls = white line). This similarity is also evident from the high values of the correlation coefficient (fusiform gyrus = .80; lateral occipital region = .89; CoS = .81), calculated for each ROI between the average activation profile of each group. Importantly, however, as evident from the figure, this similarity is not only in the overall correlation but also in the moment-by-moment waxing and waning of the activity. These results confirm the normal profile of face- and building-related activation in the CP subjects when more natural viewing conditions and stimuli are employed. Moreover, because this normal activation was found here in the absence of any behavioral task, it implies that the normal activation found in the conventional mapping experiment was not confounded by the difficulty of the behavioral task.

### Adaptation Experiment

The behavioral results reveal a clear impairment in CP individuals in unfamiliar face discrimination in a simultaneous matching task (Behrmann et al., 2005) and in a one-back memory (sequential discrimination) task (Figure 1B). These tasks are largely perceptual and do not require that a specific or individual face be represented. Indeed, CP subjects might be even more impaired than already evident when more precise face knowledge is required; their own self-testimonies suggest that ''all faces look alike.'' Using the fMR-adaptation paradigm for studying the neuronal properties of higher-order visual areas at a subvoxel resolution, it has been shown that normal subjects typically exhibit a reduction in BOLD signal with repeated presentation of a stimulus (Grill-Spector & Malach, 2001). To examine whether the face-selective activation noted above is less sensitive to face repetition in CP than in control subjects, we compared adaptation levels for face repetition across the two groups. We also examined the adaptation effect for nonface stimuli to determine whether the entire occipito-temporal region is normally sensitive to repetition (Avidan et al., 2002).

Stimuli were presented in epochs that included either 12 different stimuli (faces, building, cars) or 12 repetitions of the same identical stimulus (see Figure 5A). The activation profile was sampled from ROIs defined in-

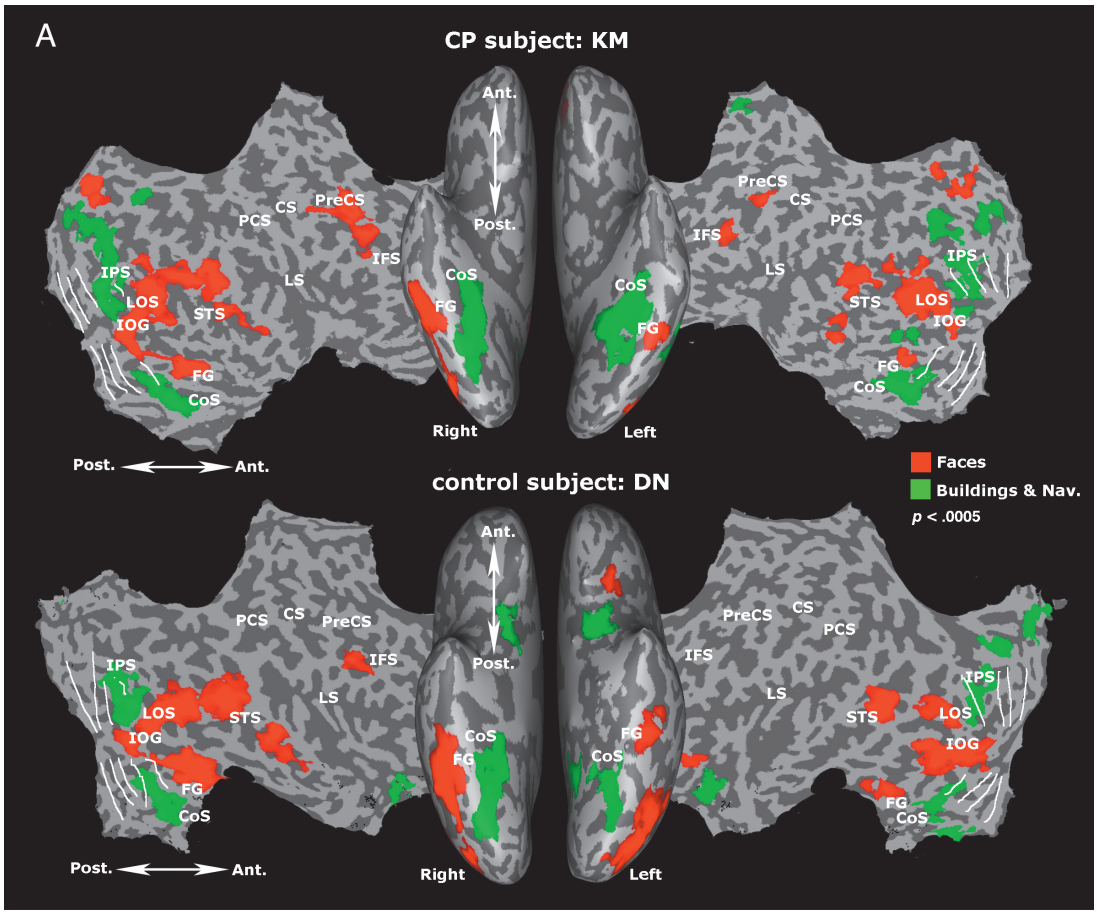


**Figure 4.** Activation maps and activation profiles from the motion pictures experiment. (A) Activation maps for faces (red) as well as buildings and navigation (green) are shown for one representative CP subject and one control subject. The data are shown on the inflated and unfolded map representation of each individual using the same statistical threshold (GLM statistics, $p < .0005$). The white dotted lines on the unfolded maps indicate the borders of the retinotopic areas that were mapped for each subject in a separate experiment. Abbreviations: LOS = lateral occipital sulcus; IOG = inferior occipital gyrus; IPS = intraparietal sulcus; PCS = postcentral sulcus. Other abbreviations as in Figures 1 and 3. (B) Averaged activation profiles of the CP (black) and control subjects (white) are shown for face-related voxels in the fusiform gyrus and lateral occipital region, and for building-related voxels in the collateral sulcus. The signal is shown along the time-axis of the experiment, and the vertical colored bars indicate the different experimental conditions. The correlation coefficient values between the entire activation profile of CP and control subjects are shown for each ROI. Error bars indicate *SEM* across subjects in each group.

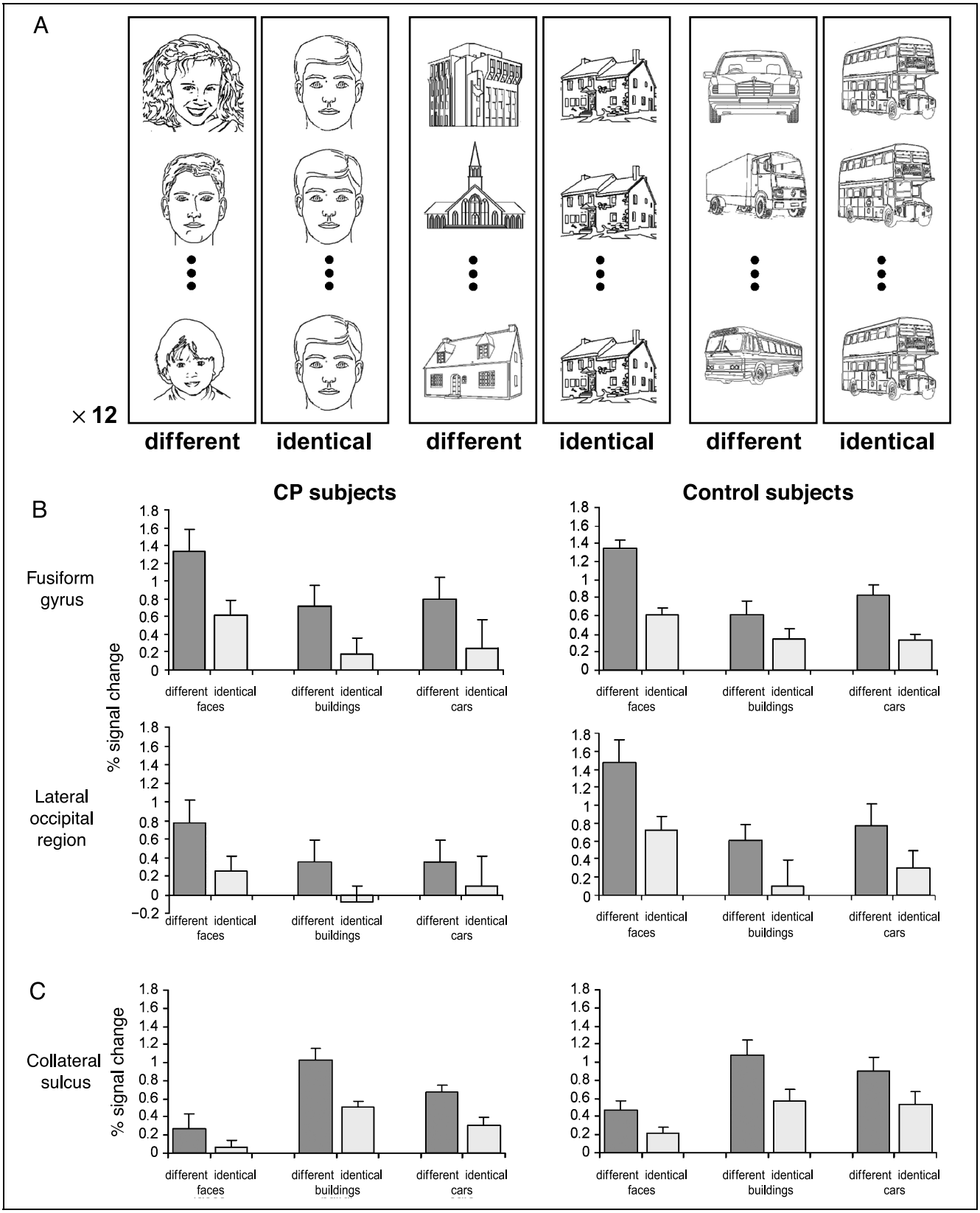


**Figure 5.** Experimental design and activation profiles of the adaptation experiment. (A) Examples of stimuli, and experimental design. Face, building, and car line drawings were presented in epochs containing either 12 different or 12 identical images. (B) Averaged activation profiles in face-related voxels in the fusiform gyrus (top) and the lateral occipital region (bottom) for the CP and control subjects. Error bars indicate *SEM* across subjects in each group. (C) Averaged activation profiles in the building-related voxels in the collateral sulcus.

dependently for each subject using the conventional mapping experiment. Figure 5B shows the activation levels within the face-related foci in the fusiform gyrus and lateral occipital region, averaged across all repetitions of each experimental condition and across the two hemispheres for the two groups. Again, despite the fact that the face-related regions were selected using an external localizer, CP individuals exhibited clear face selectivity in the ''different'' conditions in these ROIs. Note the similarity between the groups in the magnitude of the adaptation, that is, the signal decrease following face repetition (dark gray compared with light gray bars), suggesting that face representations in CP subjects are indeed sensitive to face repetition. The face-related regions also exhibit a strong adaptation effect for the nonface stimuli (buildings and cars), indicating that, like normal subjects, these regions in the CP subjects contain neurons that are highly selective for those stimuli (Avidan et al., 2002). These observations were confirmed in a repeated-measure ANOVA in which the only significant effect in both regions was a main effect of stimulus type ($p < .0001$). There was no main effect of group nor an interaction between the factors.

Figure 5C shows a similar analysis for the building-related focus in the anterior collateral sulcus. This region exhibited strong adaptation for the building stimuli as well as for the other object categories in both groups. Once again, the ANOVA revealed only a main effect of stimulus type ($p < .0001$). The strong building selectivity in the collateral sulcus combined with the finding that this region exhibits similar adaptation levels for all stimulus categories including faces further suggests that the entire occipito-temporal object representation network in CP subjects is intact and mirrors that of the normal control subjects.

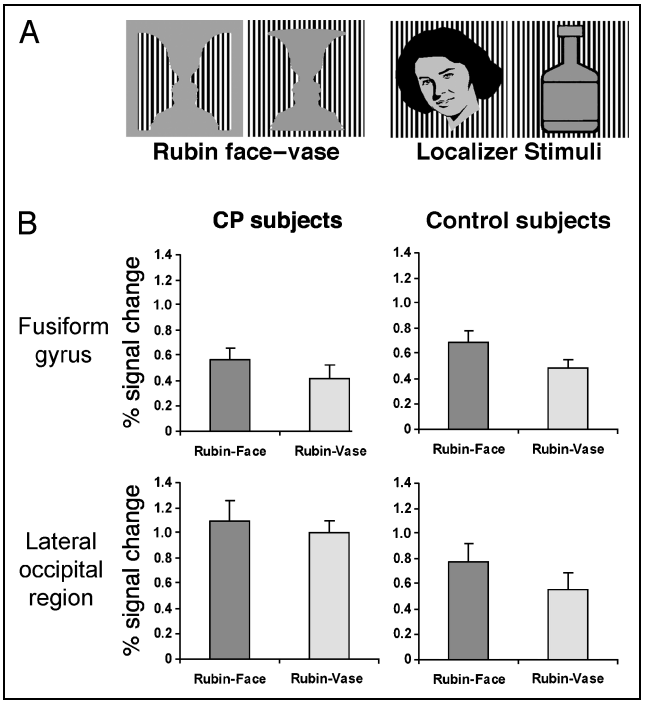


**Figure 6.** The Rubin face–vase experiment. (A) Examples of the stimuli including the Rubin face–vase stimuli (left) and frontal faces and household objects (localizer stimuli) used to independently localize face-related voxels (in the experiment the uniform surfaces shown here in gray, were colored in light pink). (B) Activation profiles for the Rubin face–vase conditions in face-related voxels in the fusiform gyrus and lateral occipital region. Error bars indicate *SEM* across subjects in each group.

## Rubin Face–Vase Experiment

One possible interpretation of the apparently normal face-selective BOLD response in the CP subjects found in the previous experiments is that it reflects a response to the presence of face parts (eyes, mouth, and nose) in the absence of an intact representation of the face as a whole. To examine whether the activation in CP is merely a product of a part-representation, we employed a paradigm used previously, which utilizes the famous Rubin face–vase illusion to demonstrate evidence for global face representations in normal subjects (Hasson, Hendler, Ben Bashat, & Malach, 2001). Critically, in the Rubin face–vase illusion, similar local elements are always present. However, depending on figure–ground segmentation and global integration, the local elements can induce two different visual percepts, either of a face or of a vase (Figure 6A). If face-selective activation in the fusiform gyrus and other face-related regions depends only on processing of the local elements, then activation in these regions should be similar in both the Rubin-face and Rubin-vase conditions (same local elements are present). However, if face representation in the fusiform gyrus and other face-related regions is affected by the global integration of the face elements into the percept of either a face or a vase, then increased activation should be found for the Rubin-face perceptual states compared to the Rubin-vase perceptual states. Indeed, in normal subjects, selective activation within face-related regions has been previously demonstrated for the Rubin-face compared to the Rubin-vase stimuli, suggesting that normal face-related activation is modulated by global grouping processes and is not only induced by the representation of local face parts (Hasson, Hendler, et al., 2001).

Here, face-selective regions were independently localized initially for each subject by contrasting the epochs of frontal faces with those of household objects (Figure 6A). Data from one control subject were excluded from this experiment, as they were too noisy to localize face-related activation. The activation profile was extracted for the Rubin-face and Rubin-vase stimuli from both the fusiform gyrus and lateral occipital foci

for each subject (see Table 2, Part 2 for foci). The averaged percent signal change across all repetitions of each condition and across the left and right hemispheres of each subject are presented in Figure 6B. As in the control group, the average fusiform gyrus activation in the CP subjects exhibited a selective response for the Rubin-face compared to Rubin-vase, indicating that this region in CP subjects is indeed involved in computing global information about faces and is sensitive to the context, not simply to the local components of the display. The similarity between the activation profiles of the two groups in the fusiform gyrus was confirmed by a repeated-measure ANOVA, which revealed only a main effect of stimulus type ($p < .01$).

The results in the lateral occipital region were, once again, more variable across subjects in both groups (see Table 2, Part 2). The ANOVA revealed a marginally significant main effect of group ($p < .06$), but not of stimulus type and no significant interaction. Note that, although not statistically significant, the selectivity for the Rubin-face compared to the Rubin-vase condition in the lateral occipital focus was somewhat reduced in the CP subjects compared to their controls. This result is analogous to the somewhat reduced face selectivity found in the lateral occipital region in the conventional mapping experiment (Figure 2A).

## DISCUSSION

In a series of four functional imaging experiments, we have shown that individuals with CP exhibit normal face- and object-related fMRI activation patterns in the ventral occipito-temporal cortex, particularly in the face-related fusiform gyrus (FFA), and largely normal activations in the lateral occipital region, despite their profound behavioral impairment. Importantly, this pattern was evident across different types of stimuli (e.g., line drawings and movie clips) and across different paradigms.

In the first study in a conventional mapping experiment, a normal pattern of BOLD activation was found when subjects viewed line drawings of face and nonface stimuli and performed a one-back memory task. This paradigm has been used extensively in the literature and serves as a rigorous baseline to demarcate areas of activation in the ventral occipito-temporal cortex. One possible interpretation of the normal activation is that the task was not sufficiently taxing for the CP individuals. Behavioral data collected concurrently with the image acquisition rules out this possibility—although the task was easy for the controls, this was not so for the CP individuals who were clearly impaired on this task. Thus, the normal face-related activation found in CP cannot merely be explained by the claim that the task was too simplistic for the CP subjects.

A second possible interpretation, and one that is diametrically opposed to the first one offered above, is that the task was excessively difficult for the CP and it is this difficulty that drove the face-related activation, particularly in the fusiform gyrus of the CP subjects. Indeed, previous studies have shown that activation in the FFA increases as a function of working memory load (Druzgal & D'Esposito, 2001). This explanation is not tenable either as the CP subjects continued to exhibit normal face-related activation even when they were not required to perform any behavioral task during the motion pictures experiment. Further research is clearly needed to unequivocally determine the contribution of task difficulty to face-related activation in CP individuals. We are now starting to parametrically explore the effects of task difficulty in these CP individuals using new paradigms. The critical point, at present, is that normal face-related activation is obtained at the very same time that the behavioral impairment is manifest.

The finding that face- and object-related activation in the ventral visual cortex is apparently normal is replicated in the motion picture experiment. As mentioned above, this replication attests to the generalizability of the finding from the first conventional mapping experiment to more natural stimuli and viewing conditions.

Importantly, the normal signature of face-related activation in CP was also found when additional experimental manipulations were used. CP subjects showed normal recovery from adaptation when different faces were shown, suggesting that neurons within these regions were sufficiently sensitive to differentiate between the face exemplars used in this experiment. Although one might think that normal adaptation is not that surprising given that the face stimuli used in this experiment were very different from each other, it is important to bear in mind that CP subjects were actually impaired in discriminating between such stimuli—in the conventional mapping experiment, similar stimuli were used and the CP subjects were impaired, suggesting that the stimuli were confusing and not as perceptually dissimilar for them as one might assume. Of note is that, in addition to the adaptation for faces found in the present experiment, CP subjects also exhibited normal adaptation levels in the fusiform gyrus and other face-related regions for nonface stimuli, suggesting that, similar to control subjects and replicating previous findings, these regions are involved in processing other object categories in addition to faces (Avidan et al., 2002; Haxby, Gobbini, et al., 2001).

Although normal adaptation for faces is apparent, determining its origin is less obvious. Because the exact same picture of an individual face was repeated during the adaptation condition, we cannot determine at this stage whether the adaptation found in the fusiform gyrus was due to the repetition of the exact same shape (i.e., based on perceptual geometry or structure) or the repetition of the same facial identity. Differentiating

between these alternatives and establishing whether neural activity in the FFA is sufficient for normal representation of fine distinctions among individual faces will require further experiments in which more subtle variations will be made to face stimuli. The use of an event-related adaptation paradigm in such future experiments will also minimize possible attentional variations that are inherent in the block-design adaptation paradigm employed here.

Finally, in the last experiment, similar to control subjects once again, CP subjects also exhibited a selective BOLD signal for Rubin-face compared to Rubin-vase stimuli in the fusiform gyrus. Importantly, these stimuli contain similar local elements but induce two different visual percepts, either of a face or of a vase, depending on figure–ground segmentation and global integration and shape processing. Hence, selectivity for the Rubin-face over the Rubin-vase stimuli implies that, as in the control group, CP subjects' face-related activation is modulated by global grouping processes and is not simply induced by the representation of local face parts (Hasson, Hendler, et al., 2001).

In sum, the CP subjects exhibit normal face- and object-related activation patterns in multiple regions of the ventral occipito-temporal cortex under various experimental paradigms. Of note, however, is that group differences between CP subjects and their controls were found in regions outside the occipito-temporal cortex, indicating that the absence of group differences is not merely a lack of statistical power. Taken together, these findings suggest that normal face-related activation in ventral occipito-temporal regions, as measured with fMRI, is not sufficient to ensure intact face processing and does not necessarily reflect normal face representation within those regions.

## Can the Behavior–BOLD Dissociation be Reconciled?

The central result is that the BOLD activation in CP in ventral occipito-temporal regions is largely not differentiable from that of the control subjects, notwithstanding their marked behavioral impairment. How might this dissociation be explained?

It has been previously suggested that the FFA is mainly involved in face detection, that is, discriminating between faces and stimuli from other object categories (Tong et al., 2000), an ability that is largely preserved in CP. The apparently normal FFA activation in the CP subjects might then reflect the intact involvement of the FFA in deriving a rather coarse and rudimentary structural representation, which suffices for some tasks (i.e., detection), but not for more taxing tasks such as identification. Evidence compatible with this possible interpretation suggests that the final stage of face identification is not completed at the level of high-order, visual face-related regions such as the FFA; rather, successful recognition requires activation in more anterior regions of the temporal lobe, where a more abstract or semantic representation of faces is derived (Haxby, Hoffman, et al., 2000; Leveroni et al., 2000; Sergent, Ohta, & Macdonald, 1992). Further support for the role of anterior temporal regions in mediating face identification and particularly for being a site of facial memory (long-term representation) comes from lesion studies. For example, Barton and Cherkasova (2003) found that patients with anterior temporal lesions were the most impaired in a task that required generating long-term representations of famous faces as in mental imagery compared to patients with more posterior occipito-temporal lesions. Similarly, patients with anterior temporal lobectomy (following intractable epilepsy) were found to be impaired in identifying familiar faces (Glosser, Salvucci, & Chiaravalloti, 2003). The source of the behavioral problem in CP might then arise in the abnormal propagation of activation from the intact FFA to more anterior temporal regions.

However, the idea that the FFA only mediates face detection is not universally accepted, and the clean division of labor between the FFA and more anterior regions might not be totally correct. Although not denying the contribution of more anterior regions to face processing and particularly to face identification, recent experimental evidence suggests that the FFA is involved not only in face detection but also in face identification. Thus, normal subjects exhibited differential responses for face detection and identification in the fusiform gyrus with the two processes resulting in either differential fMRI amplitude (Grill-Spector et al., 2004) or temporal scales (Puce, Allison, et al., 1999, and see Sugase, Yamane, Ueno, & Kawano, 1999 for similar findings from single-unit recordings in monkeys). These differential responses in the fusiform gyrus may potentially be the outcome of feedback from more anterior regions (as above) and/or from additional computation taking place within the fusiform gyrus itself. Which of these is perturbed in CP remains unclear and they are not mutually exclusive either. Propagation to or from anterior regions may be affected in CP. However, recall that CP subjects exhibit a clear deficit not only in face identification (naming of famous faces) but also in discrimination of unfamiliar faces (Figure 1B) (see also Behrmann et al., 2005). This deficit in the more perceptual (not just memorial) aspects of face processing implicates posterior occipito-temporal regions rather than exclusively the more anterior areas (Barton, Press, Keenan, & O'Connor, 2002; Wada & Yamamoto, 2001). It remains a possibility, therefore, that the fusiform activation itself may be abnormal in CP. Because the current study employed detection and discriminations tasks, the abnormality may still be uncovered under more challenging conditions such as face identification or other fine-grained face tasks.

We also cannot rule out the possibility that differences in the activation patterns in the fusiform gyrus and/or other parts of the face processing network between CP and normal control subjects might exist in the temporal domain. Such differences could underlie the behavioral dysfunction of CP subjects but may not be evident with the temporal resolution afforded by fMRI (in the order of seconds). Some evidence supporting this view comes from ERP studies showing that the relatively early, N170 potential, which shows face selectivity in normal subjects, failed to show such selectivity in CP subjects (Kress & Daum, 2003b; Bentin, Deouell, et al., 1999).

Finally, it might be that the small differences in BOLD activation in CP subjects, such as the slight reduction in face selectivity in the lateral occipital region (e.g., Figures 2A and 6B), might be ''amplified'' when translated into behavioral performance. If so, the lateral occipital region would serve as a critical link in the face processing network. Further support for the role of the occipital region in face processing comes from studies showing that acquired prosopagnosic patients often have lesions that involve not only the fusiform gyrus, but also the lateral occipital region (Barton et al., 2002; Wada & Yamamoto, 2001). Moreover, brain damage to this region, but not to the FFA, in some individuals may be associated with severe prosopagnosia (Rossion, Caldara, et al., 2003).

As is evident, there are a host of potential explanations to account for the dissociation between the impaired behavioral profile and the apparently normal BOLD activation pattern. We are currently exploring these issues using new imaging experiments and hope that these will uncover, in greater detail, the mechanisms giving rise to CP. Suffice it to say that no one explanation captures the BOLD–behavior dissociation. What is crucial, however, is that a simple assignment of face processing to the FFA is no longer defensible and a deeper examination of the computational properties of the FFA and associated regions is demanded by these findings.

### Face-related Activation Outside the Occipito-temporal Cortex

In the current study, we acquired whole-brain functional scans, and thus, were able to explore differences between the CP and control groups in the response patterns in all regions of the brain, not only in the occipito-temporal regions. A particularly novel finding was that robust bilateral face-related activation was evident in prefrontal regions (precentral sulcus, inferior frontal sulcus, anterior lateral sulcus) in the CP group. In contrast, the control group only exhibited right-lateralized activation in the precentral sulcus (Figure 3). Studies of normal individuals performing working memory tasks have revealed face-related activation in prefrontal regions (Druzgal & D'Esposito, 2003; Sala et al., 2003 Haxby, Petit, et al., 2000) and some ERP studies have detected some inferior prefrontal cortex sites that generate small but specific face-specific responses (Allison, Puce, Spencer, & McCarthy, 1999).

The poor performance exhibited by CP subjects, compared to their controls, on the one-back memory task specifically for face stimuli is consistent with the interpretation of this prefrontal activity being related to working memory. However, given that the conventional face and object mapping experiment was not specifically designed to look at the different components that usually comprise a memory study (encoding, memory delay, response), further research that specifically and parametrically manipulates the memory load of faces and other object stimuli is required in order to determine the role of this activation in face processing in CP subjects.

This study has exploited the unique possibility of examining the activation of the fusiform gyrus and other cortical regions in an unusual group of individuals with CP. Delineating the neural mechanism that gives rise to abnormal behavior and, by logical inference, normal behavior, is a critical goal of neuroscience. As might be predicted, the correspondences between the brain and behavior are not transparent and, in this study, are dissociated with the behavioral impairment being evident concomitant with normal FFA activation. Taken together, however, this study has indicated patterns of similarities and patterns of potential difference in this population of CP individuals relative to their normal counterparts. The challenge that lies before us is to use these patterns to explain the face processing deficit in detail.

## METHODS

### Subjects

Four healthy CP subjects (2 men), aged between 29 and 60 years, with no discernable cortical lesion or any history of neurological disease, participated in all experiments (for details, see Table 1). Another CP sub-

**Table 1.** Biographical Information about CP Subjects

| *Congenital Prosopagnosia (CP) Subjects* | | |
|---|---|---|
| *Subjects' Initials* | *Sex* | *Age* |
| TM | M | 27 |
| KM | F | 60 |
| MT | M | 41 |
| BE | F | 29 |

KM and TM are a mother and a son.

**Table 2.** Laterality in force-selective activation

**1. Talairach Coordinates: Fusiform Gyrus**

| | *Left Hemisphere* | | | *Right Hemisphere* | | |
|---|---|---|---|---|---|---|
| | *x* | *y* | *z* | *x* | *y* | *z* |
| CP subjects | −40 ± 2 | −53 ± 3 | −19 ± 2 | 38 ± 5 | −47 ± 8 | −17 ± 3 |
| Control subjects | −37 ± 4 | −41 ± 5 | −18 ± 4 | 36 ± 2 | −40 ± 7 | −17 ± 3 |

**2. Activation Foci**

| | *Localizer Experiment* | | | | | |
|---|---|---|---|---|---|---|
| | *Fusiform Gyrus* | | | *Lateral Occipital Region* | | |
| | *Bilateral* | *Right Lat.* | *Left Lat.* | *Bilateral* | *Right Lat.* | *Left Lat.* |
| CP subjects | 4 | – | – | 4 | – | – |
| Control subjects | 9 | 1 | – | 4 | 2 | 1 |
| | *Rubin Face–Vase Experiment* | | | | | |
| | *Fusiform Gyrus* | | | *Lateral Occipital Region* | | |
| | *Bilateral* | *Right Lat.* | *Left Lat.* | *Bilateral* | *Right Lat.* | *Left Lat.* |
| CP subjects | 4 | – | – | 1 | 3 | – |
| Control subjects | 9 | – | – | 3 | 2 | 4 |

Part 1: Talairach coordinates of the face-related activation in the fusiform gyrus of CP and control subjects extracted from the conventional face and object mapping experiment. Part 2: Number of CP and control subjects that showed bilateral, right-lateralized or left-lateralized face-related activation in the fusiform gyrus and in the lateral occipital region in the conventional face and object mapping experiment and in the Rubin face–vase experiment.

ject (NI, male, aged 40) was tested behaviorally (see Behrmann et al., 2005), but because we could not acquire his imaging data, he was excluded from the present article. Seven of the 12 control subjects who participated in the behavioral studies, along with three new participants, completed the imaging experiments. The control group included at least two age- and sex-matched controls for each CP individual. All CP and control subjects were right-handed and had normal or corrected-to-normal vision. All subjects consented to participate in the experiments, and the protocol was approved by the Institutional Review Boards of Carnegie Mellon University and the University of Pittsburgh.

## Imaging Experiments

### *Visual Stimulation*

Visual stimuli were generated using the E-prime IFIS software (Psychology Software Tools, Pittsburgh, PA, USA) and projected via LCD to a screen located in the back of the scanner bore behind the subject's head. Subjects viewed the stimuli through a tilted mirror mounted above their eyes on the head coil. Before the scan, subjects were familiarized with the visual stimuli and tasks of each of the imaging experiments.

### *MRI Setup*

All subjects were scanned in a 3-T Siemens Allegra scanner equipped with a standard head coil. Subjects participated in one scanning session that lasted 1.5 to 2 hr in which all the functional and anatomical scans were acquired. The order of the functional experiments within the scanning session was generally constant for all subjects. BOLD contrast was acquired using gradient-echo echo-planar imaging sequence. Specific parameters: TR = 3000 msec, TE = 35 msec, flip angle = 90°, FOV = 210 × 210 $mm^2$, matrix size 64 × 64, 35 axial slices, 3 mm thickness, no gap. High-resolution anatomical scans (T1-weighted 3-D MPRAGE) were also acquired to allow accurate cortical segmentation, reconstruction, and volume-based statistical analysis. Specific parameters: TE = 3.49, flip angle = 8°, FOV = 256 × 256 $mm^2$, matrix size = 256 × 256, slice thickness = 1 mm, number of slices = 160–192, orientation of slices was either horizontal or sagittal. For three of the CP subjects, the

3-D brain reconstruction was performed on images previously acquired on a 1.5-T GE scanner.

## Experiments

### *Conventional Face and Object Mapping Experiment*

Stimuli included line drawings of faces, buildings, common objects, and geometric patterns, presented in a short block design (for details, see Levy et al., 2001; Figure 1A). Each epoch lasted 9 sec and contained nine stimuli from the same category; there were eight different images and one immediate repetition of one of the stimuli. Each stimulus was presented for 800 msec followed by a 200-msec interval of blank screen. There were seven repetitions of each condition and their order was pseudorandomized across subjects. Visual epochs were interleaved with 6-sec blank epochs. The experiment lasted 450 sec and started and ended with extended blank epochs of 27 and 9 sec, respectively. Subjects were instructed to fixate on a red central fixation dot, to perform a one-back memory task, and to press a key on a response glove to indicate the repeated image. Both accuracy and reaction time were recorded.

### *The Motion Pictures Experiment*

The experiment lasted 10 minutes and was composed of 32 epochs (15 sec long) of movie clips, each containing images from one of four possible categories: people in various situations, navigation of the camera through city buildings or through open fields, and miscellaneous images of objects from different categories (machines, falling water, etc.; for details, see Hasson, Nir, et al., 2004; Figure 4). The experiment started with a 51-sec blank period followed by 9 sec of pattern stimuli and ended with a 1-minute blank. Subjects were simply instructed to watch the movie clips.

### *The Adaptation Experiment*

The experiment included line drawing images from three different categories: faces, buildings, and cars (for details, see Avidan et al., 2002; Figure 5A). Stimuli were presented in 12-sec epochs that contained either 12 different images (''different'' condition) from the same category or 12 repetitions of the same identical stimulus (''identical'' condition). Within epochs, each stimulus was presented for 800 msec followed by 200 msec of fixation only. The experiment lasted 480 sec, and started and ended with a long blank period of 21 and 15 sec, respectively. The first visual block always contained geometric patterns and was excluded from the analysis. Visual epochs were interleaved with 6-sec blank epochs, and the order of visual epochs was pseudorandomized across subjects. Subjects were instructed to continuously fixate a central red dot and to covertly categorize the images as follows: man, woman, or a child for the face stimuli; apartment, townhouse, or public facility for the buildings; and private car, truck, or bus for the vehicles.

### *The Rubin Face–Vase Experiment*

The experiment included modified versions of the Rubin face–vase stimuli as well as line drawings of front faces and household objects (for details, see Hasson, Hendler, et al., 2001; Figure 6A). The Rubin face–vase stimuli were modified so that subjects' perception was biased towards one perceptual state or the other. This was done by first uniformly coloring the vase area within each of the stimuli and placing stripes over the profile. Stimuli were then placed either over a striped background (bias towards perception of the vase due to closure of the vase stimulus) or over a uniform-color background (bias towards perception of the face due to closure of the face stimulus). Critically, the Rubin face and vase share the same local contours but give rise to different global perceptions. In order to ensure that subjects' perception remained biased to one perceptual interpretation (either the profile or vase) during the experiment, stimuli were presented briefly (200 msec) and were immediately followed by a masking grid that was presented for 800 msec. Stimuli were presented in 9-sec blocks that were interleaved with 6-sec blanks. Each condition was repeated eight times and the order of presentation was pseudorandomized across subjects. Subjects maintained central fixation throughout the experiment and performed a one-back memory task; however, due to a technical failure, their responses were not recorded. The experiment lasted 507 sec and started and ended with extended blank periods.

## Data Analysis

Data analysis was performed using the BrainVoyager 4.8 software package (Brain Innovation, Maastricht, Netherlands) and complementary in-house software. Detailed description of the data analysis is provided in Hasson, Harel, et al. (2003). Briefly, for each subject, the cortical surface was reconstructed and unfolded into the flattened format. Functional data for each subject from each experiment were analyzed separately. Preprocessing of functional scans included 3-D motion correction and filtering of low frequencies up to five cycles per experiment (slow drift). Statistical analysis was based on the GLM. For each experiment, each of the conditions (except for blank) was defined as a separate predictor; a boxcar shape was used to model each predictor and a 3-sec lag was assumed. Percent signal change for each subject in each experiment (except for the motion pictures experiment) was calculated as the percent activation from a blank baseline. For the mo-

tion picture experiment, the raw activation level in each time point for each subject was *z*-normalized and then smoothed with a moving average of three time points. These values were then averaged across all participants of each group (Figure 4B). To obtain the multisubject maps, time series of images of brain volumes for each subject were converted into Talairach space and *z*-normalized. The multisubject maps were obtained using a random-effects procedure. Significance levels of activation maps were calculated, taking into account the minimum cluster size and the probability threshold of a false detection of any given cluster. This calculation was accomplished by a Monte Carlo simulation (''AlphaSim'' software by B. Douglas Ward, which is part of the AFNI analysis package, Cox R. W., 1996). Specifically, the probability of a false-positive detection per image was determined from the frequency count of cluster sizes within the entire cortical surface (not including white matter and subnuclei) using the combination of individual voxel probability thresholding and a minimum cluster size of six contiguous functional voxels.

### *''Internal Localizer'' Test*

To obtain an unbiased statistical test within a scan, we used one set of epochs to define anatomical ROIs in the conventional face and object mapping experiment, whereas another set was used to estimate the percent signal change within each region (for details, see Lerner, Hendler, & Malach, 2002).

### *Definition of ROIs for the Motion Pictures and the Adaptation Experiments*

ROIs were independently defined using the conventional face and object mapping experiment. Face-related regions (fusiform gyrus, lateral occipital region) were selected using a face contrast (faces vs. buildings and objects) and the collateral was defined using a building contrast (building vs. faces and objects). We then extracted the unbiased activation profile from each ROI for each subject.

### *Statistical Comparison between CP Subjects and Control Group*

For the localizer, adaptation, and Rubin face–vase experiments, the statistical analysis was done by performing a repeated-measure ANOVA with group as a factor (CP/controls), the different experimental conditions as the repeated measures and the percent signal change, averaged across the left and right hemisphere, as the dependent variable. For the motion picture experiment, the correlation analyses were performed between the CP group and the control group.


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