Reduced white matter integrity is associated with face selective areas in developmental prosopagnosia

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Introduction

- Developmental prosopagnosia (DP) is characterized by an impaired face recognition, which involves an extended network of brain regions.
- Impaired face recognition in small samples of DPs has been associated with low white matter integrity in either the fibers local to right fusiform region (Gomez et al., 2012), or the long-range ventral occipital-temporal tracts (Song et.al, 2015; Thomas, 2009).
- Recent studies have indicated that there may be apperceptive (perceptual) or associative (memory specific) forms of DP (Biottie et. at, 2019). It is unclear whether DPs' impairment is related to local or more global white matter (WM) structural differences.
- Our objective was to assess whether a) structural differences (diffusion analysis) using much larger DP samples b) difference between to types of DP group.

Methods

Behavioral

- Participants were categorized as DP if CFMT< 44, PI20 >65 and FFMT < 70%; (PI-20: prosopagnosia questionnaire index, CFMT: Cambridge face memory test; FFMT: Famous faces memory test)

Diagnostic Criteria

Participants	Gender	Age	PI- 20 scores (Mean(SD))	Famous Faces Test	Cambridge Face Memory Test
Control (N=23)	13 F/ 10 M	35 (13.07)	34 (7.52)%	78 (19.8)%	57.7 (7.89)
DP (N=23)	18F/ 5M	32 (14.28)	79.78 (9.96)%	30.73 (14.2)%	39.6 (3.96)
p values		0.6	< .001	< .001	< .001

- DP group significantly differed from the control group in tests of face perception.

Perceptual Assessments

Participants	Benton Facial Recognition test	Cambridge Face Perception Test	Telling Faces Together Test	USC Face Perception Test
Control	82.5 (5.6) %	-	80.0 (7.6)%	78.7 (8.7)%
DP	74.4 (5.7) %	63.6 (10.8)%	75.5 (5.1)%	75.7 (6.9)%
p values	< .001	-	0.03	0.09

- Based on DSM-5 criteria, DPs were categorized as having mild/major perceptual deficits- **Perceptually Impaired**, <1SD on any two perceptual tests (**PI-DP**:n=12), or **Perceptually Unimpaired** DPs (**PU-DP**:n=11)

Diffusion Imaging Analysis

- Participant exclusions based on crossmodal imaging data availability

1) Whole brain FA map (TBSS) -preprocessing in FSL - *Figure 1*
2) JHU-ICMB Atlas based ROI post TBSS-*Figure 2*
3) Surface based ROI registered to diffusion- FSFAST, FSL- *Figure 3*
   - fMRI data was processed in FSFAST. Surface based ROI's were registered into the diffusion space and masks were created.
   - Mean FA values were calculated for the area within the mask. Reduced FA values indicate impaired integrity of white matter tracts.

Results

1) Whole Brain Fractional Anisotropy (FA)- TBSS

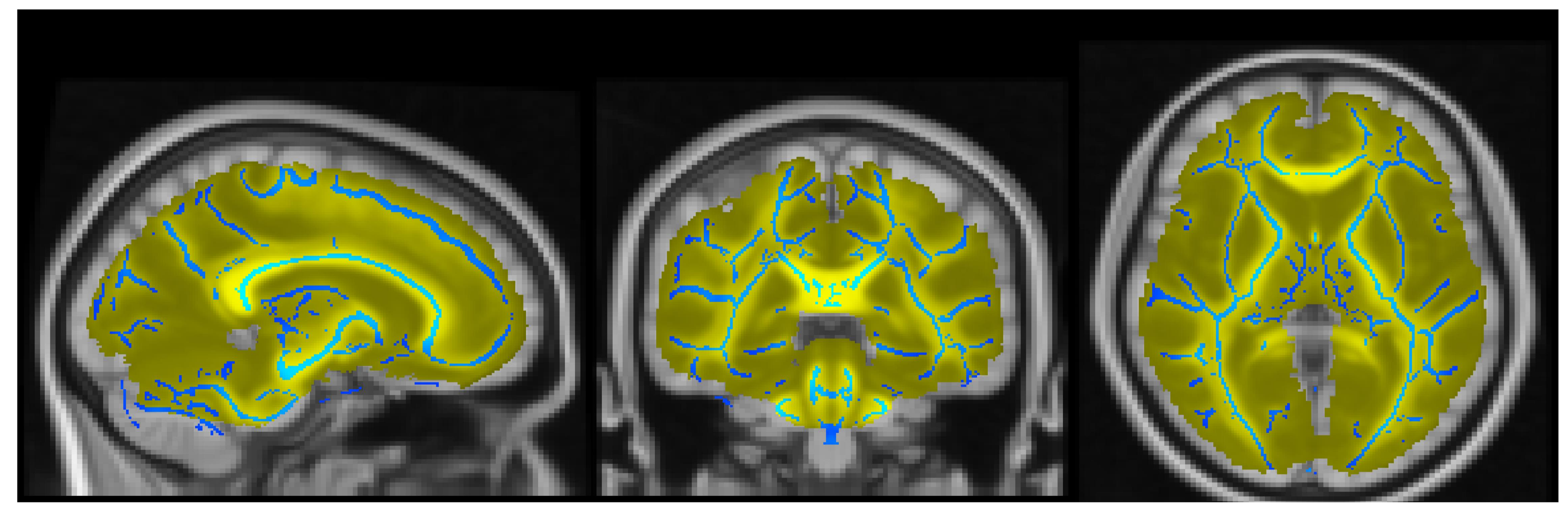

Figure 1 Results: Whole brain mean FA intensity map (yellow) overlaid with FA skeleton contrast-map (blue) across two groups of participants. We did not find any whole brain (or skeleton) FA difference between DP and Control group in the GLM analysis (*p*-corrected)

2) JHU-ICBM Atlas ROI FA analysis

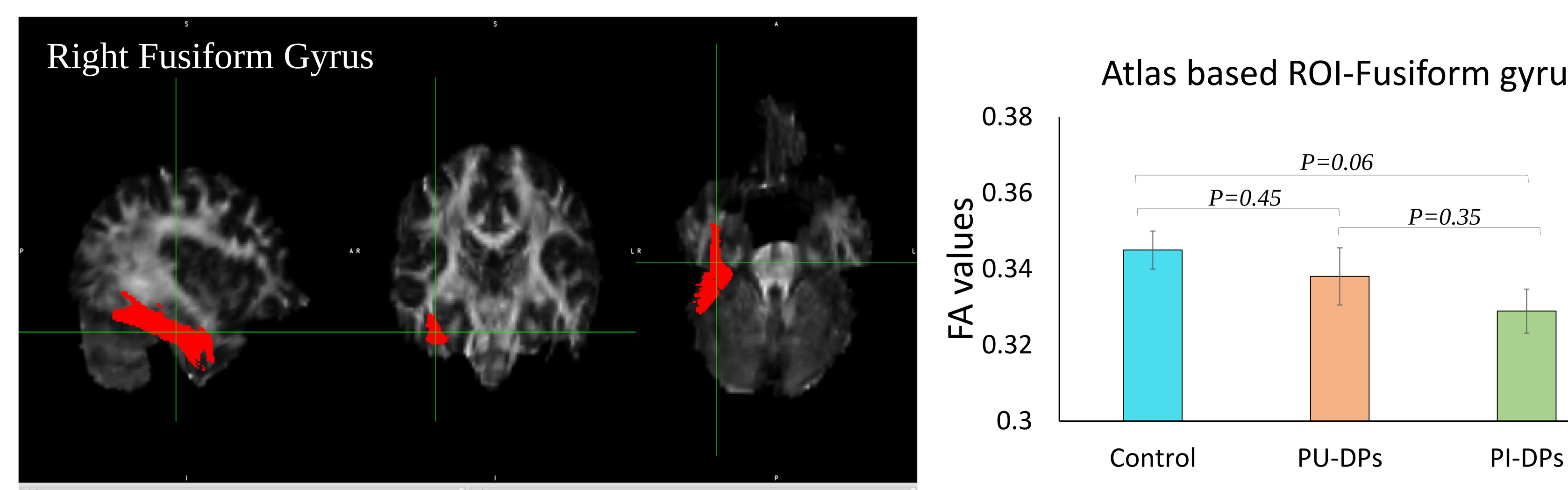

Figure 2 Results: Left figure shows that selected right hemisphere fusiform gyrus (ROI) overlaid on a FA map. Right graph shows a trend for the difference between PI-DPs and Control group but not in PU-DPs. Because the gyrus is a large area, we then used face selective ROIs that showed contrast differences in a functional localizer task between faces and objects, for the two groups

3) Using surface based fmri ROI registered to diffusion data

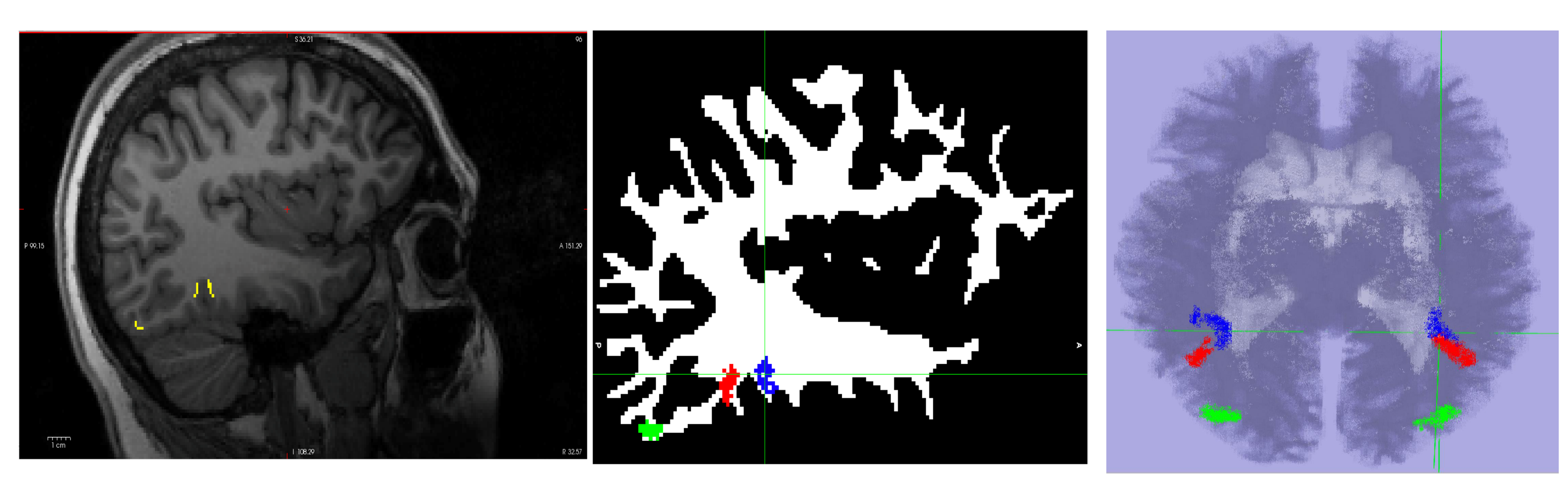

Figure 3 The above figures show the localization of surface ROIs on the right hemisphere of T1 structural brain (left, right hemisphere-saggital view) and white matter (wm) in native space (middle) and bilateral display of ROIs on white matter (right). The ROIs are projected into wm area to create masks for occipital face area (OFA- yellow, green), Posterior fusiform gyri (pFUS/FG2- yellow/red) and middle fusiform gyri (mFUS/FG4- yellow/blue).

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Results: Using surface fMRI ROIs

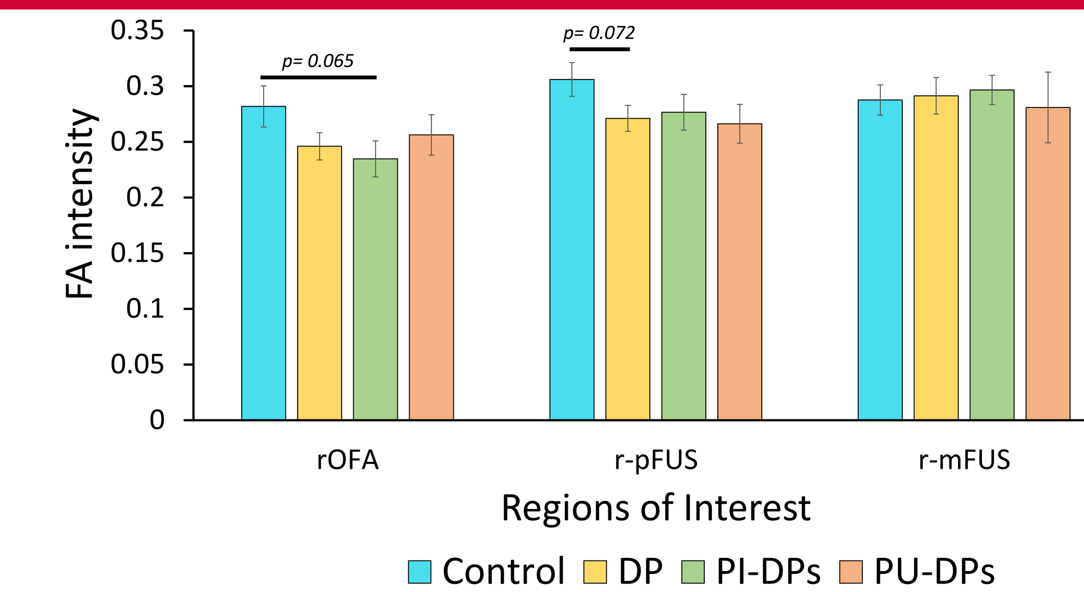

Figure 4A. FA intensity in OFA and Fusiform gyri (Right hemisphere)
The preliminary findings show a trend towards reduced integrity rOFA when comparing perceptually impaired (PI) DP's with Control group. There is also a trend for DP vs. Control group difference in r-pFUS region.

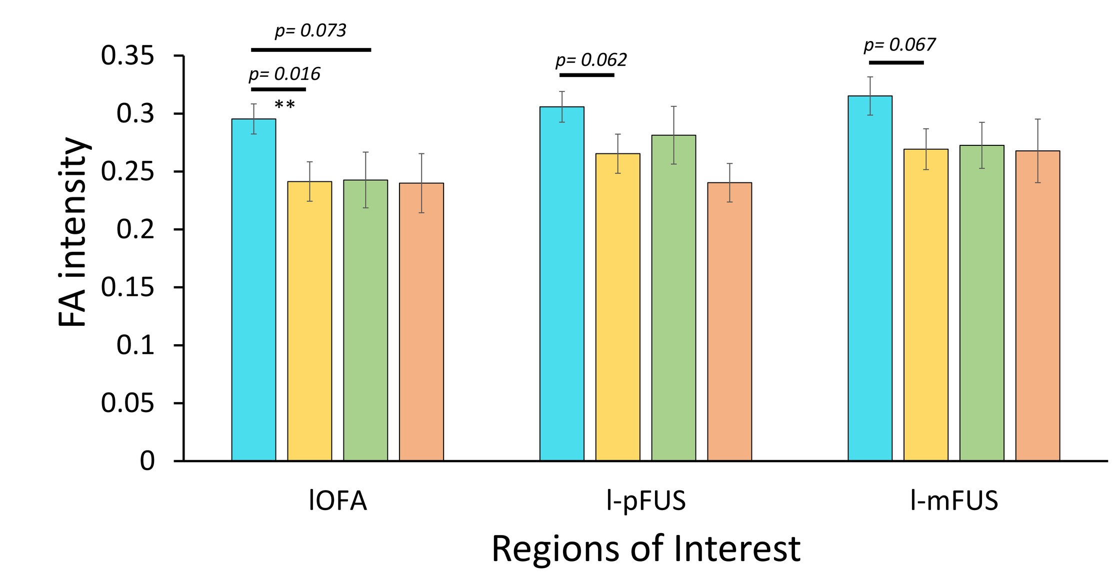

Figure 4B. FA intensity in OFA and Fusiform gyri (Left hemisphere).
More strength is observed for overall group differences in l-OFA than r-OFA and also for other face selective regions. PI-DP vs Control group differences are not strong except for a trend in the l-OFA region.

fMRI localizer task results (Li et al; CNS-2020-E118)

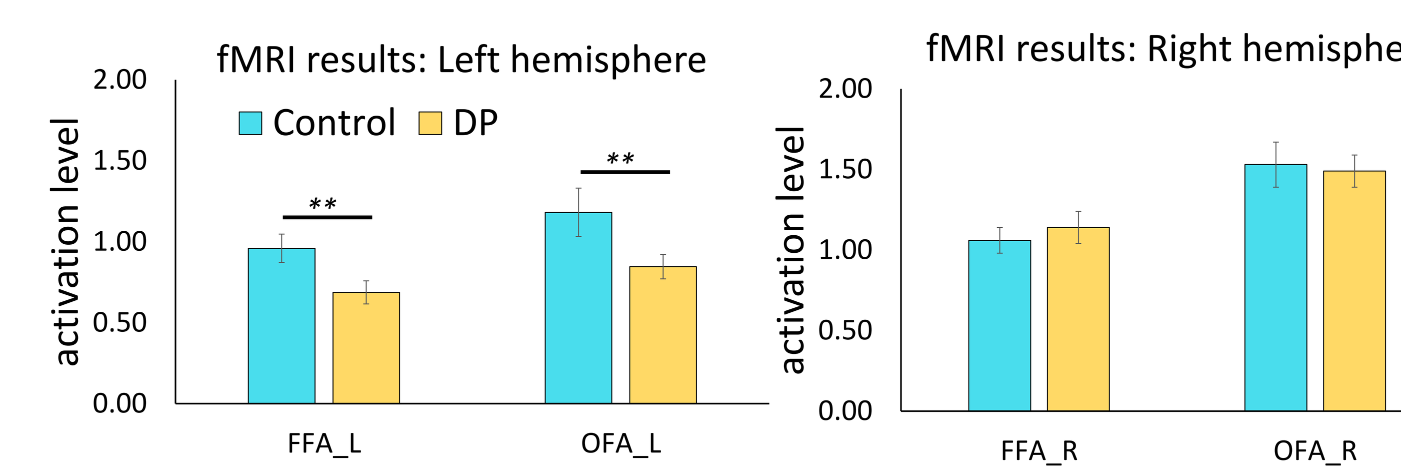

Figure 5. fMRI activations in OFA and FFA.
The diffusion results add to findings of the fMRI data on the same group of DP and Control participants, that show face selectivity group differences in left hemisphere for both OFA and FFA regions of fusiform gyrus.

Discussion

- Reduced WM integrity is observed in left hemisphere across face selective areas in DPs
- Earlier face-specific regions may be more affected in those with perceptual dysfunctions.
- Discrepancies in WM connectivity in the early brain areas might be associated with heterogeneity in the severity of perceptual deficits.
- Future directions are to map structural connectivity differences in different face selective areas using tractography and correlate with behavioral and fMRI data

References: 1) Song, S., Garrido, L., Nagy, Z., Mohammadi, S., Steel, A., Driver, J., ... & Furl, N. (2015). Local but not long-range microstructural differences of the ventral temporal cortex in developmental prosopagnosia. *Neuropsychologia*, *78*, 195-206. **2)** Thomas, C., Avidan, G., Humphreys, K., Jung, K. J., Gao, F., & Behrmann, M. (2009). Reduced structural connectivity in ventral visual cortex in congenital prosopagnosia. *Nature neuroscience*, *12*(1), 29. **3)** Gomez, J., Pestilli, F., Witthoft, N., Golarai, G., Liberman, A., Poltoratski, S., ... & Grill-Spector, K. (2015). Functionally defined white matter reveals segregated pathways in human ventral temporal cortex associated with category-specific processing. *Neuron*, *85*(1), 216-227. **4)** Biotti, F., Gray, K. L., & Cook, R. (2019). Is developmental prosopagnosia best characterised as an apperceptive or mnemonic condition?. *Neuropsychologia*, *124*, 285-298.