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Early visual deprivation from congenital cataracts disrupts activity and functional connectivity in the face network

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ABSTRACT

The development of the face-processing network has been examined with functional neuroimaging, but the effect of visual deprivation early in life on this network is not known. We examined this question in a group of young adults who had been born with dense, central cataracts in both eyes that blocked all visual input to the retina until the cataracts were removed during infancy. We used functional magnetic resonance imaging to examine regions in the “core” and “extended” face networks as participants viewed faces and other objects, and performed a face discrimination task. This task required matching faces on the basis of facial features or on the spacing between the facial features. The Cataract group (a) had reduced discrimination performance on the Spacing task relative to Controls; (b) used the same brain regions as Controls when passively viewing faces or making judgments about faces, but showed reduced activation during passive viewing of faces, especially in extended face-network regions; and (c) unlike Controls, showed activation in face-network regions for objects. In addition, the functional connections of the fusiform gyri with the rest of the face network were altered, and these brain changes were related to Cataract participants' performance on the face discrimination task. These results provide evidence that early visual input is necessary to set up or preserve activity and functional connectivity in the face-processing network that will later mediate expert face processing.

1. Introduction

Adults are experts at recognizing the identity of faces despite changes in viewpoint, lighting, or facial expression, while at the same time being adept at detecting age, race, emotional expression and direction of gaze. This expertise appears to arise from processing faces, unlike objects, as holistic gestalts and from being exquisitely sensitive to the location of features within the face and to the shape of individual facial features (Maurer, Le Grand, & Mondloch, 2002). By adulthood, all these skills are better for upright than for inverted faces, a pattern suggesting that they are tuned by experience differentiating individuals in real world interactions (Hole, 1994; Mondloch, Le Grand, & Maurer, 2002, 2003b; Young, Hellawell, & Hay, 1987). Converging evidence for a role of experience comes from the findings that holistic processing is stronger for own-race and own-species faces than for the faces of other races or most other species (Michel, Rossion, Han, Chung, & Caldara, 2006; Tanaka, Kiefer, & Bukach, 2004; Taubert, 2009) and that sensitivity to feature spacing is better for human faces than for monkey faces, other-race faces and houses (Mondloch, Maurer, & Ahola, 2006; Mondloch et al., 2010a; Robbins, Shergill, Maurer, & Lewis, 2011).

At birth, infants' attention is drawn toward faces but that preference is mediated, at least in part, by general structural properties, such as top-heaviness and congruency, rather than an innate face module (Simion, Leo, Turati, Valenza, & Dalla Barba, 2007). Already at birth infants can discriminate two faces, likely making use of featural differences (Turati, Macchi Cassia, Simion, & Leo, 2006). During infancy, rudimentary versions of the skills underlying adult expertise emerge: holistic processing by 3 months of age (Turati, Valenza, Leo, & Simion, 2005) and sensitivity to large differences in feature spacing by 5 months of age (Bhatt, Bertin, Hayden, & Reed, 2005; Hayden, Bhatt, Reed, Corbly, & Joseph, 2007), the emergence of which has already been shaped by experience because it is manifest for human and monkey upright faces but not inverted faces or houses (Zieber et al., 2013). However, recognition of facial identity continues to improve into adolescence, with improvements in recognition of a face in a novel point of view or lighting (de Heering, Rossion, & Maurer, 2012;

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Mondloch, Geldart, Maurer, & Le Grand, 2003a), in sensitivity to differences in feature spacing (Mondloch et al., 2003a), and in the magnitude of differential sensitivity to upright versus inverted faces (de Heering et al., 2012; Robbins, Maurer, Hatry, Anzures, & Mondloch, 2012). The cause of the late changes may arise from additional experience individuating upright faces of one's own race or from more general improvements in attention and cognition that impact performance on the measurement tools (Crookes & McKone, 2009). The late maturation of the neural correlates of adults' expertise, e.g., the N170 in event-related potentials (Taylor, Batty, & Itier, 2004) and the face-specific activation in the fusiform gyrus in fMRI studies (see below) suggest that at least some of the behavioral changes during adolescence are face-specific.

When visual input is missing during infancy because of bilateral congenital cataracts, the adult pattern of expertise for face processing fails to emerge later in development. Such individuals are normal at detecting the structure of a face (Mondloch et al., 2003b, 2013) and discriminate with normal accuracy between faces differing in the shape of their features (de Heering & Maurer, 2014; Le Grand, Mondloch, Maurer, & Brent, 2001; Mondloch, Robbins, & Maurer, 2010b). However, they fail to show evidence of holistic processing during childhood (Le Grand, Mondloch, Maurer, & Brent, 2004), and even as adults have difficulty discriminating upright faces that differ only in feature spacing (de Heering & Maurer, 2014; Le Grand et al., 2001; Robbins, Nishimura, Mondloch, Lewis, & Maurer, 2010). In contrast, they are normal at discriminating feature spacing in inverted faces, monkey faces, and houses (de Heering & Maurer, 2014; Le Grand et al., 2001; Robbins et al., 2010). Perhaps as a result of these perceptual deficits, even as adults they have difficulty recognizing faces with an altered point of view (de Heering & Maurer, 2014; Geldart, Mondloch, Maurer, de Schonen, & Brent, 2002) and are poor at recognizing famous faces or faces recently learned in the lab (de Heering & Maurer, 2014). Additional evidence comes from the findings of less-than-normal shifts in perception in adaptation paradigms designed to test for norm-based coding (Nishimura, Maurer, Jeffery, & Rhodes, unpublished data) and for differential representation of upright and inverted faces (Robbins et al., 2012), and from evidence that normal face detection is accompanied by abnormally large P1 and N170 responses (Mondloch et al., 2013; but see Roder, Ley, Shenoy, Kekunnaya, & Bottari, 2013, for evidence of an absence of a face-specific N170 in a sample with much longer deprivation). This pattern of deficits suggests that early visual input may be necessary to set up the neural architecture underlying adults' face expertise. When that input is missing, people may have to rely on alternate pathways not as well suited to face expertise or on the normal, but damaged, pathways. The purpose of the current experiment was to use functional magnetic resonance imaging (fMRI) to assess those alternatives while adults with a history of early visual deprivation watched faces versus other categories and while they discriminated faces based on feature shape (a task on which they perform normally) or based on feature spacing (a task on which they have large deficits).

Previous fMRI studies of adults' ability to process faces indicate that this ability is mediated by activity in a variety of brain regions, particularly those in ventral occipito-temporal cortex. These studies have identified a region in the fusiform gyrus that responds more robustly to faces than to other types of visual stimuli (e.g., Downing, Chan, Peelen, Dodds, & Kanwisher, 2006; Grill-Spector, Knouf, & Kanwisher, 2004; Haxby et al., 1994; Kanwisher, McDermott, & Chun, 1997). This area has come to be known as the fusiform face area, or FFA. The magnitude of activity in FFA depends both on whether attention is directed to the faces (O'Craven, Downing, & Kanwisher, 1999; Wojciulik, Kanwisher, & Driver, 1998) and on the task demands involved in processing them (Druzgal & D'Esposito, 2003; Ishai & Yago, 2006; Lee, Anaki, Grady, & Moscovitch, 2012; Nestor, Vettel, & Tarr, 2008).

Despite agreement that the FFA is especially sensitive to faces, there has been considerable debate as to its precise role in face processing, including whether it is truly selective for faces, or rather mediates the differentiation of objects with which one has developed an expertise (Gauthier, Skudlarski, Gore, & Anderson, 2000; Gauthier, Tarr, Anderson, Skudlarski, & Gore, 1999; Grill-Spector et al., 2004; Joseph & Gathers, 2002). There is evidence of FFA involvement in both holistic (Schiltz, Dricot, Goebel, & Rossion, 2010; Schiltz & Rossion, 2006) and part-based face processing (Yovel & Kanwisher, 2004). Although there is considerable evidence that the FFA is specialized for representing face identity (Grill-Spector et al., 2004; Mazard, Schiltz, & Rossion, 2006; Nestor, Plaut, & Behrmann, 2011; Nestor et al., 2008; Rhodes, Byatt, Michie, & Puce, 2004), some have argued that the FFA is involved in the individuation of non-face objects (Haist, Lee, & Stiles, 2010). There are also regions adjacent to FFA in the fusiform gyrus that appear to be involved in some aspects of face processing (Maurer et al., 2007b; Schiltz et al., 2010).

Despite the focus on the FFA, face processing in the brain goes quite a way beyond this one region. In addition to the FFA, visual representation of faces involves a region in posterior occipital cortex (the occipital face area, or OFA), thought to provide input to FFA (Nichols, Betts, & Wilson, 2010; Rossion et al. 2003), and the superior temporal sulcus (STS), which is involved in the processing of eye gaze (Hoffman & Haxby, 2000; Itier & Batty, 2009). Other regions that are thought to primarily represent non-face objects, such as the lateral occipital region (Grill-Spector, Kushnir, Edelman, Itzchak, & Malach, 1998; Malach et al. 1995), also show activity related to face processing (Axelrod & Yovel, 2012; Haxby et al., 2001; Natu, Raboy, & O'Toole, 2011). Indeed, there is evidence that distinct patterns of activity across the entire ventral occipito-temporal cortex can be used to predict when participants are viewing faces (Haxby et al., 2001). One recent model of face processing (Gobbini & Haxby, 2007) proposes that there is a "core" system concerned with the visual analysis of faces, and an "extended" system for extracting person knowledge and processing the emotional and reward aspects of faces. The core system includes the occipital and temporal areas that are sensitive to face stimuli (FFA, OFA, and STS), whereas the emotional part of the extended system includes the amygdala, insula, and striatum, all of which have been implicated in emotion or reward (e.g., Adolphs, Tranel, Damasio, & Damasio, 1994; Haber & Knutson, 2010; Lane, Reiman, Ahern, Schwartz, & Davidson, 1997; Phillips et al., 1997). The person-knowledge segment of the extended system consists of the anterior temporal cortex, medial prefrontal cortex, and medial parietal/posterior cingulate cortex (PCC), regions involved in personal semantics, self-reference and theory of mind (Graham, Lee, Brett, & Patterson, 2003; Grigg & Grady, 2010a; Northoff & Bermpohl, 2004; Spreng & Grady, 2010). In this model, the core system provides input to the two parts of the extended system, which in turn modulate the activation of the core system through feedback. Although this model does not include frontal regions, other work (Fairhall & Ishai, 2007; Ishai, Schmidt, & Boesiger, 2005) has suggested that the inferior frontal gyrus (IFG) and orbitofrontal cortex (OFC) should be considered as a part of the extended face network. The IFG may be involved in the semantic processing of faces (Ishai, Haxby, & Ungerleider, 2002; Leveroni et al., 2000) whereas the OFC is involved in reward, decision making and top down processing of faces (Fellows, 2007; Li et al., 2010; Rolls, 2000). Studies assessing functional connectivity of these regions, including the frontal areas, have provided further evidence for the idea that face processing is supported by an interacting network of regions (Fairhall & Ishai, 2007; Li et al., 2010; McIntosh et al., 1994).

Developmental neuroimaging studies have shown that the areas of ventral occipital cortex are responsive to faces even in infants (Tzourio-Mazoyer et al., 2002), although the response in these areas is less specific during infancy than at older ages. Activity in core network regions increases during development, being lower and less extensive in children and adolescents, relative to young adults (Cohen Kadosh, Cohen Kadosh, Dick, & Johnson, 2011; Golarai, Liberman, Yoon, & Grill-Spector, 2010; Haist, Adamo, Han Wazny, Lee, & Stiles, 2013). Functional connectivity within the core system also changes during development (Haist et al., 2013; Joseph et al., 2012) and is less sensitive to task manipulations in children than in young adults (Cohen Kadosh et al., 2011), indicating that maturation of both mean activity and connectivity parallels the development of face processing abilities.

In the current study, we examined the influence of congenital cataracts on brain activity during face processing, with a particular focus on regions previously described as core and extended face processing areas. We used fMRI to study a group of young adults who had been born with dense, central cataracts in both eyes that blocked all visual input to the retina until the cataracts were removed during infancy and the eyes given compensatory contact lenses. Compared to age-matched Controls, we expected larger group differences when faces were being viewed, relative to other kinds of objects. Also since congenital cataracts have larger effects on face processing based on spacing among facial features rather than on the features themselves (Maurer, Mondloch, & Lewis, 2007a; Mondloch et al., 2010b), we expected that the areas involved in processing the spacing of features should show larger group differences than areas involved when face discrimination was based on the features per se. In addition to this examination of task-related activity, we also assessed functional connectivity in the two groups to determine if face sensitive regions in the fusiform gyrus would show disrupted connectivity (i.e., correlated activity) with other areas in the face network. Given evidence that deprivation of the right hemisphere is critical for face processing deficits after congenital cataracts (Le Grand, Mondloch, Maurer, & Brent, 2003), we predicted that the right fusiform gyrus would show reduced functional connectivity with other face network regions in individuals with congenital cataracts, which might be accompanied by increased strength of connections involving the left fusiform gyrus. We considered all of our results in the context of the core and extended components of the face network to determine if the influence of cataracts on face processing lies mainly in core regions, which would suggest a primary effect on face perception, or areas in the extended system, which might indicate an effect on the transfer of information to, or feedback from, these areas and the core.

2. Methods

2.1. Participants

Fourteen healthy Controls participated in the experiment. All (10 females, four males, mean age=22.7 years) were Caucasian, right-handed (score >45 on the McMaster Handedness Questionnaire, a modified version of the Edinburgh Handedness Questionnaire, Mondloch et al., 2002) and had an average of 16.6 years of education. Each had normal or corrected-to-normal linear letter acuity tested with the Lighthouse Visual Acuity chart and normal stereo-acuity as measured by the Titmus test. None of the participants took medications that might affect brain function, and none had overt brain abnormalities revealed by a structural MRI scan obtained during the same session.

Ten young adults with bilateral cataracts at birth (all removed within the first year) also participated. All were Caucasian and all but one were right-handed (four females, six males). The duration of the deprivation from birth until compensatory contact lens fitting after surgery ranged from 64 to 237 days ($M=143$ days). At the time of the scan, the Cataract group had a mean age of 22.4 years, and had an average of 14.2 years of education. The acuity in the better eye ranged from 20/25 to 20/100. As with the Controls, none of the bilateral group had overt brain abnormalities revealed by a structural MRI scan.

The Ethics Committees of Baycrest, Sunnybrook Health Science Centre, The Hospital for Sick Children, and McMaster University approved this experiment and each participant gave informed consent.

2.2. Stimuli and tasks

For the Localizer task, participants viewed 24-s blocks of gray-scale photographs from each of three categories: faces, houses, and common household objects. Viewing was passive, and no response to the stimuli was required.

The stimuli for the Jane task were identical to those described previously in our behavioral studies (Le Grand et al., 2001; Mondloch et al., 2002). Briefly, gray scale digitized images of Caucasian female faces were taken under standard lighting. A photograph of a single face (called “Jane”) was modified with Adobe Photoshop to create eight new versions (“Jane's sisters”). The four modified faces in the featural set were created by replacing the model's eyes and mouth with the features of the same length from different females. On every “different” trial, the two faces had different eyes and mouth. The four modified faces in the spacing set were created by moving the eyes of the original face up, down, closer together, or farther apart, and the mouth up or down. We used all possible combinations of the five faces; because there were only two mouth positions, on 20% of the different trials the mouth was in the same location in the two faces and only the location of the eyes differed. According to anthropomorphic norms (Farkas, 1981), the movements correspond to shifts in Jane's eyes of 1.3 SDs up or down, of 2.4 SDs closer together, or of 3.2 SDs farther apart, and shifts of Jane's mouth by 0.79 SDs up or down. Thus, the differences covered most of the variations in spacing among adult female faces in the population, without being so large that the faces appeared deformed or unnatural. Control stimuli consisted of scrambled Jane images created using custom MATLAB software. The original images were cut digitally into 20 × 20 pixel sections and reassigned randomly to positions in the display. Edges between the pieces were smoothed by convolving a Gaussian filter with the scrambled image (see Fig. 1 for examples of the stimuli).

2.3. Procedure

Prior to the experimental session, participants practiced the task outside the MRI scanner. They were shown Jane and her sisters and told that they would see one of the faces flash quickly on the screen followed by another face. They were instructed to press a key with the index finger if the second face matched the first face and to press with the middle finger if the two faces were different. The speed of responding was emphasized in addition to accuracy. Participants also practiced making same/different judgments about the scrambled images.

After the practice session, participants were positioned in the MRI scanner with their head stabilized with snug foam cushions. They were fitted with MRI-compatible Silent Vision Goggles (Avotec Inc.), which were adjusted to correct vision (up to 6 diopters) independently for each eye. Following anatomical scans, two or three 5-min functional Localizer scans were performed during which each picture in the 24-s block of faces, houses or objects was presented for 1900 ms, with an ISI of 100 ms. Each Localizer run consisted of three sequences of an 8-s fixation block, followed by object/house/face blocks (with stimulus-block order counterbalanced), followed by a final fixation block. The instructions given during the practice session were repeated before the first run. In the Jane task each trial consisted of the presentation of the first face for 200 ms, an inter-stimulus interval of 300 ms, followed by the second face for 1500 ms, with no inter-trial interval. On half the trials, the correct response was “different.” Conditions (Spacing, Featural, or Scrambled) were blocked with 22 trials in each block. Blocks lasted 45 s each and were presented in a fixed order during each run (scrambled, spacing, feature, spacing, feature, scrambled, spacing, feature, spacing, feature, scrambled). Trial types were segregated to allow time for each style of processing to emerge, but the subjects were not explicitly informed about the distinctions. Each Jane run lasted 495 s, and participants performed three to five runs, resulting in a total of 540–900 s of data from each of the three face tasks across the runs. Responses were collected through a RURB (Rowland Universal Response Box, Rowland Institute for Science, Cambridge, MA).

Imaging was performed with a 1.5 T whole-body GE Signa MRI scanner with a standard head coil (CV/i hardware, LX8.3 software; General Electric Medical Systems, Waukesha, WI). During the functional scans, the blood oxygenation level dependent (BOLD) MRI signal was measured in 26 5 mm slices (no gap). The imaging sequence was a single shot T2*-weighted pulse sequence with spiral readout, offline gridding, and reconstruction ($TR=2000$ ms, $TE=40$ ms, flip angle 80°). Structural scans were obtained prior to task performance by using a 3D T1-weighted pulse sequence ($TR=35.0$ ms, $TE=6.0$ ms, flip angle 35°, 22 × 16.5 field of view, 124 axial slices, 1.4-mm thick). For the functional scans, the in-plane resolution was 3 mm × 3 mm and the slice thickness was 5 mm.

2.4. Image processing and task analysis

Preprocessing of the fMRI data was performed with AFNI (Cox, 1996) and consisted of physiological motion correction (Glover, Li, & Ress, 2000), rigid-body

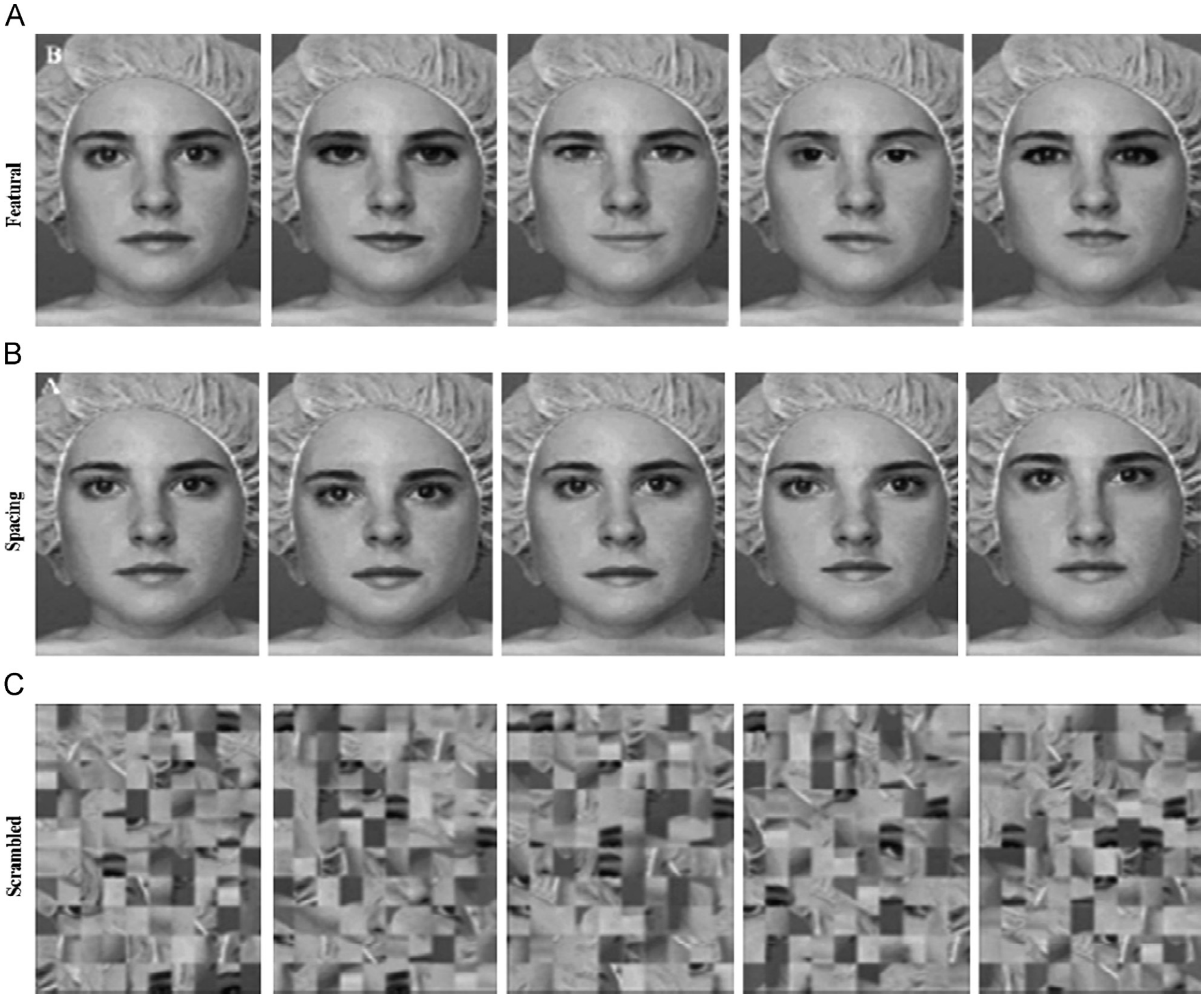

Fig. 1. Examples of stimuli from the Jane task for Feature (A), Spacing (B), and Scrambled (C) conditions.

motion correction, spatial normalization to the MNI template (resampling our data to 4 mm isotropic voxels), and smoothing (full-width half-maximum, 8 mm).

For the Localizer data, all time points for each condition (across all runs) for each subject were averaged and these averages were included in the analysis. For the analysis of the Jane data, we divided the three conditions into early (average of runs 1 and 2) and late conditions (average of runs 3 and 4) to gain power from replications across runs. A first analysis included the Scrambled, Spacing, and Feature conditions, and a second compared just the Spacing and Feature conditions to remove the influence of the Scrambled condition and focus on face processing differences. For the Jane analysis there were 13 Controls and 9 Cataract participants with sufficient data (the analysis of the Localizer data included all participants).

Image analysis was performed with partial least squares, or PLS (McIntosh, Bookstein, Haxby, & Grady, 1996; McIntosh & Lobaugh, 2004), a multivariate analysis approach that robustly identifies spatiotemporal patterns related to varying tasks (task-PLS) or correlated to neuronal activity (seed-PLS). Because the decomposition of the data matrix is done in a single analytic step, no correction for multiple comparisons is required for this approach. PLS performs block-based signal normalization (i.e., normalizing to the first time point in each block) and then uses singular value decomposition to extract patterns of activity that characterize the covariance between activity in all voxels and the experimental conditions or seed activity. In task-PLS, each latent variable (LV) contains a spatial activity pattern depicting the brain regions that, as a whole, show the strongest relation to (e.g. are covariant with) the task contrast identified by the LV. Each brain voxel has a weight, known as a salience, which is proportional to the covariance of activity with the task contrast on each LV. The significance for each LV as a whole was determined by using a permutation test (McIntosh et al., 1996), using 500 permutations. In addition to the permutation test, a second and independent step was to determine the reliability of the saliences for the brain voxels characterizing each pattern identified by the LVs. To do this, all saliences were submitted to a bootstrap estimation (100 bootstraps) of the standard errors (SE, Efron, 1981). Reliability for each voxel was determined from the ratio of salience value to the SE for that voxel (bootstrap ratio, or BSR). Clusters of activity were identified using a BSR of ≥ 3.0 ($p < 0.005$), and a cluster size of 10 voxels. The local maximum for each cluster was defined as the voxel with a salience/SE ratio higher than any other voxel in a 2-cm cube centered on that voxel. Locations of these maxima are reported as coordinates in MNI space and labeled according to gyrus or sulcus. Finally, to obtain summary measures of each participant's expression of each LV pattern, we calculated "brain scores" by multiplying each voxel's salience by the BOLD signal in the voxel, and summing overall brain voxels for each participant. This resulted in a brain score for each participant in each condition, for each LV. These brain scores were then mean-centered (using the grand mean across groups) and confidence intervals (95%) for the mean brain scores in each condition were calculated from the bootstrap. Differences in activity between conditions within groups, as well as differences between groups per condition, were determined via a lack of overlap in these confidence intervals.

The primary analyses included both groups so that patterns of activity to which each group contributed, as well as any group differences in these patterns of activity, could be assessed directly. These were followed up with analyses assessing each group separately to confirm these similarities and differences.

2.5. Functional connectivity analysis

For this analysis, we were interested in examining functional connectivity among face processing regions independently of task effects to get an estimate of intrinsic connectivity. This is typically done by measuring functional connectivity during resting state scans (e.g., Allen et al., 2011; Fox et al., 2005). Since we did not obtain such scans on our participants, we took another approach, which was to treat the first run for all participants (a Localizer run) as if it were a resting state run. To do this we divided the run into 28 sequential "blocks" of data, each 10 s in length, which ignores the timing of stimulus presentation, thus blurring any task effects present in the data. This results in patterns of functional connectivity that

Table 1
Behavioral data for the Jane Task.

Condition	Control group	Cataract group
Accuracy (proportion correct)		
Spacing	0.77 ± 0.12	0.61 ± 0.10
Feature	0.88 ± 0.11	0.79 ± 0.12
Scrambled	0.91 ± 0.14	0.88 ± 0.09
Response time (ms)		
Spacing	781 ± 100	868 ± 124
Feature	752 ± 115	840 ± 127
Scrambled	704 ± 97	782 ± 111

closely resemble those calculated from "true" resting state scans (Grigg & Grady, 2010b), and similar approaches have been used by others (Al-Aidroos, Said, & Turk-Browne, 2012). For our purposes here, we assessed functional connectivity of two fusiform gyrus regions based on their proximity to the right and left FFA, as defined in the literature (see Supplementary Table 1 for an average estimate of FFA location). The seed coordinates were obtained from an LV identified by the task-PLS analysis of the Localizer, which showed a group difference in face-specific activity (see Table 2b, results for LV2). The aim of this analysis was to test the idea that cataracts would alter the functional connectivity of these regions with other areas in the face network. For this analysis, we included both regions (or seeds) and both groups because we wanted to determine the common set of regions that would be functionally connected with the two seeds in the groups, as well as the group differences in the strength of functional connections in this network.

For this analysis, we used seed PLS, which involved extracting the mean signal for each seed voxel from the 28 "blocks" in the first scan, and correlating these values with the mean signal in all other brain voxels, across participants in each group. These correlations (one for each block) were then compared across blocks and groups; this analysis was data-driven, as were the task analyses. The first LV identified a common network that was strongly correlated with both seeds in both groups, and it is this pattern that we report here. To provide a measure of how strongly seed activity covaried with the whole-brain pattern of activity, correlations between brain scores and seed activity were computed for each group, for each block. We compared the distribution of the correlations across the 28 blocks between groups using *t*-tests (note that the same results were obtained with *t*-tests after converting the *r* values to *Z* values using a Fisher transformation, and when using an independent samples non-parametric test), and the correlation strength between right/left seeds within each group with paired *t*-tests. Because this type of correlation analysis is sensitive to outliers, one cataract participant who was shown to be an outlier in preliminary analyses was omitted. To assess functional connectivity of these fusiform regions in a "true" resting state for comparison, we carried out a similar analysis in an independent group of 45 healthy young adults, who were scanned at rest in other experiments (Campbell, Grady, Ng, & Hasher, 2012; Campbell, Grigg, Saverino, Churchill, & Grady, 2013; Grigg & Grady, 2010a), using the same two seed regions.

3. Results

3.1. Behavioral data

The behavioral data for the Jane task are shown in Table 1. There was a significant main effect of task on accuracy ($F(2,40)=84.4$, $p<0.001$) and a significant effect of group ($F(1,20)=8.5$, $p<0.005$). These main effects were moderated by a significant group × task interaction ($F(2,40)=8.5$, $p=0.001$). Tests of group differences for the tasks done separately revealed a significant group difference for the Spacing task ($F(1,20)=10.8$, $p<0.005$), a non-significant trend for the Feature task ($F(1,20)=3.2$, $p=0.09$), and no group difference for the Scrambled task ($F<1$). All mean performance scores were significantly above chance, which would be 50% (all t's >3, p's <0.01). Because we analyzed the brain data in early and late phases of the Jane task, we also examined the behavioral data in this way. The effect of task phase on accuracy was not significant ($F(1,19)=2.6$, $p>0.10$), and neither was the interaction of phase × group ($F(1,19)=1.9$, $p>0.10$), phase × task ($F(1,19)=1.4$, $p>0.20$), nor the 3-way interaction of phase × group × task ($F<1$).

For RT, there was a significant main effect of task ($F(2,40)=41.2$, $p<0.001$). All pairwise comparisons between the tasks were significant ($p<0.01$, Bonferroni corrected). The effect of group and the interaction of task × group were not significant, although there was a trend for the Cataract group to be slower than Controls ($F(1,20)=3.2$, $p=0.09$). The effect of early vs. late phase was not significant for RT ($F(1,19)=2.5$, $p>0.10$), or the phase × group interaction ($F(1,19)=2.6$, $p>0.10$), or the 3-way interaction ($F(2,38)=1.1$, $p>0.30$). However the phase × task interaction was significant ($F(2,38)=3.5$, $p<0.05$). Paired *t*-tests done on each task separately showed no difference in early vs. late phase for Feature or Scrambled, but RT was faster in the late phase during the Spacing task (early $M=835$ ms, late $M=798$ ms, $t(20)=3.2$, $p<0.01$).

3.2. Brain activity during the Localizer scan

PLS analysis of brain activity during the Localizer scan identified three significant patterns of activity. The first ($p<0.002$, accounting for 37.8% of the covariance) showed brain regions where the activity was higher during all the visual stimulus conditions relative to fixation, with the most activity seen for objects (Fig. 2A). More activity for the visual stimuli was seen in both groups in a widespread area of bilateral extrastriate cortex, including the fusiform gyri, extending into the left superior parietal lobe (Table 2A). More activity also was found in extensive areas of left IFG. Therefore, this pattern of activity engaged core and extended face-network regions, as well as broader regions of posterior cortex. Activity in these regions was reduced during fixation, but there were no regions with more activity during fixation that exceeded the BSR threshold. In addition, there were no group differences in any of the visual stimulus conditions, although the reduction of activity during fixation was less in the Cataract group relative to Controls. As can be seen in Table 2 A, the increase in activity above fixation, averaged across the three stimulus conditions, was comparable in the two groups in the regions making a robust contribution to this pattern of activity. Analyses of the Localizer data in each group separately (see Supplementary Figure 1) showed that both Control and Cataract groups had a significant pattern of activity that very closely resembled the one seen in Fig. 2A, with no group differences in the independently generated brain scores. Thus, the within-group analyses, as well as the direct group comparison, indicate no group differences in how this pattern of activity contrasting the stimulus categories to fixation was expressed.

An additional pattern of activity from the Localizer scans (LV3, $p=0.03$, accounting for 13.6% of the covariance) also showed no group differences. This LV differentiated faces from all other conditions, especially objects, in both groups (Fig. 2B). More activity for faces was observed in a restricted group of face-network regions, consisting of right fusiform and middle temporal gyri, bilateral inferior occipital gyri, and right amygdala (Table 2D). Activity was increased for objects, relative to faces, in a widely distributed set of regions, including the lingual and parahippocampal gyri, bilateral parietal cortex, and left middle frontal gyrus (Table 2E). As with the first LV, the magnitude of activity in these regions for faces or objects, relative to fixation, was similar in the two groups (Table 2D and E). Analysis of the groups separately showed no significant pattern of activity resembling the ones seen in Fig. 2B in either group, indicating that this effect was a relatively weak one that could only be identified when the statistical power was increased by including both groups.

A third pattern of activity (LV2, $p<0.002$, accounting for 28.8% of the covariance) showed a group difference specific to faces. This LV differentiated faces from all other conditions in Controls, with the maximal difference between faces and houses (Fig. 3A). More activity for faces than houses or objects was seen in a distributed set of regions, including both core and extended face network areas. Core regions with more face-related activity included

Table 2
Brain areas identified in the analysis of the Localizer scan.

Brain region	BA	*X*	*Y*	*Z*	BSR	Δ Control[a]	Δ Cataract
(A) All object categories > fixation (LV1)							
R inferior frontal gyrus[b]	47	48	24	−16	4.1	0.24 ± 0.10	0.00 ± 0.10
L inferior frontal gyrus[b]	45	−40	24	12	8.0	0.14 ± 0.03	0.06 ± 0.06
L middle frontal gyrus	10	−44	52	8	3.7	0.23 ± 0.12	0.12 ± 0.09
L superior frontal gyrus	9	−16	52	32	6.4	0.33 ± 0.06	0.09 ± 0.08
L inferior occipital gyrus	18	−24	−92	0	13.8	0.76 ± 0.08	0.54 ± 0.10
R middle occipital gyrus	18	28	−92	4	13.9	1.02 ± 0.10	0.80 ± 0.16
R inferior occipital gyrus[b]	19	44	−72	−16	10.1	0.59 ± 0.07	0.71 ± 0.15
L inferior occipital gyrus[b]	19	−44	−76	−8	10.1	0.41 ± 0.07	0.47 ± 0.09
R fusiform gyrus[b]	37	32	−56	−20	8.0	0.49 ± 0.09	0.25 ± 0.16
L fusiform gyrus[b]	37	−36	−60	−12	11.8	0.25 ± 0.10	0.24 ± 0.08
L intraparietal sulcus	7	−28	−68	44	4.5	0.20 ± 0.18	0.05 ± 0.05
(B) Faces > houses (LV2)							
R medial frontal gyrus[b]	9	8	44	28	5.6	0.08 ± 0.04	−0.07 ± 0.03
R middle frontal gyrus	10	32	64	8	7.6	0.10 ± 0.13	−0.16 ± 0.13
R middle frontal gyrus	8	36	8	44	5.2	0.09 ± 0.06	0.02 ± 0.05
L middle frontal gyrus	46	−40	48	8	5.8	0.17 ± 0.07	0.04 ± 0.05
L middle frontal gyrus	8	−48	8	48	4.6	0.47 ± 0.15	0.02 ± 0.26
L superior frontal gyrus	10	−24	52	20	4.9	0.04 ± 0.06	0.06 ± 0.08
R middle temporal gyrus	37	48	−64	−4	8.5	0.16 ± 0.09	0.28 ± 0.10
L middle temporal gyrus[b]	37	−52	−68	4	6.9	0.30 ± 0.11	0.14 ± 0.09
R middle temporal gyrus[b]	21	60	−16	−12	4.6	0.11 ± 0.09	−0.26 ± 0.07
L amygdala/globus pallidus[b]		−20	−12	−12	4.6	0.31 ± 0.09	0.00 ± 0.07
R anterior inferior parietal lobe	40	60	−44	40	5.8	0.10 ± 0.15	−0.45 ± 0.08
L intraparietal sulcus	7	−32	−52	52	4.8	0.19 ± 0.08	0.01 ± 0.06
R precuneus/posterior cingulate[b]	31	8	−68	28	7.9	0.28 ± 0.11	−0.18 ± 0.10
R fusiform gyrus[b]	37	44	−40	−20	4.2	0.22 ± 0.11	0.45 ± 0.12
L fusiform gyrus[b]	37	−44	−48	−20	4.8	0.24 ± 0.15	0.34 ± 0.12
R thalamus		4	−28	4	4.8	0.08 ± 0.07	0.06 ± 0.14
R caudate/putamen[b]		16	8	12	6.0	0.08 ± 0.05	−0.06 ± 0.05
L caudate[b]		−16	0	16	7.1	0.02 ± 0.09	−0.05 ± 0.05
(C) Houses > faces (LV2)							
R middle occipital gyrus	18	28	−88	4	−5.4	1.03 ± 0.12	0.59 ± 0.13
L lingual gyrus	18	−16	−92	−4	−5.0	0.94 ± 0.15	0.44 ± 0.13
R parahippocampal gyrus	36	28	−44	−12	−4.3	0.24 ± 0.11	0.19 ± 0.07
(D) Faces > objects (LV3)							
R amygdala[b]		28	0	−20	4.5	0.32 ± 0.07	0.27 ± 0.11
R fusiform gyrus[b]	37	40	−44	−24	4.9	0.65 ± 0.16	0.78 ± 0.16
R middle temporal gyrus[b]	21	52	−56	4	5.5	0.29 ± 0.08	0.08 ± 0.04
R inferior occipital gyrus[b]	19	44	−80	−16	7.6	1.09 ± 0.17	1.13 ± 0.15
L inferior occipital gyrus[b]	19	−40	−80	−20	4.4	1.15 ± 0.18	1.23 ± 0.27
(E) Objects > faces (LV3)							
L middle frontal gyrus	9	−32	40	20	−4.2	−0.04 ± 0.09	0.13 ± 0.07
R superior temporal gyrus	22	64	8	−4	−5.6	0.32 ± 0.18	−0.07 ± 0.21
L inferior temporal gyrus	37	−56	−60	−12	−4.8	0.35 ± 0.08	0.22 ± 0.09
R posterior cingulate gyrus	31	8	−44	40	−5.2	0.01 ± 0.09	0.00 ± 0.06
R parahippocampal gyrus	36	28	−44	−12	−7.8	0.28 ± 0.11	0.20 ± 0.08
L lingual gyrus	19	−24	−60	−8	−5.7	0.43 ± 0.07	0.29 ± 0.10
R superior occipital gyrus	19	40	−80	24	−5.9	0.40 ± 0.15	0.08 ± 0.14
L middle occipital gyrus	19	−36	−84	8	−6.1	0.84 ± 0.11	0.57 ± 0.13
L superior temporal gyrus	41	−64	−24	12	−4.9	0.03 ± 0.14	0.08 ± 0.12
R precuneus	7	20	−76	40	−8.3	−0.05 ± 0.11	0.16 ± 0.13
L precuneus	7	−16	−76	40	−7.2	0.16 ± 0.12	0.10 ± 0.14
L intraparietal sulcus	40	−48	−36	40	−3.7	0.03 ± 0.11	0.08 ± 0.04

Note: BA, Brodmann area; *X*, right/left; *Y*, anterior/posterior; *Z*, superior/inferior; BSR, bootstrap ratio.

[a] Δ refers to a difference between conditions for each effect (mean ± S.E., all values were mean − centered prior to calculating the difference): A, average of stimulus minus fixation across all categories; B, face minus fixation; C, house minus fixation; D, face minus fixation; E, object minus fixation.

[b] Region that is similar in location to an area proposed to be a part of the face network (including core and extended areas; see Supplementary Table for locations of core regions).

bilateral fusiform gyri, and left middle temporal gyrus; emotion regions included bilateral striatum, left amygdala and left insula; and person-knowledge regions included medial PFC, PCC, and right anterior temporal cortex (Table 2B). More activity for faces in regions outside the face network was seen in bilateral middle frontal gyri and bilateral parietal cortex. More activity for houses than faces was seen in right parahippocampal/lingual gyrus and bilateral posterior extrastriate cortex. The Cataract group showed equivalent activity for houses, but less activity than Controls in face-sensitive regions, as indicated by the non-overlapping confidence intervals for the mean brain scores between the two groups in the face condition (Fig. 3A). Indeed, a number of these regions showed less activity for faces than for fixation in the Cataract group (Table 2B). Interestingly, the extended face-network regions that were part of this pattern of activity (e.g., amygdala and precuneus) appeared to show greater decrements in face-sensitive activity in the Cataract group than did the core regions (i.e., bilateral fusiform and left middle temporal gyrus, Table 2B). To test whether the

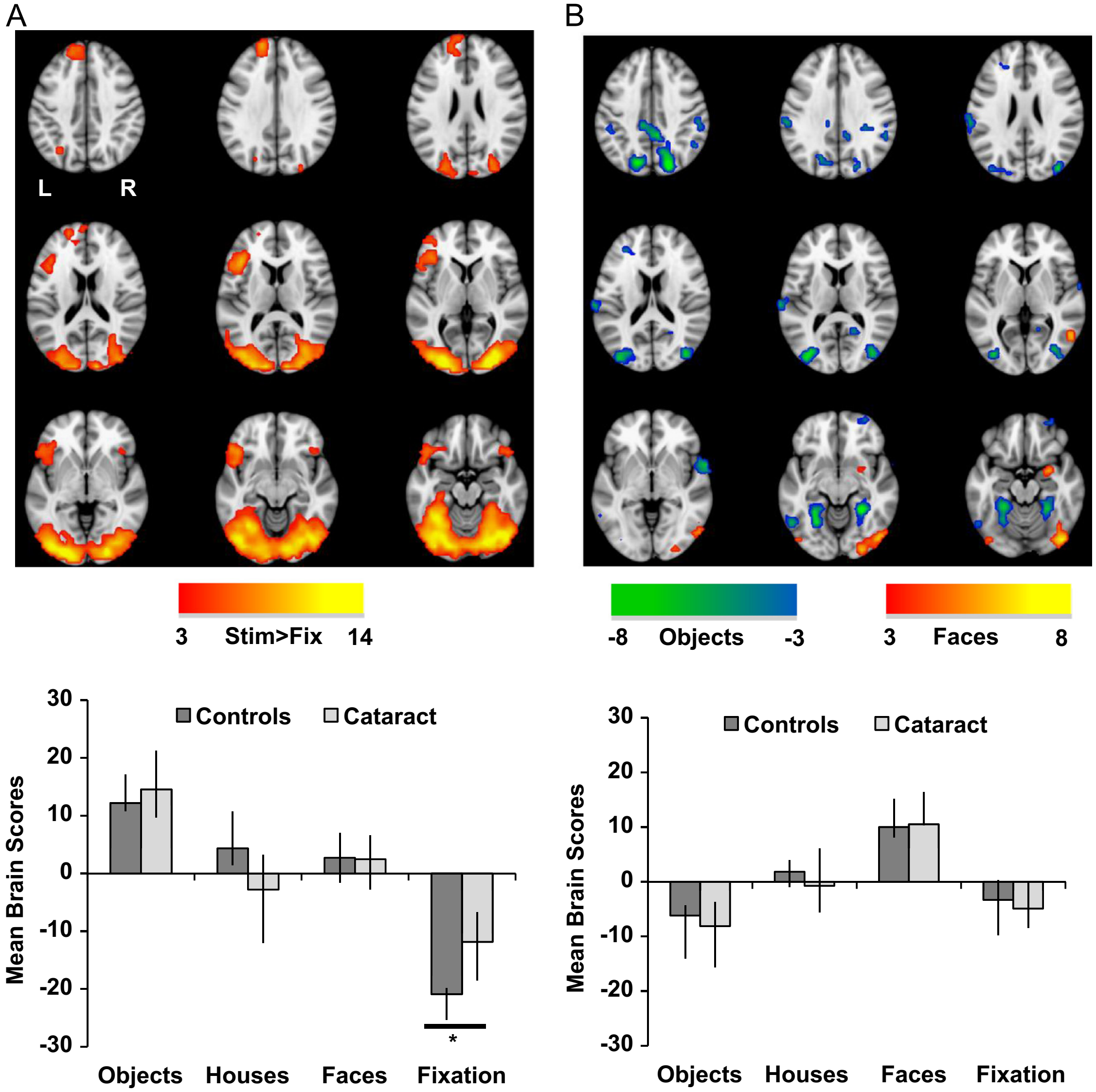

Fig. 2. The result of the analysis of the Localizer scans, showing two LVs on which there were no group differences for any of the visual category conditions. (A) The warm colored brain areas (associated with positive brain scores) are those with increased activity for objects, faces and houses relative to fixation in both groups. The graph shows the average of the mean-centered brain scores for each condition in each group (error bars are the 95% confidence intervals, CIs). The only group difference was seen in the fixation condition (indicated by "*"). In this and all subsequent figures, non-overlapping CIs between bars indicate reliable differences in activity, whereas overlapping CIs indicate no differences. CIs that overlap with zero on the graph indicate activity that does not differ from the mean activity across all conditions and groups. (B) The warm-colored areas (associated with positive brain scores) are those with increased activity mainly for faces in both groups. Cool colored areas (associated with negative brain scores) have more activity for objects. Overlapping CIs between groups for all conditions indicate no group differences. The color bars indicate the range of BSRs shown in the images. In this and subsequent figures the left and right hemispheres are indicated by "L" and "R", respectively. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

activity in the core face-network regions was maintained in the Cataract group, compared to the extended network regions, we conducted a two-factor ANOVA (group and region type [core, extended]) on the mean activity for the three core regions and the mean activity for the extended network regions (regions are indicated by asterisks in Table 2B). The group by region type interaction was significant ($F[1,22]=5.5$, $p=0.03$); follow-up *t*-tests showed that the activity for core regions did not differ between groups ($t[22]<1$), but the Cataract group had significantly less activity for extended-network regions ($t[22]=4.5$, $p<0.001$). Finally, unlike Controls, the activity for objects was significantly increased above baseline in the Cataract group.

When the Control and Cataract groups were analyzed separately, each group showed a significant LV that replicated the pattern seen in the between-group analysis. In Controls the primary contrast was between faces and houses ($p<0.002$), as was seen in the analysis of both groups (compare Fig. 3B to A). In the Cataract group the largest difference in activity was between objects and houses, with little contribution of faces and fixation ($p=0.004$, compare Fig. 3C to A). Thus, the within-group analyses, as well as the between-group analysis, suggested a group by condition interaction, such that Controls had more activity for faces than objects, whereas the Cataract group showed the opposite. An ANOVA on the face and object brain scores from the between-group analysis (i.e., those seen in Fig. 3A) showed a significant group by condition interaction ($F[1,22]=6.4$, $p=0.02$), confirming that the face-sensitive regions in Controls tended to be more object-sensitive in the Cataract group.

3.3. *Brain activity during the Jane task*

The task-PLS analysis of data from all three conditions of the Jane runs resulted in a single significant LV ($p<0.002$, accounting for 43.6% of the covariance). This LV identified a set of regions

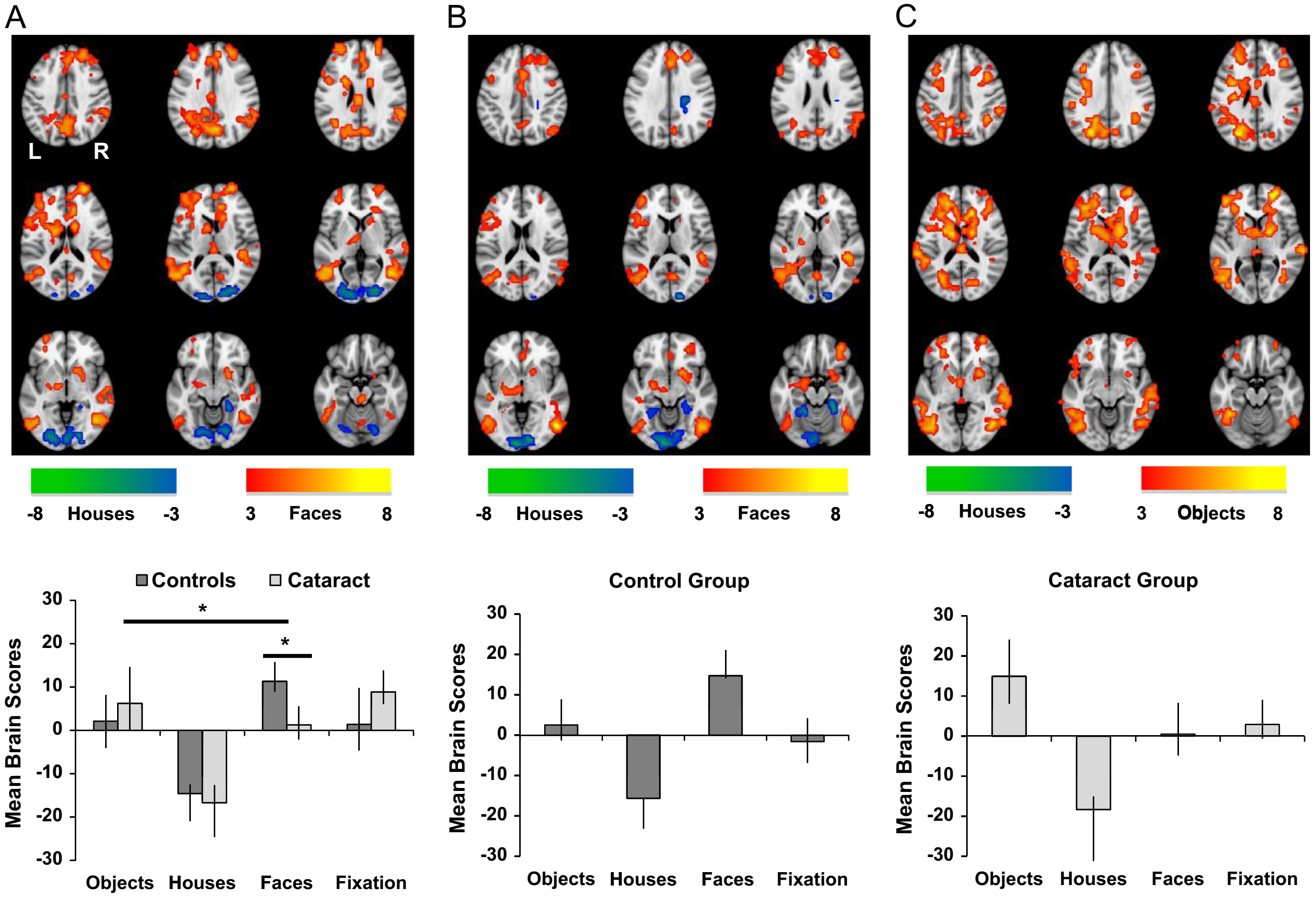

Fig. 3. An additional LV from the Localizer that showed a group difference for face-specific activity. (A) Warm-colored brain areas (associated with positive brain scores) are those with more activity for faces vs. the other conditions and cool colors (associated with negative brain scores) indicate more activity for houses in Controls. For the Cataract group, the activity for faces does not differ from the mean, or differ from objects, and is less than that seen in controls. There was a group difference in activity for faces and a significant interaction of group by condition for the face and object conditions (both indicated by "*"). (B) Analysis of the Control group only, showing condition contrasts that closely resemble the pattern for Controls in A. (C) Analysis of the Cataract group only, showing condition contrasts that closely resemble the pattern for this group in A. Error bars in the graphs are the 95% confidence intervals. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

where activity differentiated the Scrambled condition from the Spacing and Feature conditions (Fig. 4a) for early and late runs in both groups, with no group differences. There was greater activity for scrambled faces in an extensive set of occipital and parietal regions and in left inferior frontal gyrus (see Table 3A for the magnitude of these activity increases), similar to the set of regions with more activity for objects, houses and faces, relative to fixation, seen in Fig. 2a. This occipital activity is likely due to the increased number of edges and "objects" seen in the scrambled images. More activity for the Spacing and Feature conditions, relative to Scrambled, was seen only in two face network regions, ventromedial prefrontal cortex, including OFC, and bilateral amygdala (Fig. 4a, Table 3B). The late blocks showed reduced differences in brain activity between the Jane and Scrambled conditions because the activity during the Scrambled condition declined in both groups over time (Fig. 4a, Table 3A and B). When the groups were analyzed separately, significant patterns showing the same effect as in Fig. 4a were found, with no differences between groups in the expression of this pattern (see Supplementary Figure 2).

When the Scrambled condition was omitted from the analysis, a single significant pattern of activity differentiating the Spacing and Feature conditions was identified ($p=0.02$, accounting for 26.7% of the covariance, Fig. 4b). Both the Cataract and Control groups showed activity that differentiated early and late Spacing conditions from the Feature conditions, and there were no group differences in the expression of this pattern. However, the Cataract group had reliably less activity in the early Spacing condition than the late condition, whereas Controls showed no early/late differences (non-overlapping confidence intervals for early vs. late Spacing in the Cataract group, Fig. 4b). Regions with more activity for Spacing than for Feature were all in the right hemisphere, including frontal areas of the extended face network (IFG and dorsomedial frontal cortex, Table 3C). More activity for the Feature condition was seen in left ventromedial prefrontal cortex, left putamen and right cerebellum (Table 3D). When the groups were analyzed separately, only the Controls showed a significant pattern differentiating the Spacing and Feature conditions (accounting for 42.9% of the covariance, $p=0.01$), indicating that this effect was weaker in the Cataract group ($p=0.15$), although still detectable when both groups were included in the analysis.

Neither the right nor left fusiform gyrus showed a Spacing/Feature difference during the Jane task. However, we probed activity in this region further, given that in our previous study (Maurer et al., 2007b), which reported data from 10 of the control participants included in the current report, we found a region in the right posterior fusiform gyrus (within the boundary of the FFA as defined here) that was more active in Controls during the Spacing condition than during the Feature condition. To determine if the failure to find such a region in the current analysis was due to the influence of the Cataract group, we carried out a task PLS analysis including just the Controls. This analysis revealed a region in the right posterior fusiform with more activity for Spacing

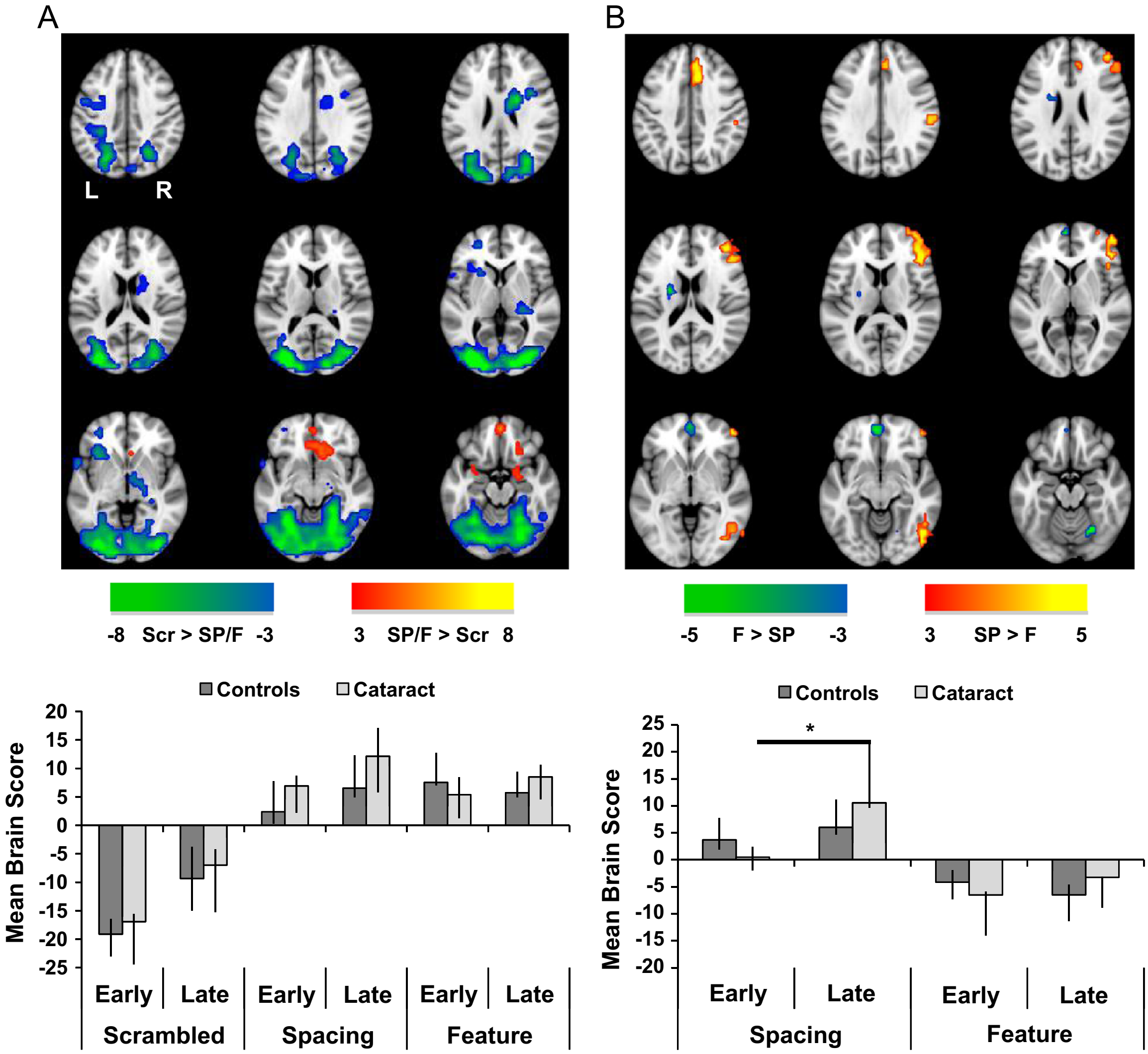

Fig. 4. Results of the analysis for the Jane task. (A) The warm-colored areas (associated with positive brain scores) have increased activity for Spacing and Feature vs. Scrambled, and cool colored regions (associated with negative brain scores) indicate more activity for Scrambled stimuli. The graphs in this figure show the average of the mean-centered brain scores for each condition in each group. Both groups show distinct activity for Spacing/Feature vs. Scrambled, with no group differences. (B) The warm-colored areas are those with increased activity for Spacing and cool colors indicate more activity for Feature. The activity for both Spacing conditions differed from both Feature conditions, and no group differences in activity were seen. In Controls there were no differences between early and late runs for either Spacing or Feature, but the Cataract group showed less activity for the early Spacing condition than the late Spacing condition (indicated by "*"). The color bars indicate the range of BSRs shown in the images. Error bars in the graphs are the 95% confidence intervals. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

($X=52$, $Y=-60$, $Z=-24$, similar to our previously reported region: $X=56$, $Y=-64$, $Z=-20$). When the activity from this region was extracted for the Cataract group, there was no difference in activity between the Spacing and Feature conditions ($F<1$, Fig. 5).

3.4. Functional connectivity of right and left fusiform gyri

The network of regions that showed positive functional connectivity with the right and left fusiform seeds when both groups were included is shown in Fig. 6a (25.6% of the covariance, $p<0.002$). This set of regions included widespread extrastriate areas, bilateral frontal cortex (including IFG and OFC), medial parietal cortex, bilateral amygdala and left striatum. This group of regions therefore included both core face-network areas and extended areas (Table 4). Mean connectivity strength across the 28 blocks of the run was positive for both seeds and both groups, and did not differ between groups for the right fusiform seed ($t<1$). However the connectivity strength did differ for the left fusiform region, and was stronger in the Cataract group compared to Controls ($t(54)=3.5$, $p=0.001$). In addition, the Cataract group had significantly weaker functional connectivity in the right fusiform compared to the left (paired $t(27)=-3.4$, $p<0.005$), whereas the Control group showed no hemispheric difference ($t<1$). Thus, this analysis identified regions with strong functional connections to the fusiform gyri that were common to both groups. Although we did not find weaker right fusiform connectivity in the Cataract group, relative to Controls, we did see reductions compared to their own left hemisphere connectivity, which in turn was increased relative to Controls. The group difference was therefore not in the regions that were functionally connected to the fusiform gyri, but in the strength of correlations between these regions and the left fusiform region. Separate functional connectivity analyses in the two groups revealed very similar patterns of activity to that seen in Fig. 6a and almost identical mean correlation values (see Supplementary Figure 3).

To assess whether the pattern of functional connectivity seen here using our estimate of intrinsic connectivity during the first

Table 3
Brain areas identified in the analysis of the Jane Task.

Brain region	BA	X	Y	Z	BSR	Δ Con early[a]	Δ Con late	Δ Cat early	Δ Cat late
(A) Spacing & Feature > Scrambled									
R anterior cingulate	25	8	20	−12	5.0	0.10 ± 0.10	0.27 ± 0.10	0.11 ± 0.14	0.15 ± 0.14
R orbitofrontal cortex[b]	11	4	48	−20	5.1	0.41 ± 0.12	0.10 ± 0.17	0.60 ± 0.14	0.03 ± 0.29
L inferior frontal gyrus	47	−16	28	−16	4.1	0.24 ± 0.09	−0.07 ± 0.18	0.29 ± 0.14	0.06 ± 0.16
R amygdala[b]		24	−8	−28	6.3	0.21 ± 0.10	0.13 ± 0.11	0.26 ± 0.10	−0.10 ± 0.15
L amygdala[b]		−20	−8	−28	5.0	0.33 ± 0.16	0.08 ± 0.13	0.23 ± 0.15	−0.08 ± 0.19
(B) Scrambled > Spacing & Feature									
R inferior frontal gyrus	44	40	4	24	−5.0	0.18 ± 0.06	0.11 ± 0.03	0.05 ± 0.05	0.11 ± 0.04
L insula/inferior frontal	47	−32	24	−8	−4.6	0.17 ± 0.06	0.09 ± 0.08	0.10 ± 0.10	0.21 ± 0.07
L precentral gyrus	6	−36	−4	44	−7.0	0.18 ± 0.07	0.12 ± 0.07	0.13 ± 0.05	0.14 ± 0.05
R intraparietal sulcus	7	20	−64	48	−6.6	0.21 ± 0.05	0.18 ± 0.08	0.30 ± 0.04	0.27 ± 0.11
L intraparietal sulcus	7	−24	−60	40	−7.4	0.20 ± 0.08	0.14 ± 0.07	0.20 ± 0.06	0.11 ± 0.06
R middle occipital gyrus	18	32	−88	0	−9.9	0.57 ± 0.08	0.47 ± 0.13	0.47 ± 0.08	0.35 ± 0.13
L middle occipital gyrus	18	−28	−88	0	−16.3	0.80 ± 0.07	0.60 ± 0.09	0.44 ± 0.06	0.31 ± 0.06
R lingual/fusiform gyrus	19	24	−68	−16	−11.5	0.44 ± 0.07	0.35 ± 0.14	0.62 ± 0.06	0.43 ± 0.07
R caudate		16	0	20	−6.0	0.10 ± 0.06	0.07 ± 0.05	0.19 ± 0.05	0.05 ± 0.04
(C) Spacing > feature									
R middle frontal gyrus	10	44	56	8	5.3	0.23 ± 0.15	0.40 ± 0.12	0.14 ± 0.14	0.37 ± 0.15
R inferior frontal gyrus[b]	45	48	32	8	5.1	0.20 ± 0.06	0.18 ± 0.08	0.08 ± 0.04	0.26 ± 0.09
R medial frontal gyrus[b]	32	8	20	40	5.7	0.20 ± 0.06	0.10 ± 0.04	0.10 ± 0.06	0.14 ± 0.03
R intraparietal sulcus	40	60	−24	36	3.7	0.33 ± 0.10	0.33 ± 0.15	0.05 ± 0.10	0.18 ± 0.09
R inferior temporal gyrus	37	48	−64	−8	4.9	0.16 ± 0.09	0.03 ± 0.07	0.11 ± 0.06	0.19 ± 0.05
(D) Feature > spacing									
L medial frontal gyrus	10	−4	60	4	−4.0	0.17 ± 0.09	0.09 ± 0.11	0.12 ± 0.15	0.29 ± 0.07
R cerebellum		24	−64	−20	−4.4	−0.07 ± 0.10	0.29 ± 0.07	0.20 ± 0.06	0.30 ± 0.11
L putamen[b]		−24	−4	16	−3.9	0.02 ± 0.06	0.14 ± 0.07	0.11 ± 0.07	0.09 ± 0.04

Note: Con, control; Cat, cataract; BA, Brodmann area; *X*, right/left; *Y*, anterior/posterior; *Z*, superior/inferior; BSR, bootstrap ratio.

[a] Δ refers to the difference between conditions for each effect (mean ± S.E., all values were mean-centered prior to calculating the difference): A, mean of spacing and feature minus scrambled; B, scrambled minus mean of spacing and feature; C, spacing minus feature; D, feature minus spacing.

[b] Region that is similar in location to an area proposed to be a part of the face network (including core and extended areas; see Supplementary Table for locations of core regions).

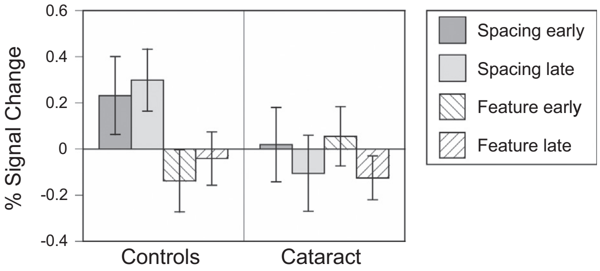

Fig. 5. Mean activity for a region of the right posterior fusiform gyrus that was more active for Spacing than for Feature when the controls were analyzed separately (see text for coordinates). Plotted values are mean ± S.E.

Table 4
Brain areas that are functionally connected with the right and left fusiform gyri.

Brain region	BA	X	Y	Z	BSR
R inferior frontal gyrus	9	56	8	40	8.1
R superior frontal gyrus	9	20	56	20	7.1
R inferior frontal gyrus	9	60	16	28	10.0
L inferior frontal gyrus[a]	45	−52	24	12	9.2
Orbitofrontal gyrus[a]	10	−4	56	−8	7.8
R inferior occipital gyrus[a]	18	28	−88	−20	7.5
L inferior occipital gyrus[a]	18	−32	−88	−16	9.3
R middle temporal gyrus[a]	21	64	−12	−24	9.4
L anterior inferior parietal lobe	40	−52	−40	44	7.7
R posterior inferior parietal lobe	40	36	−64	48	6.7
R precuneus[a]	31	4	−64	32	6.4
R amygdala[a]		20	−8	−20	8.6
L amgydala/hippocampus[a]		−20	−12	−24	6.7
L putamen[a]		−20	4	4	7.5

Note: BA, Brodmann area; *X*, right/left; *Y*, anterior/posterior; *Z*, superior/inferior; BSR, bootstrap ratio.

[a] Region that is similar in location to an area proposed to be part of the face network (including core and extended areas; see Supplementary Table for locations of core regions).

localizer run resembles the functional connectivity of these fusiform regions during a true resting state scan, we also carried out the seed PLS analysis in an independent group of healthy young adults. The resting functional connectivity pattern of the right and left fusiform regions is shown in Fig. 6b (47.5% of the covariance, $p < 0.002$). This pattern is more spatially extensive, probably due to increased statistical power, but is nevertheless very similar to that seen in the Control and Cataract groups. Importantly, there was no difference in connectivity between the right and left fusiform regions in this independent sample at rest. This lends support to the idea that the functional connectivity identified in the Control and Cataract groups is a reasonable estimate of intrinsic connectivity and that the hemispheric difference seen in the Cataract group deviates from what one would expect to see in healthy young adults.

To summarize the results of the brain activity and functional connectivity analyses, the Control and Cataract groups had equivalent activity during both the Localizer and Jane runs in extrastriate regions consistent with general activity evoked by meaningful visual stimuli. The participants with congenital cataracts also had face-specific activity in a limited set of regions that was equivalent to that of Controls. Although the Cataract group had no overall reductions in activity discriminating the Spacing and Feature conditions from the Jane task, relative to Controls, they did show less activity during the early Spacing conditions compared to the activity they showed in the later conditions, and failed to activate the right fusiform gyrus during Spacing trials. There were two

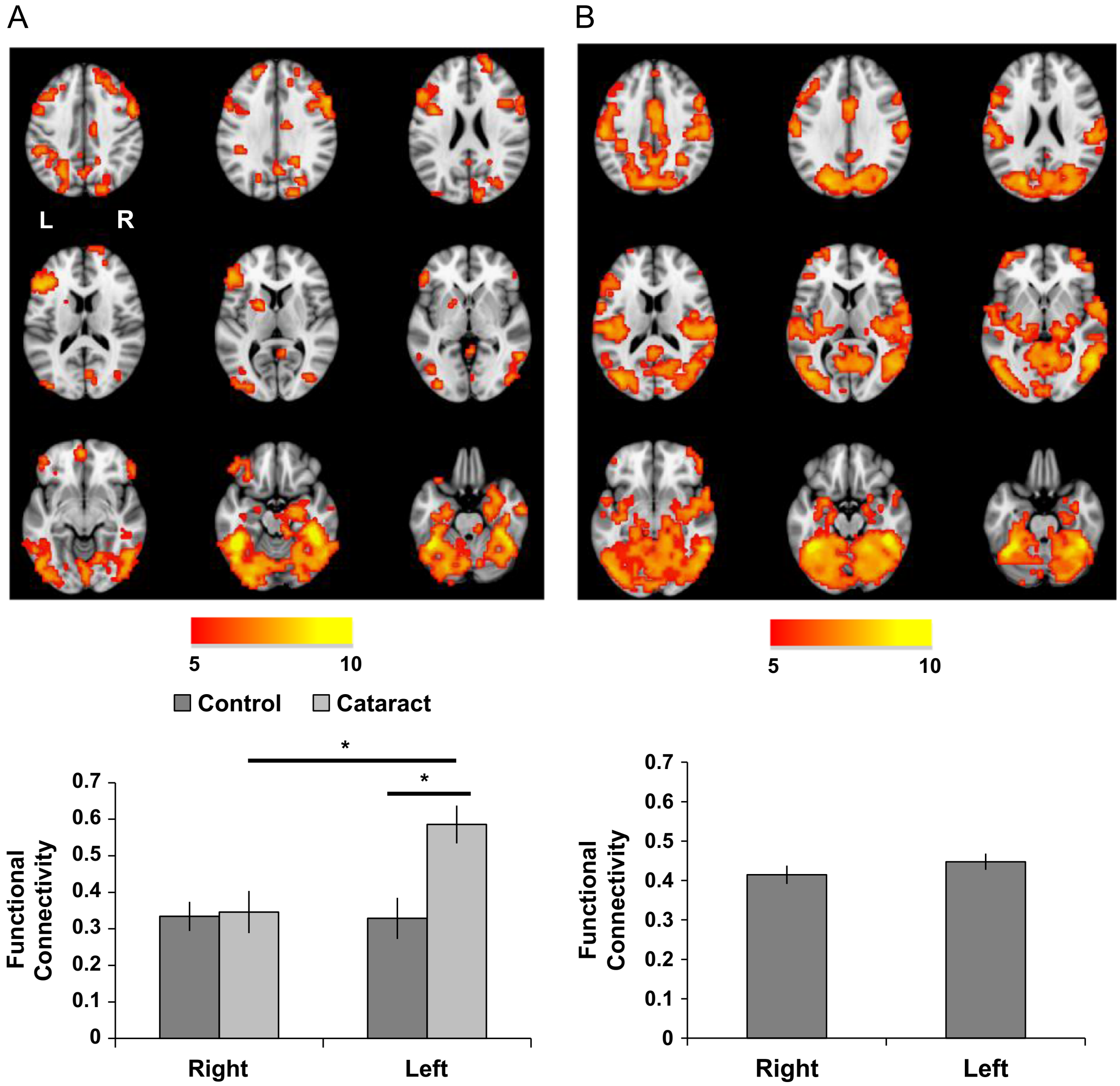

Fig. 6. (A) The set of regions where the activity was robustly correlated with right and left fusiform seeds in the Cataract and Control groups is shown in warm colors. The color bars indicate the range of BSRs shown in the images. The graph shows the strength of the functional connectivity for both regions and groups, i.e., the mean correlation over the 28 blocks between each seed's activity and a score expressing activity in all the regions seen in the figure (the brain score). The Cataract group had stronger functional connectivity for the left fusiform gyrus seed relative to Controls and relative to their own connectivity for the right fusiform seed (both effects are indicated by "*"). (B) Regions where resting activity was robustly correlated with right and left fusiform seeds in an independent group of young adults are shown in warm colors. The color bars indicate the range of BSRs shown in the images. The graph shows the strength of the functional connectivity for both regions, measured as the mean correlation (over 29 blocks) between each seed's activity and the brain score. The error bars in the graphs are the S.E. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this paper.)

robust group differences. First, the Controls showed face-specific activity in a broad set of regions, including core and extended face-network regions, and activity in this distributed group of brain areas was markedly reduced for faces in the Cataract group, who instead had activation for objects in these regions. The reduction in face-specific activity was more pronounced for extended face-network regions than for core regions. Second, the bilateral fusiform seed regions had strong functional connections to core and extended-network areas in both groups, but these connections were greater with the left fusiform region in the Cataract group relative to Controls.

3.5. Brain activity and behavior

We next assessed whether any of the brain activity patterns seen during the Localizer or Jane scans were related to performance on the Jane task. To address this question, we assessed four different regression models (using backward regressions) for accuracy on the Spacing and Feature tasks. In two models, the predictors were the brain scores from the face condition in the three Localizer LVs, and the three interaction terms of these scores with the group, and the dependent variable was accuracy on the Spacing (or Feature) task. The other two models included the brain scores from early and late Spacing (or Feature) conditions, the brain score in the Spacing (or Feature) condition vs. the Scrambled condition (averaged across early and late runs), and the interaction terms of these scores with the group, to predict the accuracy. The group interaction terms were included so that we could assess whether there were group differences in brain/behavior associations. For the Spacing performance, the model using the Localizer data was significant ($F(1,20)=5.0$, $p<0.05$, $R^2=0.20$). The only significant predictor of Spacing accuracy was face-specific activity in the brain regions identified in LV2 of the Localizer data ($t=2.2$, $p<0.05$, $\beta=0.48$). This indicates that, in both groups (Fig. 7A), better performance on the Spacing task was related to more activity in the distributed set of face-network regions that

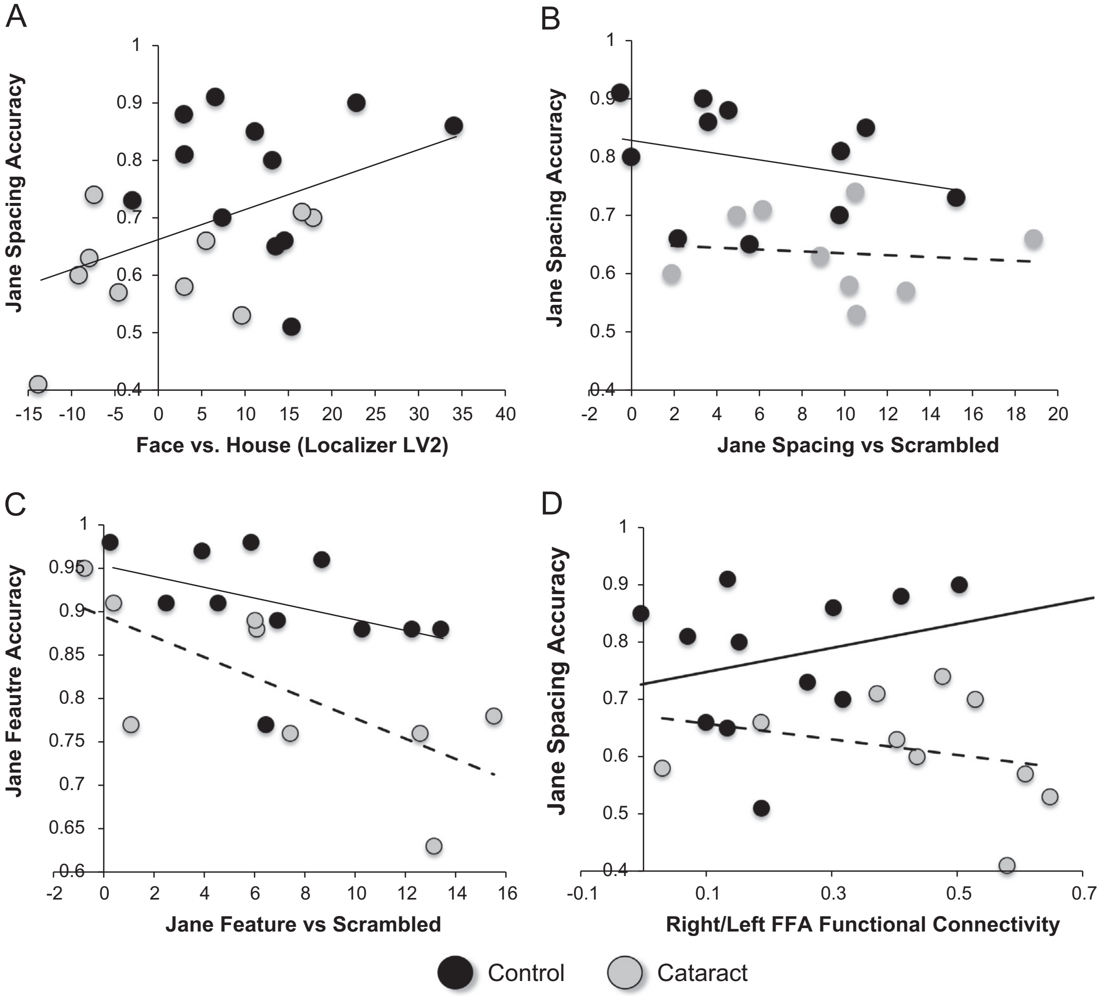

Fig. 7. Associations between performance on the Jane task and significant predictors identified from the regression analyses are shown. (A) Scatterplot showing the relation between Spacing accuracy and face-specific activity from Localizer LV2. (B) Scatterplot showing the relation between Spacing accuracy and activity during the Spacing condition vs. the Scrambled condition. (C) Scatterplot showing the relation between Feature accuracy and activity during the Feature condition vs. the Scrambled condition. (D) Scatterplot showing the relation between Spacing accuracy and the functional connectivity between right and left fusiform seeds (expressed as the mean correlation between activity in the two seeds).

differentiated faces primarily from houses. The model using brain activity during the Spacing task itself also was significant[1] ($F(1,18)=7.5$, $p<0.02$, $R^2=0.29$). In this model only the interaction of the group and brain score for the Spacing vs. the Scrambled condition was a significant predictor ($t=2.7$, $p<0.02$, $\beta=0.54$). As can be seen in Fig. 7B, the accuracy in Controls tended to be higher in those who had less activity in those regions differentiating the Spacing task from the Scrambled task, whereas no relation was seen in the Cataract group.

For Feature accuracy, the model using the Localizer brain scores was not significant ($F(1,20)=3.4$, $p=0.08$), but the model using scores from the Feature task was significant[2] ($F(2,17)=8.7$, $p<0.01$, $R^2=0.51$). In this model, two predictors were significant: activity for Feature vs. Scrambled ($t=-2.5$, $p<0.05$, $\beta=-0.43$) and the interaction of Feature vs. Scrambled and group ($t=2.9$, $p<0.01$, $\beta=0.51$). Fig. 7C shows that overall there was a negative relation between accuracy and brain activity in the Feature condition vs. Scrambled, but this effect was stronger in the Cataract group. Interestingly, brain activity differentiating Spacing from Feature was not related to the performance for either condition.

In a second set of analyses we used similar regression models to assess the relation between functional connectivity of the right and left fusiform regions and behavior on the Jane task. Because the seed PLS analysis assessed functional connectivity across participants, it did not provide individual measures of functional connectivity. So for these regression models we used each participant's mean correlation between the right and left fusiform seeds across the 28 blocks of the scanning run as the predictor. These individual correlation values and the interaction term of group × correlation value were entered into two regression models, one with Spacing accuracy as the dependent variable and one for Feature accuracy. The model for Feature was not significant ($F(1,20)=3.8$, $p=0.07$), but was significant for Spacing ($F(1,20)=12.9$, $p<0.005$, $R^2=0.39$). For Spacing, the group × functional connectivity variable was the only significant predictor of accuracy ($t=3.6$, $p<0.005$, $\beta=0.63$). Because of the trend for a positive association in Controls and a negative association in the Cataract group, the difference between groups in accuracy on the Spacing

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[1] Note that for this analysis, one control participant had outlying values on one of the brain scores ($>$ 2.5 SD), and so was omitted.

[2] Note that for this analysis, as for the one carried out for Spacing, one control participant had outlying values on one of the brain scores ($>$ 2.5 SD), and so was omitted.

task increased as a functional connectivity between right and left fusiform regions increased (Fig. 7D).[3]

A final set of correlations was carried out in the Cataract group to assess relations between visual acuity or days of deprivation prior to cataract removal and: (1) the brain scores from the Localizer and Jane analyses; and (3) functional connectivity between the right and left fusiform seed regions. None of the correlations with acuity were statistically significant, and only one of the correlations with days of deprivation was significant. This was the correlation between deprivation duration and activity for faces from LV3 in the Localizer analysis ($r=0.66$, $p<0.05$), indicating that longer deprivation was associated with more activity for faces in the few face-network regions seen in this pattern (warm colored regions in Fig. 2B).

4. Discussion

In this study, we compared brain activity in young adults treated for congenital cataracts to that of a control group, to determine the influence of early visual deprivation on face processing. The first finding of note is that the effect of congenital cataracts on visual processing is not a general one, despite the reduced acuity in the Cataract group. There were no group differences in the general patterns of visual activity identified in the Localizer and Jane runs, and the Cataract group showed no reductions in the brain activity accompanying processing of either houses or objects. Instead, like the behavioral findings in previous studies (de Heering & Maurer, 2014; Mondloch et al., 2010b; Robbins et al., 2010) and the behavioral findings during the Jane task of this study, the fMRI data indicate that the deficit is specific for faces. The second novel finding is that the individuals with congenital cataracts had reduced brain activity in both core and extended face-network regions, including prefrontal regions, when viewing faces in the Localizer scan. Interestingly, we found no evidence that early visual deprivation from congenital cataracts led to engagement of different brain regions from those of Controls; instead, there were reductions in the use of the areas normally engaged for face processing. Third, we found that the brain activity characterizing faces vs. other stimuli was related to performance on the Jane task in both Controls and Cataract participants, although again there were group differences in the strength of these associations. Finally, the functional connectivity of the fusiform gyri was altered in the Cataract group such that connectivity with the left fusiform and other face-network regions was increased. Additionally, the functional connectivity between right and left fusiform regions was differentially associated with the performance on the Jane task in the two groups. The implications of these results are discussed below.

4.1. Activity during the Localizer

Analysis of the Localizer data showed three different patterns of brain activity across the conditions. The general visual network (LV1) was active for houses, faces, and objects, relative to fixation, as would be expected, and included areas thought to be sensitive to each of the visual categories (including the fusiform and lingual gyri, and lateral occipital cortex). The pattern distinguishing faces from houses in Controls (LV2) was similar to the distinctive regions reported by others, in that it showed fusiform activity for faces and activity in parahippocampal/lingual gyrus for houses (e.g., Epstein, Graham, & Downing, 2003; Large, Cavina-Pratesi, Vilis, & Culham, 2008; Maurer et al., 2007b; Spiridon, Fischl, & Kanwisher, 2006). Activity for faces also included the left STS (a core network region) and extended-network regions involved in face recognition (Gobbini & Haxby, 2007), such as the amygdala (responsive to emotional expressions in faces), precuneus/posterior cingulate and medial PFC (person knowledge), and caudate/striatum (social reward). The third Localizer pattern consisted of increased activity in core face-network areas and the amygdala during face presentation in both groups, and a much more widely distributed set of regions active for objects. Note that although we identified these areas using a group analysis instead of individual analyses as is often done, we found activity in regions that are similar in location to those defined functionally for each visual category and reported in the literature (see Supplementary Table 1). However, because we used a whole brain, multivariate approach, we also were able to identify a much wider range of activity, including most of the face network.

Only the second of these Localizer patterns showed less activity in the Cataract group relative to Controls when viewing faces. Although this distributed pattern of activity was reduced as a whole in the Cataract group, the magnitude of the reduction was greater in extended face-network regions than in core regions. This suggests that the major effect of visual deprivation is not in core face-network regions per se, but in extended face-network regions, suggesting altered communication within the broader network. In addition, the activity in these regions overall was robust for objects in the Cataract group, not for faces; this lack of face-specific activity was particularly evident when the Cataract group was analyzed separately (see Fig. 3b). This suggests the interesting possibility that the face network has been “co-opted” for object processing instead of face processing, which would be an important aspect for future research.

Interestingly, the fusiform gyrus contributed to two patterns, one with (LV2) and one without (LV1) group differences. This is consistent with the idea that the activity within nodes of a network can fluctuate up or down in response to task demands relatively independently of one another or may participate in multiple networks to flexibly respond to task demands or processing states (Bressler & Menon, 2010; McIntosh, 2000). It also should be noted that the particular fusiform regions that contribute to LV1 and LV2 are somewhat different in location, with the face-specific regions being more anterior. Our results indicate that the posterior fusiform covaried with other general visual areas in a non-specific way across all the visual categories (LV1), and there was no reduction of activity in these regions in the Cataract group. In contrast, the anterior fusiform covaried with other face-network regions specifically during face presentation (LV2), and the Cataract group had reduced activity overall in this group of regions. These anterior/posterior fusiform regions are similar in location to those reported by Pinsk et al. (2009) in a study comparing face sensitive regions in humans and monkeys. Our results, taken together with theirs, suggest some level of specialization within the fusiform regions that are sensitive to face stimuli, although the exact nature of such a specialization is not yet known.

Early visual deprivation impacted activity in most of the extended face-network regions in at least one hemisphere during the Localizer scan. Indeed, there was a more marked reduction in extended network regions than in core regions, suggesting that the face-processing deficit of these individuals is not in face perception per se, but in how face information is transmitted to, or processed by, the extended areas. This interpretation is consistent with evidence that individuals with congenital cataracts confuse subtle facial expressions with each other and do not make normal judgments of the similarity among facial expressions (Gao,

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[3] Note that the significant group × brain measure interactions do not imply that the within-group correlations between these measures and behavior were significant. Only one of the correlations depicted in Fig. 7 was significant (Fig. 7c, between Feature accuracy and Feature vs. Scrambled brain scores in the Cataract group, $r=-0.68$, $p<0.05$).

Maurer, & Nishimura, 2013). In addition, reduced activity in person-knowledge regions may contribute to these patients' deficit in recognizing famous faces (de Heering & Maurer, 2014). Interestingly, the majority of the frontal regions in the extended face network showed no reduction of face-specific activity during the Localizer, but did show differences in activity during the early and late phases of the Jane task in the Cataract group, to which we turn next.

4.2. *Activity during the Jane task*

The set of regions more active during the Scrambled condition, compared to Spacing and Feature, were very similar to those active during all object categories during the Localizer runs, which we attributed to general visual activity. The finding that the activity for scrambled faces declined in both groups across the Jane runs, despite the lack of any changes in accuracy or RT in the Scrambled condition, likely represents adaptation to stimuli that are initially quite novel but become less so with repeated presentations (Grill-Spector, Henson, & Martin, 2006). The finding of equivalent activity in these diffuse occipital regions both for multiple object categories vs. fixation and scrambled faces vs. real faces in the two groups is strong evidence for a lack of effect of congenital cataracts on brain activity associated with presumably low level visual analysis of stimuli sufficiently large and containing sufficient contrast to be above any visibility threshold.

In terms of regions with more activity for the Spacing and Feature conditions than the Scrambled condition, we did not find a difference in the fusiform gyri. This may be due to the nature of our scrambled images, in which one can see contours and some face parts. Studies that define the FFA using a functional localizer typically do so using objects, houses or scenes as the contrasting stimuli (e.g., Epstein et al., 2003; Gauthier et al., 2000; Grill-Spector et al., 2004; Kanwisher et al., 1997), and find robust activity in the fusiform gyri, as we did in our Localizer scan. A few studies used scrambled images to define face-sensitive regions (Fairhall & Ishai, 2007; Hoffman & Haxby, 2000; Ishai et al., 2005), but these used phase scrambling, which obscures all face parts and object-like contours. So it would seem that the response of the fusiform gyri to scrambled images of faces might depend critically on how the scrambling is done. Although we did not find more activity in core network regions for Spacing and Feature compared to Scrambled, there was more activity in OFC and the bilateral amygdala, both extended-network regions. The OFC is thought to be involved in emotional regulation (Gillihan et al., 2011; Northoff et al., 2004; Wheeler & Fellows, 2008) and is often active during face tasks (Fairhall & Ishai, 2007; Lee, Grady, Habak, Wilson, & Moscovitch, 2011; Li et al., 2010) so that it has been included in the extended face network. The amygdala is also critically involved in emotional perception and memory, as indicated above. Because the increased activity was seen for both Spacing and Feature conditions, it may thus represent a general emotional response to the Jane faces, and the lack of a group difference in the activity of these regions suggests that the emotional response to these faces, although not required for the task, was equivalent in the two groups. However, the activity in these face-network regions was related to length of deprivation in the Cataract group. This correlation could have been due to chance (as it was the only one out of 11 correlations between deprivation and brain measures that was significant). Alternatively, it might suggest that the activity in these regions increases to compensate for the duration of visual deprivation, as does the P1/N170 amplitude over parietal and occipital regions recorded with event-related potentials when these patients are presented with pictures of faces, houses, and objects (Mondloch et al., 2013).

Unlike the other brain activity patterns seen here, comparison of the Spacing and Feature conditions showed a rather striking hemispheric asymmetry, with right hemisphere regions active for Spacing and left hemisphere regions active for Feature. This asymmetry is consistent with evidence of a prominent role of the right hemisphere in face processing (for a review see Behrmann & Plaut, 2013) and with evidence that deprivation of the right hemisphere is critical for face processing deficits after congenital cataracts (Le Grand et al., 2003). The most extensive regions with more Spacing activity were in right prefrontal cortex. For example, the region that included IFG, an extended face network area, is similar to one that is thought to be involved in processing higher-order relations among object features (Bunge, Helskog, & Wendelken, 2009), consistent with its role here in processing second-order relations among facial features. In addition, the cingulate/dorsomedial prefrontal region with more Spacing activity also is part of the extended face network and is involved in self-reference and theory of mind (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Grigg & Grady, 2010a; Northoff & Bermpohl, 2004; Spreng & Grady, 2010). In particular, this region shows evidence of reduced face-specific activity in the Cataract group (during the Localizer, LV2) and an early/late difference on Jane spacing, so processing in this region, perhaps reflecting the processing of other people's faces in relation to ones' self, may be particularly impacted by early cataracts. There was more activity for Feature vs. Spacing in the ventromedial prefrontal cortex, which is involved in a network of regions known as the default mode network that is thought to represent self-reference and other social cognitive processes (e.g., Buckner, Andrews-Hanna, & Schacter, 2008; Grigg & Grady, 2010a; Gusnard, Akbudak, Shulman, & Raichle, 2001; Spreng, Mar, & Kim, 2009). The default network shows reduced activity during externally driven tasks, such as the Jane task, particularly when the task is difficult (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Persson, Lustig, Nelson, & Reuter-Lorenz, 2007). Because the Feature task was easier than the Spacing task, more activity in ventromedial PFC during the Feature task may be due to less deactivation of the default network in an easier task, and not anything specific to faces. Plotting the regions more active for Feature vs. Spacing at a lower threshold supports this idea (see Supplementary Figure 4), as this shows more default network regions, such as the posterior cingulate. Overall, the contrast of Spacing and Feature processing during the Jane task suggests that the difference is driven by Spacing activity in right hemisphere frontal regions involved in social aspects of the extended face network. Given that the Cataract group showed reliably increased activity for Spacing only in the later trials, our results suggest that early visual deprivation is associated with less consistent activation of these regions when using a spacing strategy for face discrimination.

4.3. *Functional connectivity of the fusiform gyri*

The seed analysis supported the notion that the strength of functional connectivity is altered in the Cataract group within the network of regions that are functionally connected to the fusiform gyri in both groups. This indicates that the network itself is not altered spatially after early visual deprivation, but deprivation does affect how strongly the nodes of the network are interconnected. Although we would have expected to see weaker functional connectivity of the right fusiform region in this group if the right hemisphere is a primary target of early deprivation (Le Grand et al., 2003), this was not the case. It is possible that other aspects of this region's connectivity might be altered, for example the fiber tracts connecting it to other areas, or its functional connections outside the face network. Even though the right fusiform was not reliably weakened within the face network, we did find enhanced connectivity of the left fusiform in the Cataract group. The lack of a hemispheric difference in functional connectivity in both the Control group and the independent sample of young adults scanned at rest supports the interpretation that the asymmetry seen in the Cataract group is not what one would expect to see in those with typical development of the visual system. We cannot determine from these data whether the enhanced functional connectivity of the left fusiform is a consequence of alterations in its right hemisphere homolog, but this is an intriguing possibility. According to one recent theory (Behrmann & Plaut, 2013), both right and left fusiforms contribute to face processing early in life, but during development the left region becomes more strongly connected with language areas as its role in word processing increases, and the right fusiform becomes more finely tuned for faces as a consequence. Our result would suggest that early visual deprivation from bilateral cataracts alters the developmental process so that this asymmetry fails to mature fully, leaving the left hemisphere more strongly connected to other face processing regions.

The regions that were functionally connected to the right and left fusiform seeds, and that showed increased connectivity with the left fusiform in the Cataract group, included most of the regions in the extended face network, at least in one hemisphere, with the exception of dorsomedial prefrontal cortex, insula and superior temporal sulcus. This finding, along with the reduced face-specific activity during the Localizer and less consistent activity in the Jane scans in the Cataract group, adds further support to the conclusion that early visual deprivation influences the integrated activity of the distributed set of regions active for the various aspects of processing faces. There is not much in the literature about how functional connectivity in the face network might be altered under different conditions, but there is evidence in healthy aging that the functional connectivity between right and left fusiform gyri during same/different discrimination of faces is disrupted relative to young adults, with a concomitant increase in connectivity between right fusiform and OFC (Burianova, Lee, Grady, & Moscovitch, 2013). This finding, taken together with our results here, indicates that functional interactions between right and left fusiform gyri are important for face processing, and for how well one can carry out this processing, as we discuss next.

4.4. Associations between brain activity and behavior

The patterns of activity and functional connectivity identified in our analyses not only differentiated the groups but also were associated with how well participants carried out the tasks. The relation between face-specific activity seen in the Localizer scan and better performance on the Jane Spacing task is intriguing, as it indicates that activity in the extended face network is important for the ability to identify faces based on feature spacing. Despite the fact that the Cataract participants had particular difficulty with this task, as well as less activity in these brain regions, they nevertheless showed the same brain/behavior association as Controls, suggesting that their face processing also depends on this network. This result is further support for the idea that early visual deprivation impairs the ability to engage the extended face network, or perhaps hampers its efficiency, but does not result in a major reorganization of the network.

Accuracy on both Spacing and Feature tasks was associated with activity during these tasks relative to that seen during scrambled faces. In both cases, the relation was such that more activity in OFC and amygdala during the face tasks, compared to Scrambled, was associated with worse performance on the tasks. In addition, this relation was stronger for Controls in the Spacing task, and stronger for the Cataract group in the Feature condition. If activity in these regions is associated with emotional processing of the faces, as we suggest above, this difference in how activity predicts performance implies that responding to the emotional aspects of the faces in this task, where emotion is not relevant to the task, is disruptive to identifying them. This group difference in which task shows the larger impact may depend on which strategy individuals tend to use more readily when processing faces, that is, a more holistic approach in Controls and a feature-based strategy in the participants with early visual deprivation.

Finally, a group difference was found in the relation between functional connectivity between right and left fusiform regions and performance on the Spacing task. The trend for Controls was for a positive association between functional connectivity and performance, whereas this trend was negative for the Cataract group, suggesting that functional interactions between these two core face regions no longer carry the same information after early deprivation. Importantly, this interaction also indicates that the difference in Spacing performance between the groups increases as functional connectivity increases. This is further evidence, along with the increased functional connectivity between the left fusiform gyrus and other face processing regions, at the expense of right fusiform connectivity, that activity within the face network is disrupted by early deprivation, especially so for face processing that depends on spacing among facial features.

4.5. Limitations

One potential limitation of the study is that the Cataract group performed more poorly on the Jane task, so a concern might be that the observed brain differences would simply reflect this behavioral difference. We do not think that this is a major concern because the main group difference in brain activity was seen during the Localizer and no response was required during these runs. It therefore seems unlikely that the reduced activity in face-processing regions in the Cataract group during the Localizer can be explained by behavioral differences. This reduction in face-specific activity likely reflects some difference in how the faces are processed even during passive presentation. Similarly, the relations among brain activity during the Localizer scan, functional connectivity and Jane performance (seen in Fig. 7a and d) are unlikely to be influenced by behavioral differences because the brain measures were obtained from an independent scan. Nevertheless, group differences in the performance on the Jane task may have influenced some of the relations between performance and brain activity measured during this task. Finally, the lack of significant correlations between acuity and the brain measures suggests that the effects that we observed in the Cataract group were not due to their relatively poor acuity.

Another potential limitation is that we did not have a resting-state scan from our participants for assessing intrinsic functional connectivity, and instead approximated this connectivity by dividing a task run into sequential “blocks”, thus disrupting the hemodynamic response to stimulus presentation. The similarity of functional connectivity patterns seen in the Control and Cataract groups to that seen in the group of participants scanned at rest indicates that the method used here to identify the functional connectivity of the fusiform gyri does indeed approximate the “true” intrinsic connectivity of these regions. However, we cannot completely rule out some influence of residual task effects on functional connectivity, as changes in functional connectivity have been reported in other networks between task and rest states (Betti et al., 2013; Mennes, Kelly, Colcombe, Castellanos, & Milham, 2013). For example, the apparently smaller extent of regions functionally connected to the fusiform gyri in the current sample relative to the larger, independent sample scanned at rest (see Fig. 6) could be due either to reduced statistical power (smaller sample size) or to some as yet unidentified influence of task on face-network functional connectivity.

4.6. Conclusions

We found that adults who experienced visual deprivation from cataracts during infancy appear to use the normal face processing network when passively viewing faces or making judgments about whether or not two faces are the same. However, there is less than normal activation, particularly in the extended face-processing network. In addition, functional connectivity in the face network is altered, and all these brain changes have a more marked impact on the ability to make judgments about feature spacing than on judgments based on features per se. Thus, early visual input is necessary to set up or preserve the connections in the extended face-processing network that will later mediate expert face processing.

Future fMRI studies would be useful to determine whether the patterns observed here represent the partial recovery of face processing networks as the cataract-reversal patients gain experience with faces, or whether they represent stable deficits. For example, it is possible that patients initially use mainly an undifferentiated and compromised network for processing both faces and objects, but as they attempt to remember more and more faces as they enter first primary and then high school, the object and face networks differentiate to some extent, with the late-differentiating face network remaining disadvantaged. This hypothesis is consistent with evidence that the object and face networks become increasingly differentiated during childhood in children with normal eyes. Future fMRI studies would also be useful on the effects of early visual deprivation on other aspects of face processing at which adults excel: detecting direction of eye gaze; decoding facial expressions; and integrating information about identity, eye gaze, age, race, and facial expression.

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Appendix A. Supporting information

Supplementary data associated with this paper can be found in the online version at http://dx.doi.org/10.1016/j.neuropsychologia.2014.03.005.

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