Developmental prosopagnosics have widespread selectivity reductions across category-selective visual cortex

Guo Jiahui[a,1], Hua Yang[a], and Bradley Duchaine[a]

[a]Department of Psychological and Brain Sciences, Dartmouth College, Hanover, NH 03755

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Developmental prosopagnosia (DP) is a neurodevelopmental disorder characterized by severe deficits with facial identity recognition. It is unclear which cortical areas contribute to face processing deficits in DP, and no previous studies have investigated whether other category-selective areas function normally in DP. To address these issues, we scanned 22 DPs and 27 controls using a dynamic localizer consisting of video clips of faces, scenes, bodies, objects, and scrambled objects. We then analyzed category selectivity, a measure of the tuning of a cortical area to a particular visual category. DPs exhibited reduced face selectivity in all 12 face areas, and the reductions were significant in three posterior and two anterior areas. DPs and controls showed similar responses to faces in other category-selective areas, which suggests the DPs' behavioral deficits with faces result from problems restricted to the face network. DPs also had pronounced scene-selectivity reductions in four of six scene-selective areas and marginal body-selectivity reductions in two of four body-selective areas. Our results demonstrate that DPs have widespread deficits throughout the face network, and they are inconsistent with a leading account of DP which proposes that posterior face-selective areas are normal in DP. The selectivity reductions in other category-selective areas indicate many DPs have deficits spread across high-level visual cortex.

face perception | visual recognition | developmental disorder | prosopagnosia | scene perception

Individuals with developmental prosopagnosia (DPs) have great difficulty with facial identity recognition despite normal low-level vision, normal intelligence, and no history of brain damage (1, 2). DPs' problems with faces are a significant social handicap and can lead to chronic social anxiety (3, 4). Although neural differences between DPs and participants with normal face recognition have been identified, fundamental issues concerning the neural basis of DP remain unclear. These questions include (*i*) which regions in the face-processing system function abnormally in DP, (*ii*) whether areas outside the face processing system contribute to DPs' deficits with faces, and (*iii*) whether DPs show functional abnormalities in response to categories other than faces. Here we address these questions by presenting controls and a relatively large group of DPs with videos of faces and other categories and then comparing the selectivity of their responses.

Facial identity recognition depends on a set of face-selective cortical regions that extend from the occipital lobe to the anterior temporal lobe (5–7), and the location of DPs' neural deficits within the face network is controversial. One view proposes DP results from a disconnection between posterior face-selective areas and anterior face-selective areas (8, 9). Support for this view comes from findings suggesting posterior face areas function normally in DPs (10–12), whereas white matter tracts in DPs linking posterior and anterior face areas are compromised (13) and anterior temporal areas in DPs exhibit reduced activation (8, 10) as well as reduced structural integrity (14). However, an alternative view suggests DPs have deficits in both posterior and anterior face-selective areas. This distributed account is supported by the findings indicating anterior abnormalities, in combination with studies indicating DPs have reduced face selectivity (15, 16) and functional connectivity in posterior face-selective areas (17–19) as well as structural abnormalities in the vicinity of posterior face areas (14, 15). In addition, two recent studies of white matter tracts in DP found deficits local to ventral temporal face areas but no abnormalities in long-range tracts linking posterior and anterior face areas (20, 21). Because the findings reviewed above, particularly the fMRI studies, paint an inconsistent picture, often used small samples, and did not investigate the entire face-processing system, it is critical to thoroughly compare anterior and posterior face areas in a large group of DPs.

fMRI investigations of DP have focused solely on face-selective areas, but we believe it is also essential to examine responses in areas selective for other visual categories. The response of these areas to their preferred categories (e.g., scene selectivity in scene areas) will shed light on the extent of the cortical anomalies associated with DP and may provide insight into the developmental processes that lead to DP. Face input to the visual system early in life appears to be necessary for normal face recognition later in life (22, 23), and it has been hypothesized DP may result from a lack of exposure to faces early in life (24, 25), possibly due to deficits in subcortical mechanisms that lead infants to preferentially attend to faces (26). If DP results from inadequate face input in the context of normal exposure to other categories, DPs would be expected to show impairments only in face-selective areas while other category-selective areas should respond normally to preferred categories. However, if non-face category-selective areas respond abnormally in many DPs, it would suggest DP often results from impairments to neurobiological

Significance

People with developmental prosopagnosia (DP) have extremely poor face recognition and even have problems recognizing the faces of family and close friends. We carried out a comprehensive investigation of the neural basis of DP by comparing brain responses to multiple visual categories in DPs and people with normal face processing. The DPs showed widespread abnormalities in areas specialized for face processing and areas that respond preferentially to scenes and bodies. The abnormalities in scene and body areas indicate cortical problems in many DPs extend beyond face areas and open the door to investigations of developmental disorders impacting recognition of categories other than faces.

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[1]To whom correspondence should be addressed. Email: jiahui.guo.gr@dartmouth.edu.

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factors with broader effects rather than insufficient experience with faces. An event-related potential study indicated DPs have abnormal neural responses to bodies (27), but the responses of non-face category-selective areas in DP have not been examined.

To address the issues discussed above, we carried out a systematic analysis of category selectivity in DP. We first compared the distribution of category selectivity in DPs and controls using whole-brain results. Then, to more precisely quantify the selectivity differences, we adopted a data analysis approach we refer to as the "variable window" method to conduct group comparisons of selectivity in category-selective areas that were individually defined for each participant (28, 29). For each region of interest (ROI), we first created an anatomical mask around the expected location for all participants. To compare results at a variety of ROI sizes, we then computed the percent signal change to different categories across a range of selectivity percentages within the mask (top 5%, top 10%, etc.) for each individual. This method provides an objective means to generate individualized functionally defined ROIs. It also avoids omitting results from participants with responses below typically used threshold and fairly compares selectivity between groups that often have unequal cluster sizes (16, 30).

Materials and Methods

Participants. Twenty-two DPs (seven males, mean age 41.9 y) and 25 typical adults (10 males, mean age 42.3 y) participated in the study. DPs were recruited from www.faceblind.org, and all reported problems in daily life with face recognition. To assess their face recognition, DPs were tested with the Cambridge Face Memory Test (CFMT) (31), a famous face test (32), and an old–new face discrimination test (32). All DPs except one performed two or more SDs below the mean of published control results in at least two of the three diagnostic tests (33, 34). The DP who did not reach −2 SD on two tests scored poorly on two of the three tasks (CFMT: z = −1.9; famous face: z = −7.1; old–new: z =−0.5), so we included her to increase the sample size. *SI Appendix*, Fig. S1*A* shows the Z-score of all DPs on the three diagnostic tests. All participants had normal or corrected-to-normal vision (*SI Appendix*, Table S2) and had no current psychiatric disorders. Participants provided written informed consent before doing the tasks, and all procedures were approved by Dartmouth's Committee for the Protection of Human Participants.

Stimuli and Procedures. Participants did a one-back task during a dynamic localizer scan containing five visual categories (faces, scenes, bodies, objects, and scrambled objects). Stimuli in the localizer were brief video clips of each category. Face and object stimuli were obtained from video clips used in Fox et al. (35), scene and body video clips came from Pitcher et al. (36), and scrambled objects were created by scrambling the video clips of the objects spatially into 24 × 16 grids. Each video clip subtended ∼18.5° × 12.3° of visual angle for width and height.

Each participant completed five scans. Each scan comprised 10 12-s category blocks of video clips interleaved with 12-s fixation blocks, which in total lasted about 4.2 min. Each visual category was displayed twice in each scan in a quasi-random order across scans. In each category block, six 1,500-ms video clips were presented interleaved by blank fixation screens presented for 500 ms (*SI Appendix*, Fig. S1*B*). Stimuli were presented using Superlab 4.5.3 (www.superlab.com/) and displayed to the participant via a PanasonicDT-4000UDLP projector (resolution: 1,024 × 768; refresh rate: 60 Hz) at the rear of the scanner.

Leave One Run Out. The five runs were divided into localization runs and test runs to carry out a "leave-one-out" analysis (28, 29). In each of the leave-one-out combinations, four of the five runs for a participant were used to localize the voxels that showed the strongest preference for the preferred category (e.g., largest z-value for faces > objects contrast). To avoid the double-dipping problem (37), the responses of the selected voxels to each stimulus condition were then measured in the left-out run. All five combinations were analyzed and then averaged to produce the final result for each participant.

Category Selectivity. Category selectivity was used to measure how strongly tuned a cortical area was to a particular category. Selectivity for faces was defined as the difference between the response to faces and the response to objects. Objects were also used as the comparison category to compute scene selectivity and body selectivity. Object selectivity was defined as the difference between the response to objects and the response to scrambled objects.

The Variable-Window Method. To avoid both the subjectivity of manually setting thresholds and the problem of how to deal with data from participants who have responses below typically used thresholds, we adopted the "variable-window" method used in several recent papers (28, 29, 38, 39). We first made surface masks at the expected location for each ROI we planned to analyze. The mask was manually prepared by referring to the category-selective voxels of both groups at a liberal threshold ($P < 0.05$), so as to include all voxels that could be considered part of a particular category-selective area (see *SI Appendix*, Fig. S2 to view the masks). We then identified each participant's ROI by selecting the most selective voxels in the mask. To determine whether our results are consistent across different ROI sizes, we compared selectivity between DPs and controls at varied ROI sizes, ranging from 5 to 35% in 5% steps. This method provided a simple but effective way to balance the trade-off between extent and selectivity and ensured a fair comparison between controls and DPs.

Results

Normal Organization of Category-Selective Areas in DP. To compare the overall distribution of category-selective responses in the 22 DPs and 27 controls, a group-level analysis was performed for each category and each group of participants. In Fig. 1*A*, each of the category-selective significance maps shows the clusters that were more responsive to either faces, scenes, bodies, or objects than the contrast category. For all four contrasts, controls and DPs had similar category-selectivity maps. Clusters that were significantly face-selective appear in the fusiform gyrus, along the

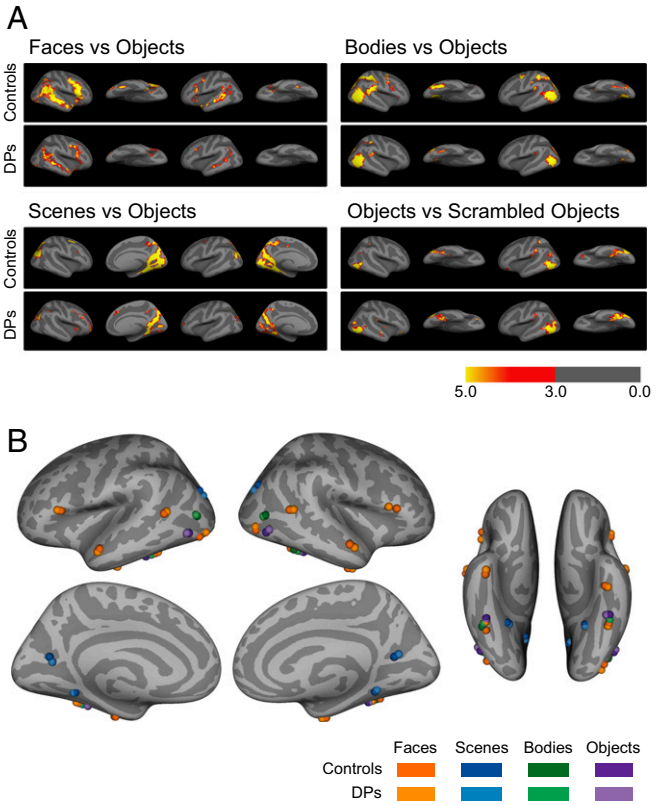

Fig. 1. Whole-brain organization of category-selective areas in DPs and controls. (*A*) The whole-brain significance maps for each visual category ($P < 0.001$, clusterwise-corrected). The location of selective areas in controls and DPs was similar for all categories, but the DPs had noticeably weaker activations and smaller cluster sizes for all categories except objects. (*B*) Group peak coordinates extracted for each functional ROI analyzed. Darker dots display peaks for the control group, and lighter dots represent peaks for the DPs. DPs and controls had very similar peak coordinates.

superior temporal sulcus (STS), and in the frontal lobe. Scenes selectively activated areas spread from occipital cortex to medial parietal cortex and parahippocampal gyrus. Body-selective and object-selective areas were distributed mainly along the fusiform gyrus and occipital cortex. Except for object-selective areas, clusters in DPs were noticeably smaller and exhibited weaker significance than the same clusters in controls. The average peak coordinates for each ROI showed DPs and controls had extremely similar peak coordinates (Fig. 1*B* and *SI Appendix*, Table S1; see *SI Appendix* for how the peak coordinates were located). These comparisons indicate the general organization of visual recognition in DPs is comparable to that found in participants with normal face processing.

Widespread Deficits in Face-Processing System. Having compared the category-selective organization in DPs and controls, we next investigated the tuning profiles in the face-selective areas using the variable-window method. Before comparing category selectivity, we confirmed that controls and DPs had similar amounts of head motion in the scanner and that the functional signal-to-noise ratios of all ROIs were comparable for the two groups (see *SI Appendix*, *SI Analysis* for details).

We first report results from analyses using the 10% most face-selective voxels as the ROI, as was done in previous reports (28, 29, 38, 39). In four of the six face-selective ROIs in the right hemisphere, DPs had significantly weaker face selectivity than controls [Fig. 2*A*; fusiform face area (FFA): $t(45) = 2.96$, $P = 0.005$; posterior STS (pSTS): $t(45) = 3.48$, $P = 0.001$; anterior STS (aSTS): $t(45) = 3.29$, $P = 0.002$; inferior frontal gyrus (IFG): $t(45) = 2.78$, $P = 0.008$]. These reductions in selectivity were driven by reduced responses to faces, not increased responses to objects (Fig. 2*B*; Tukey test; FFA: face, $z = 3.93$, $P < 0.001$, object, $z = 0.63$, $P = 0.53$; pSTS: face, $z = 2.95$, $P = 0.003$, object, $z = -0.82$, $P = 0.41$; aSTS: face, $z = 4.04$, $P < 0.001$, object, $z = -0.27$, $P = 0.79$; IFG: face, $z = 2.53$, $P = 0.01$, object, $z = 0.62$, $P = 0.54$). Significance values of all four ROIs remained significant after correction with the Holm–Bonferroni method for multiple comparisons (40–42). DP face selectivity in the other two ROIs in the right hemisphere was also weaker than control selectivity, but these differences were not statistically significant [Fig. 2*A*; occipital face area (OFA): $t(45) = 1.10$, $P = 0.28$; anterior temporal lobe (ATL): $t(45) = 1.82$, $P = 0.08$].

DP face selectivity in all face ROIs in the left hemisphere was weaker than selectivity in controls, but only left FFA reached significance [Fig. 2*A*; $t(45) = 3.01$, $P = 0.005$; Holm–Bonferroni-corrected] while left OFA was marginally significant [Fig. 2*A*; $t(45) = 1.94$, $P = 0.06$]. As above, the selectivity reductions in these two regions resulted primarily from weaker responses to faces in DPs, not stronger responses to objects (Fig. 2*B*; FFA: face, $z = 2.89$, $P = 0.004$, object, $z = 0.37$, $P = 0.71$; OFA: face, $z = 2.20$, $P = 0.03$, object, $z = 0.97$, $P = 0.33$). None of the other face-selective ROIs in the left hemisphere reached significance for face selectivity [Fig. 2*A*; pSTS: $t(45) = 1.15$, $P = 0.25$; aSTS: $t(45) = 1.62$, $P = 0.11$; IFG: $t(45) = 1.57$, $P = 0.12$; ATL: $t(45) = 1.37$, $P = 0.18$].

We validated our parametric results by doing a bootstrap analysis with 10,000 repetitions. This nonparametric analysis generated the same results as described above (Holm–Bonferroni-corrected). Examination of individual DP's face selectivity suggested the group differences in face areas did not result from a subset of DPs with extremely low selectivity across many of the ROIs (*SI Appendix*, Figs. S10 and S11).

A 2 (anterior/posterior) × 2 (control/DP) × 6 (ROIs) ANOVA revealed comparable reductions in face selectivity in the anterior and posterior ROIs [*SI Appendix*, Fig. S3*C*; $F(1,45) = 1.47$, $P = 0.23$]. Results of the individual ROI analyses found significant differences in four right hemisphere areas but only one left hemisphere area, but a 2 (left/right) × 2 (control/DP) × 6 (ROIs) ANOVA did not reveal a significant right hemisphere bias [*SI Appendix*, Fig. S3*C*; $F(1,45) = 1.80$, $P = 0.19$]. Similarly, a 2 (dorsal/ventral) × 2 (control/DP) × 6 (ROIs) ANOVA on the dorsal and ventral stream ROIs across hemispheres did not find a difference in the reduction of face selectivity between ROIs in the two streams [*SI Appendix*, Fig. S3*C*; $F(1,45) = 0.62$, $P = 0.43$].

To evaluate the consistency of our findings at different ROI sizes, we calculated face selectivity for ROIs of different sizes by changing the percentage of voxels selected (Fig. 2*C*). Each ROI included the top X% (range: 5–35) of voxels in each functional mask with the strongest response preference for faces over objects. As expected (28, 39), the magnitude of face selectivity dropped as the percentage increased, but the difference in face selectivity between DPs and controls at different percentages was similar to what was found at 10% across all ROIs (Fig. 2*C* and *SI Appendix*, Fig. S3*B*). Across the different percentages, selectivity differences were driven by reduced responses to faces in DPs and not increased responses to objects (*SI Appendix*, Fig. S3*A*).

Face-Selectivity Deficits Are Restricted to Face Network. The analyses above demonstrate the DPs had weaker face selectivity across the face network and that this reduction was driven by reduced responses to faces. Areas selective for scenes, bodies, and objects also show responses to faces (43), so we next examined whether DPs also show abnormal responses to faces in these areas. To answer this question, we analyzed commonly investigated scene-, body-, and object-selective ROIs (43–45) using a procedure similar to that used for the face-selective ROIs. In each functional mask covering the expected location of a category-selective area, the top 10% of voxels that were most scene-, body-, or object-selective were selected as ROIs. Face selectivity in each category-selective ROI was then calculated for both groups by contrasting the response to faces and objects. Because many of the masks for the nonface ROIs overlapped with face masks, they often contained a substantial number of face-selective voxels that were analyzed as part of the face ROIs discussed above. To make sure the results were not affected by those face-selective voxels, we carried out the analyses after removing face-selective voxels (see *SI Appendix*, *SI Analysis* for analysis details). Face selectivity in the DPs was not significantly reduced in any of the nonface ROIs [Fig. 3; ROI abbreviations are defined in the text (l indicates left and r indicates right); rPPA: $t(45) = -1.59$, $P = 0.12$; rOPA: $t(45) = -1.21$, $P = 0.23$; rMPA: $t(45) = -0.33$, $P = 0.74$; lPPA: $t(45) = -1.79$, $P = 0.08$; lOPA: $t(45) = -0.43$, $P = 0.67$; lMPA: $t(45) = -0.51$, $P = 0.61$; rEBA: $t(45) = 0.96$, $P = 0.34$; rFBA: $t(43) = -0.01$, $P = 0.99$; lEBA: $t(45) = 0.08$, $P = 0.93$; lFBA: $t(41) = 0.53$, $P = 0.60$; rLO: $t(45) = 0.83$, $P = 0.41$; rpFs: $t(45) = 0.35$, $P = 0.73$; lLO: $t(45) = -0.86$, $P = 0.39$; lpFs: $t(45) = 0.28$, $P = 0.78$]. Similarly, if the analyses included the removed voxels, none of the ROIs showed significant differences (*SI Appendix*, Fig. S4). These results indicate that DP face-selectivity deficits are limited to the face system and tentatively suggest their behavioral deficits with faces do not result from impairments in other category-selective regions.

Broad Deficits in Visual-Recognition Mechanisms. Little is known about the extent of the cortical abnormalities associated with DP, so we next compared selectivity to the preferred category in areas selective for scenes, bodies, and objects between DPs and controls.

Selectivity to scenes in scene-selective areas. In the scene-selective areas, we used the variable-window method to measure selectivity. Masks were created for three ROIs [parahippocampal place area (PPA), occipital place area (OPA), and medial place area (MPA)] in each hemisphere and the top 10% of the voxels that were most scene-selective based on the contrast of scenes > objects were analyzed. The ROI size was also varied in a later step from 5 to 35%.

In the right hemisphere, DP scene selectivity at the 10% level was significantly weaker than control selectivity in all three ROIs [Fig. 4*A*; PPA: $t(45) = 3.65$, $P < 0.001$; OPA: $t(45) = 2.02$,

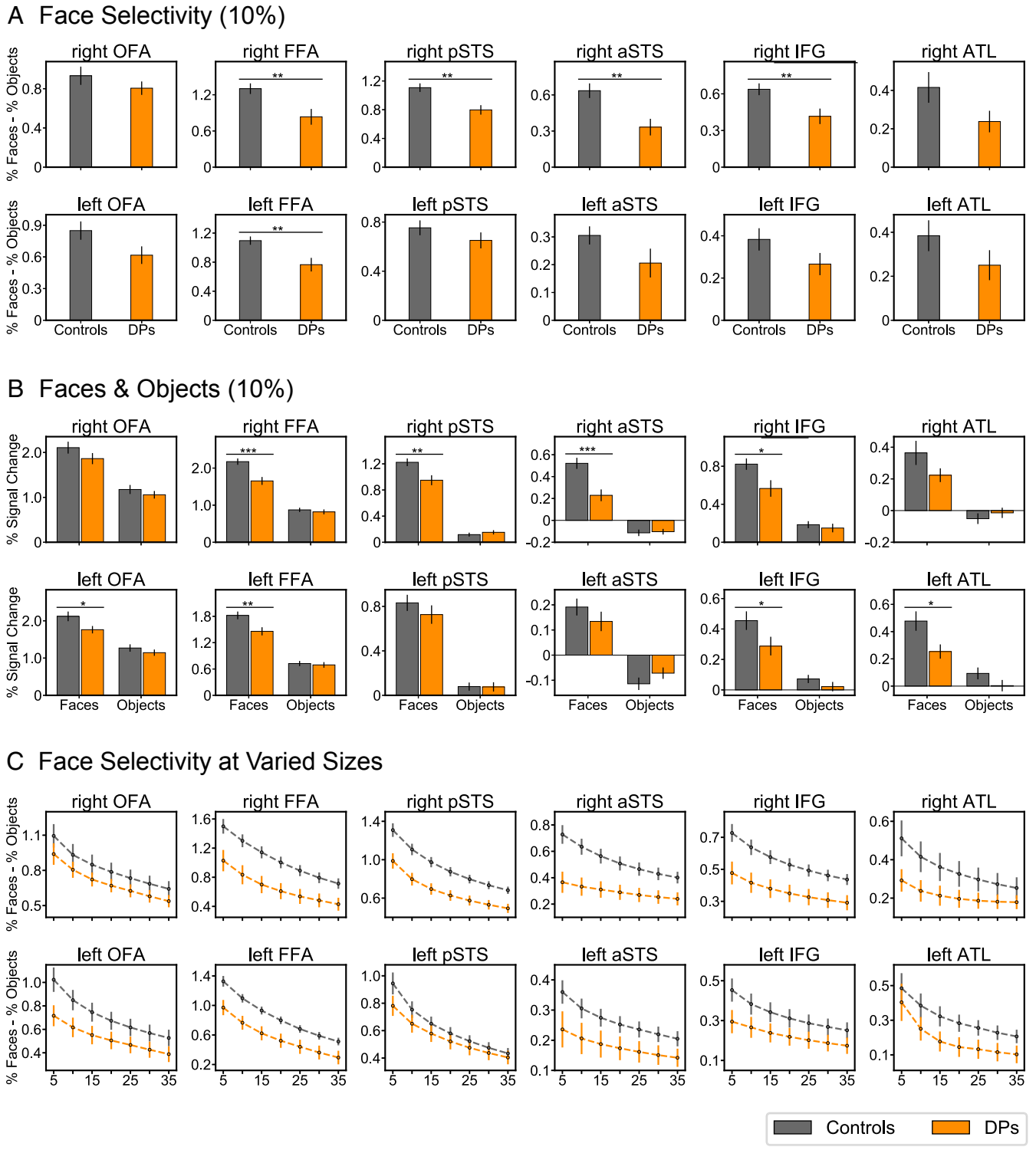

Fig. 2. DPs had widespread selectivity reductions in the face processing network. (*A*) Face selectivity and (*B*) responses to faces and objects in all face-selective ROIs at the 10% size. Significant reductions of face selectivity were found in four right-hemisphere ROIs and one left-hemisphere ROI, and the reductions in face selectivity were driven by weaker responses to faces. (*C*) Face selectivity at ROI sizes from 5 to 35%. The differences at 10% were comparable to results at other sizes. In all panels, error bars stand for ±1 SE for each group. ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

$P = 0.05$; MPA: $t(45) = 3.73$, $P < 0.001$; all passed the Holm–Bonferroni correction]. The difference was driven primarily by weaker responses to scenes rather than increased responses to objects (Fig. 4*B*; Tukey test; PPA: scenes, z = 2.75, $P = 0.006$, objects, z = 0.73, $P = 0.47$; OPA: scenes, z = 1.75, $P = 0.08$, objects, z = 0.88, $P = 0.38$; MPA: scenes, z = 3.03, $P = 0.002$, objects, z = −0.09, $P = 0.93$). In the left hemisphere, scene selectivity in the DPs was significantly reduced in PPA [Fig. 4*A*; $t(45) = 2.64$, $P = 0.01$, Holm–Bonferroni-corrected], reduced, though not significantly, in OPA [$t(45) = 1.12$, $P = 0.27$], and was

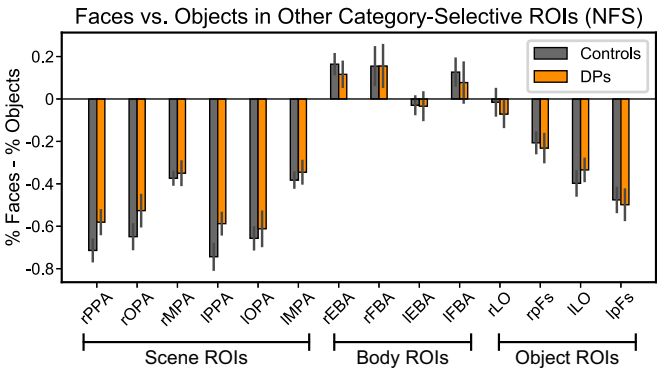

Fig. 3. Face selectivity in controls and DPs was comparable in ROIs outside the face network. Face selectivity in ROIs outside the face processing system when face-selective voxels ($P < 0.05$) were excluded from body ROIs (bilateral EBA and LO) and object ROIs (bilateral FBA and pFs). Face selectivity was comparable for controls and DPs across scene, body, and object ROIs. Error bars stand for ±1 SE for each group. NFS, non-face-selective.

marginally significant in MPA [$t(45) = 1.96$, $P = 0.06$]. Bootstrap analysis revealed similar results (Holm–Bonferroni-corrected). In left PPA, we found a significant reduction in the response to scenes (Fig. 4*B*; Tukey test; scenes, z = 2.67, $P = 0.008$, objects, z = 1.16, $P = 0.25$). The reductions to scenes in left OPA and left MPA were not significant (Tukey test; OPA: scenes, z = 0.10, $P = 0.92$, objects, z = −0.96, $P = 0.34$; MPA: scenes, z = 1.08, $P = 0.28$, objects, z = −0.65, $P = 0.52$). We did a 2 (left/right) × 2 (DP/control) × 3 (ROIs) ANOVA, which showed that group differences were more pronounced in the right hemisphere [$F(1,45) = 5.70$, $P = 0.02$].

Next, we varied the ROI percentage within each mask. The magnitude of selectivity decreased as ROI size increased, but the differences between the controls and DPs remained comparable (Fig. 4*C* and *SI Appendix*, Fig. S5 *A* and B).

Selectivity to human bodies in body-selective areas. Body-selective ROIs, based on bodies > objects contrasts, were examined with the variable-window method. Two ROIs in each hemisphere were included in the analysis: one on the lateral cortex (EBA) and the other on the fusiform gyrus (FBA). The difference in body selectivity between DPs and controls was marginally significant in EBA bilaterally [Fig. 5*A*; right EBA: $t(45) = 2.01$, $P = 0.05$; left EBA: $t(45) = 1.88$, $P = 0.07$]. Although the selectivity of bilateral FBA in the DPs was weaker than the selectivity in controls, the difference was not significant [Fig. 5*A*; right FBA: $t(45) = 1.48$, $P = 0.15$; left FBA: $t(45) = 0.26$, $P = 0.80$]. Bootstrap analysis generated similar results (Holm–Bonferroni-corrected). The response to bodies in the DPs was reduced relative to the controls, but none of the reductions reached significance (Fig. 5*B*; Tukey test; right EBA: body, z = 0.64, $P = 0.53$, object, z = −1.20, $P = 0.23$; right FBA: body, z = 1.26, $P = 0.21$, object, z = 0.05, $P = 0.96$; left EBA: body, z = 0.77, $P = 0.44$, object, z = −0.70, $P = 0.48$;

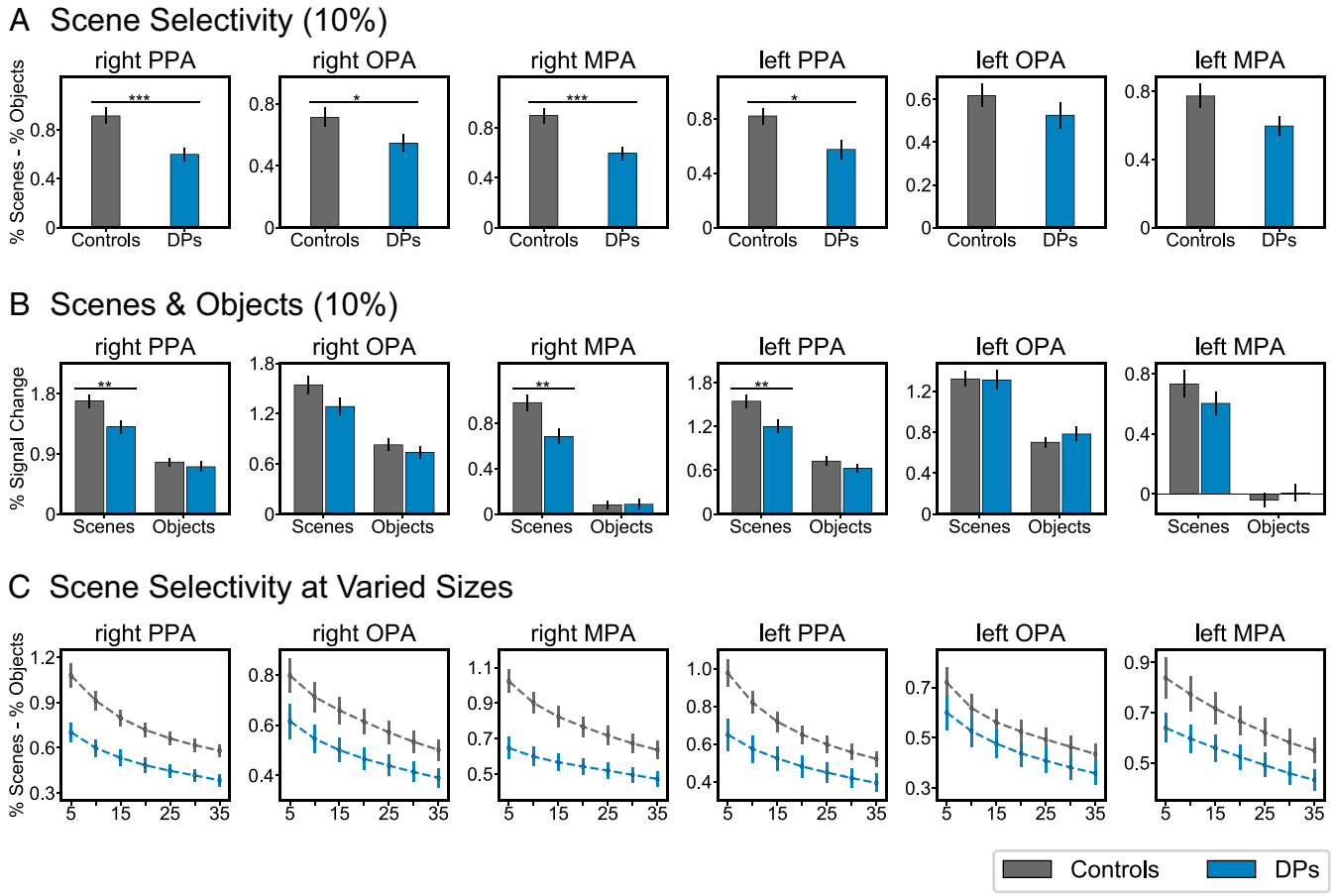

Fig. 4. DPs had scene-selectivity reductions in scene-selective ROIs. (*A*) Scene selectivity and (*B*) responses to scenes and objects in all scene-selective ROIs at 10% size. Significant reductions of scene selectivity were found in all three right ROIs and one left ROI, and the reductions of scene selectivity were driven by weaker responses to scenes. (*C*) Scene selectivity at ROI sizes from 5 to 35%. The results at 10% were similar to those at other sizes. In all panels, error bars stand for ±1 SE for each group. ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.

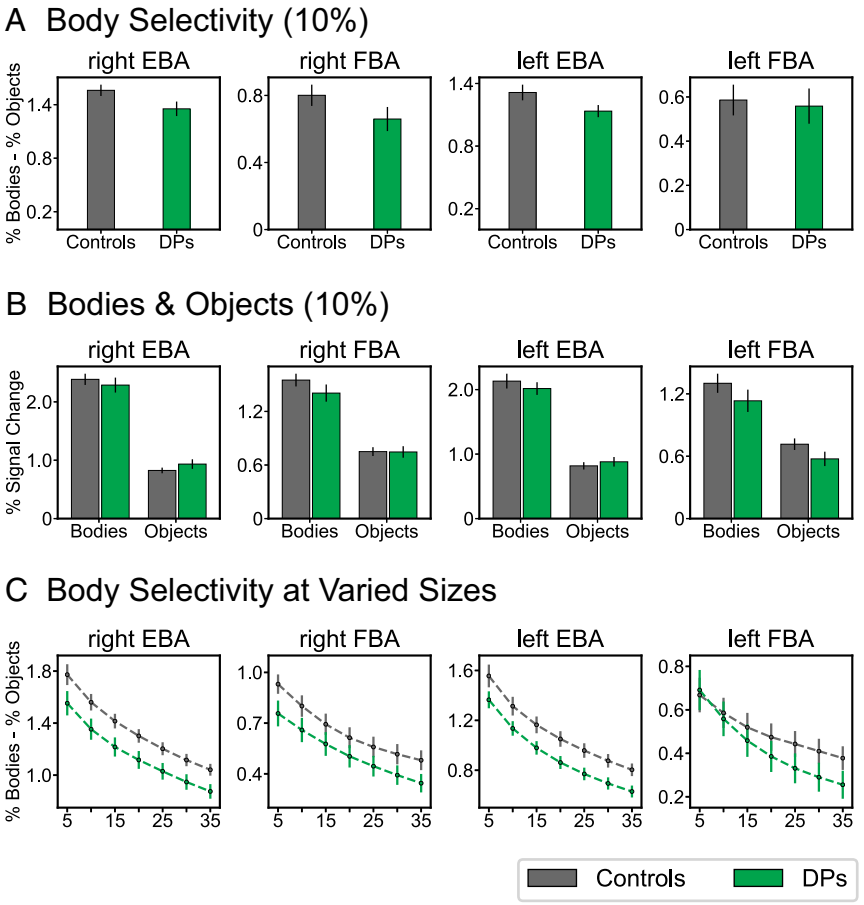

Fig. 5. DPs had marginal body-selectivity reductions in body-selective ROIs. (*A*) Body selectivity and (*B*) responses to bodies and objects in all body-selective ROIs at 10%. Marginally significant reductions of body selectivity were found in right EBA ($P = 0.05$) and left EBA ($P = 0.07$). (*C*) This panel displays body selectivity at ROI sizes from 5 to 35%. The results at 10% were similar to the results at other sizes. In all panels, error bars stand for ±1 SE for each group.

left FBA: body, z = 1.23, $P = 0.22$, object, z = 1.64, $P = 0.10$). The results were similar at different ROI sizes (5–35%) (Fig. 5*C* and *SI Appendix*, Fig. S5 *C* and *D*).

Some voxels in EBA and FBA overlapped with face-selective ROIs so we excluded those voxels ($P < 0.05$ in face vs. object contrast) from the body-selective ROIs to prevent the face-selective voxels from contributing to group differences. The results were unchanged in either selectivity or in the responses to bodies (*SI Appendix*, Fig. S6).

Object selectivity in object-selective areas. Two object-selective ROIs [lateral occipital area (LO) and object-selective posterior fusiform area (pFs)] were localized in each hemisphere using the contrast of objects > scrambled objects. Unlike the other three category-selective contrasts, object selectivity in the DPs was similar to controls in all object-selective ROIs [Fig. 6*A*; right LO: $t(45) = -0.38$, $P = 0.71$; right pFs: $t(45) = 0.14$, $P = 0.89$; left LO: $t(45) = 1.48$, $P = 0.15$; left pFs: $t(45) = -0.20$, $P = 0.84$]. Bootstrap analysis also did not reveal any significant differences (Holm–Bonferroni-corrected). In all object-selective ROIs, DPs and controls showed comparable responses to objects and scrambled objects (Fig. 6*B*; Tukey test; right LO: objects, z = 0.24, $P = 0.81$, scrambled objects, z = 0.59, $P = 0.56$; right pFs: objects, z = −0.50, $P = 0.62$, scrambled objects, z = −0.53, $P = 0.59$; left LO: objects, z = 0.36, $P = 0.72$, scrambled objects, z = −0.87, $P = 0.39$; left pFs: objects, z = 0.71, $P = 0.48$, scrambled objects, z = 1.00, $P = 0.32$). The results were similar at different ROI sizes (*SI Appendix*, Fig. S7*D*). We again excluded the face-selective voxels ($P < 0.05$) from the object-selective ROIs, and DPs and controls continued to show similar object selectivity and responses at all ROI percentages (*SI Appendix*, Fig. S7).

Selectivity reductions were limited to the preferred category in all ROIs. To examine whether selectivity differences to scenes and bodies were restricted to areas showing a preferential response to these categories, we separately tested for group differences in selectivity to scenes, bodies, and objects in the ROIs that showed selective responses to other categories. Scene selectivity was calculated in face-, body-, and object-selective ROIs. No significant group differences were discovered (*SI Appendix*, Fig. S8, Holm–Bonferroni-corrected). Similarly, for body and object selectivity, no significant differences between controls and DPs were seen in the ROIs that did not prefer those categories (*SI Appendix*, Fig. S8, Holm–Bonferroni-corrected). To exclude the effect of face-selective voxels in the body- and object-selective ROIs, those voxels were again excluded at $P < 0.05$ and the same analysis of group differences was then carried out. Again, no significant differences between the groups were found for the three categories in their nonpreferred ROIs (*SI Appendix*, Fig. S8, Holm–Bonferroni-corrected).

Discussion

Using the variable-window method, dynamic stimuli, and a relatively large sample size, our study was able to answer fundamental questions about the neural basis of DP and call attention to issues that will be important for future work. Comparison of the whole-brain distribution of category-selective areas and the peak

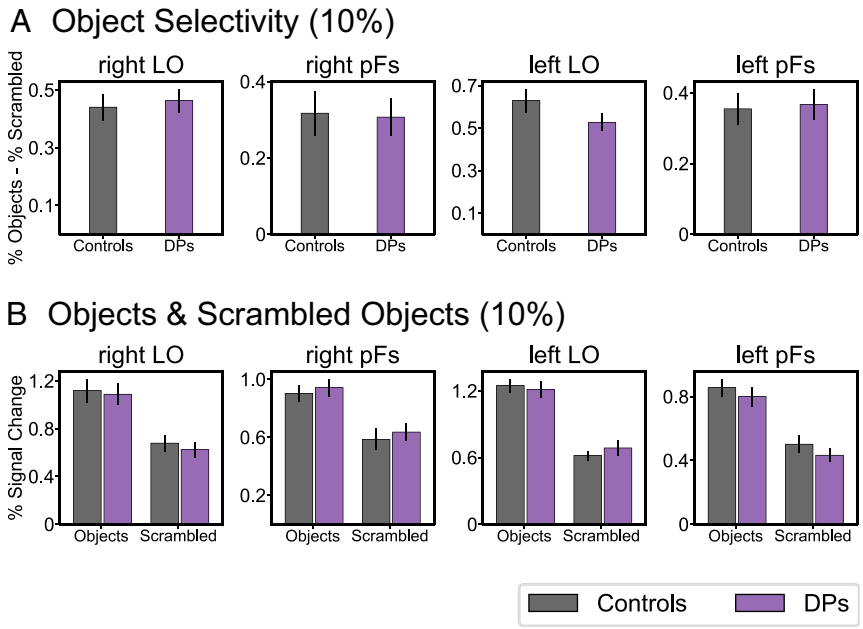

Fig. 6. No deficits were found in object-selective ROIs. (*A*) Object selectivity and (*B*) responses to objects and scrambled objects in all object-selective ROIs at 10% size. No significant results were found in any ROIs. Figures displaying selectivity at different ROI percentages can be found in *SI Appendix*, Fig. S7*D*. In all panels, error bars stand for ±1 SE for each group.

voxel locations in DPs and controls (Fig. 1) indicated that visual recognition mechanisms in DP are organized normally (46), contrary to suggestions that individuals with selective developmental disorders have functional architectures that differ from neurotypical individuals (47, 48). Analyses of these ROIs, however, revealed that DPs have reduced selectivity for faces in face-selective areas and reduced selectivity for preferred categories in other category-selective areas.

Face Selectivity in DP. A leading neural account of DP proposes that it results from a disconnection between posterior face-selective areas (e.g., OFA and FFA) and ventral temporal anterior regions that process facial identity (9). While we found that DPs showed a nearly significant difference in face selectivity in the face ROI in the ventral anterior temporal lobe (ATL-FA), significant reductions in face selectivity were also present in right FFA, left FFA, and right pSTS-FA, contrary to what a disconnection hypothesis would predict. In addition, comparison of the selectivity differences between DPs and controls in anterior face ROIs (ATL-FA, aSTS-FA, and IFG-FA) vs. posterior face ROIs (OFA, FFA, and pSTS-FA) did not reveal a difference. Our results thus suggest that functional differences in posterior face-selective areas contribute to the face recognition deficits in DP. This conclusion is consistent with previous findings that also indicated abnormalities affecting or in the vicinity of posterior face areas (14–18, 20, 21) and with event-related potential studies that reported the N170, an early face-selective component generated by posterior face-selective areas (49, 50), responds atypically in a large proportion of DPs (51). Thus, our results support a distributed account rather than a disconnection account. The selectivity reductions we observed in some face ROIs may reflect the impact of reduced face selectivity in other face ROIs, but functional connectivity analyses will be necessary to better understand the interactions between face areas.

Our analyses of face selectivity in the face ROIs also allowed us to examine whether DPs showed differential reductions in ventral areas vs. dorsal areas. In the most prominent model of face processing (5, 52), ventral face areas are critical for the representation of invariant aspects of faces such as identity and sex whereas dorsal face areas represent changeable aspects of faces like expression and gaze. Many DPs perform normally with facial expression (53, 54) and eye gaze (55), so we expected selectivity in ventral areas would be more strongly reduced in DPs than selectivity in dorsal areas. However, selectivity in all three right hemisphere dorsal face areas was significantly weaker in DPs than in controls, and ventral-area selectivity was not more strongly reduced than dorsal-area selectivity. Previous DP imaging studies have tended to focus on ventral face areas, but dorsal, particularly STS, abnormalities have been reported as well (10, 14, 16, 56). The clear abnormalities we found in DP dorsal face areas raise questions about the computations carried out in these areas and suggest it would be valuable to carry out further testing of changeable aspects of face processing in DPs and to systematically examine DP performance with other STS-mediated abilities such as voice perception/recognition and biological motion perception (57).

Although pronounced reductions in face selectivity in face-selective ROIs were present in the DPs, we found no reductions in face selectivity in other category-selective areas. The restriction of face-selectivity reductions to face areas provides evidence that DPs' behavioral deficits with faces may result from problems limited to the face network. Nevertheless, the absence of group differences in non-face areas should be treated cautiously and further examined in future work. The normal response to faces in other category-selective areas also suggests the reductions found in face-selective areas are caused by deficient processing within the face network rather than reduced responses to faces in early visual areas, because problems originating in early visual areas would be expected to impact the response to faces in all category-selective ROIs.

DPs also Show Reduced Selectivity to Preferred Categories in Other Category-Selective Areas. Our study investigated the functioning of non-face category-selective areas ROIs in DP, and we found reductions in selectivity to the preferred category in a number of these ROIs. Selectivity to scenes in all scene-selective areas and to bodies in all body-selective areas was weaker in DPs than in controls. This weaker selectivity was significant in all three right-hemisphere scene-selective ROIs and one left-hemisphere

scene-selective ROI. For body-selective areas, two of the four ROIs were marginally significant. Similar to the findings in face-selective areas, these reductions were driven by weaker responses to the preferred category. As we found for face selectivity, scene-selectivity and body-selectivity reductions were restricted to the ROIs showing a preferential response to those categories. Surprisingly, the size of the group differences in two scene-selective ROIs (rMPA, rPPA) were comparable to the differences found in the face-selective ROIs exhibiting the largest group differences. It is possible that the use of bodies that were mostly covered by clothes may have underestimated the group differences in body-selective ROIs, because clothed bodies do not appear to fully engage body processing mechanisms (58).

Because selectivity in the DPs was weaker in all face, scene, and body areas, we considered several factors that might contribute to these differences. One possibility is that the DPs have impairments to early visual cortex so that category-selective areas receive insufficient input. However, deficits in upstream processes are unlikely to explain the reductions, because the responses to nonpreferred categories in DPs and controls were comparable (*SI Appendix*, Fig. S9). The group differences were also not the result of differences in head motion or functional signal-to-noise ratios (*SI Appendix*, *SI Methods*).

Are there other potential mechanisms that might cause the widespread selectivity deficits? One possibility concerns the nature of the information about the preferred category delivered to category-selective mechanisms. Normal participants show substantial variability in the location they initially fixate when viewing faces (59), and behavioral performance peaks when observers fixate faces at their preferred fixation location (60). It is possible that unlike normal participants, DPs do not preferentially fixate their optimal fixation location on the face. It is not known whether fixating away from one's optimal fixation location reduces neural responses to faces, but if it does, a mismatch between DPs' fixation locations and their optimal positions may contribute to the selectivity reductions in face ROIs. Another factor that may contribute to the selectivity reductions is the size of receptive fields in category-selective areas. A study with a small sample of DPs found that estimates of population receptive field size in posterior face-selective areas were smaller in DPs than in controls (61). Smaller receptive fields would be expected to reduce the quality of face input to face areas and lead to reduced responses. If DPs' receptive fields are small across a variety of category-selective areas, receptive field size may also account for weaker responses to scenes in scene areas and bodies in body areas.

The selectivity reductions found in non-face areas in the DPs may represent the neural correlates of behavioral deficits some DPs have with recognition tasks involving categories other than faces. These deficits include impairments with bodies (27, 53, 62), scenes (32), and objects (32, 33, 63, 64). Future studies can test this possibility by comparing selectivity in scene and body areas in DPs with normal scene and body recognition and DPs who have deficits with these categories. The common occurrence of object recognition deficits in DP (64) suggests the normal selectivity exhibited by the DPs in object-selective areas should be interpreted cautiously. It is worth noting that a number of DP cases with behavioral deficits limited to faces have been reported (32, 64–66), and the group differences we found in many of the non-face ROIs are not inconsistent with the presence of face-specific deficits in individual DPs. We expect that, similar to what is seen in acquired brain damage, face-selective cases of DP likely result from highly circumscribed cortical dysfunction whereas DPs with broad deficits have more extensive cortical dysfunction.

Developmental Factors Contributing to DP. Several findings suggest early face input is necessary for the face network to function normally later in life (22, 23, 67). These findings have led to suggestions that DP may result from a lack of exposure to faces in childhood (24, 26, 68), but we are unaware of previous evidence that speaks to whether insufficient exposure to faces contributes to the emergence of DP. We believe, however, that the selectivity reductions in the DPs in scene-selective and body-selective areas indicate that inadequate experience with faces is unlikely to account for the face deficits in many of the participants tested here, because reduced face input would not be expected to lead to selectivity reductions in other category-selective areas. Restricted visual input during development might lead to reduced selectivity across many category-selective areas (69), but none of the DPs tested here had impaired scores on tests of low- and midlevel vision and none reported visual problems early in life.

The widespread neural deficits found in the DPs instead indicate DP often results from factors affecting the development of cortex well beyond face-selective areas. Many factors could be involved (e.g., neurotransmitter systems, myelination, pruning, etc.), and it seems likely that such factors would be unlikely to be limited to particular functional areas. Thus, these sorts of neurobiological factors would be expected to affect both face-selective areas and other category-selective areas in similar brain regions. Ramus has proposed an influential theory that developmental disorders such as DP, dyslexia (70), dyscalculia (71), and amusia (72) result from a particular neurobiological problem: neural migration errors. These errors lead to focal cortical disorganization, and according to this view, the type of behavioral deficit that results from the disorganization depends on the computations normally carried out in the affected cortex. For example, anomalies in left perisylvian cortex will tend to cause phonological deficits, whereas anomalies to face-selective areas of right fusiform gyrus might result in prosopagnosia. Autopsies of dyslexic brains found that cortical anomalies were concentrated in regions critical for speech and language but were also present in lower concentrations in neighboring regions (73–75). Further support for the role of neural migration in dyslexia comes from studies showing that the majority of genes associated with dyslexia play a role in neural migration (76). Ramus (70) has suggested this neural migration model of dyslexia may be applicable to DP, and the extensive selectivity reductions in the DPs tested here as well as the heritability of DP (33, 77–79) fit with his proposal. Looking ahead, the well-characterized functional organization of visual recognition provides a unique opportunity to assess the neural scope of a selective developmental disorder, and it will be informative to determine how often DPs have functional abnormalities in regions surrounding those examined here.

Summary and Future Directions

DPs exhibited reduced face selectivity across many face-selective ROIs, and these reductions were not concentrated within particular divisions of the face network. Selectivity reductions were also present for scenes and bodies in areas selective for those categories. These widespread selectivity reductions suggest face recognition deficits in a substantial proportion of DPs are only the most noticeable visual recognition deficit, and we hope the recognition of these broader abnormalities encourages visual neuropsychologists to widen the lens beyond DP to address the variety of developmental visual recognition disorders that occur.

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