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Research report

Three cases of developmental prosopagnosia from one family: Detailed neuropsychological and psychophysical investigation of face processing

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ABSTRACT

A number of reports have documented that developmental prosopagnosia (DP) can run in families, but the locus of the deficits in those cases remains unclear. We investigated the perceptual basis of three cases of DP from one family (67 year-old father FA, and two daughters, 39 year-old D1 and 34 year-old D2) by combining neuropsychological and psychophysical methods. Neuropsychological tests involving natural facial images demonstrated significant face recognition deficits in the three family members. All three members showed normal facial expression recognition and face detection, and two of them (D2, FA) performed well on within-class object recognition tasks. These individuals were then examined in a series of psychophysical experiments. Intermediate form vision preceding face perception was assessed with radial frequency (RF) patterns. Normal discrimination of RF patterns in these individuals indicates that their face recognition difficulties are higher in the cortical form vision hierarchy than the locus of contour shape processing. Psychophysical experiments requiring discrimination and memory for synthetic faces aimed to quantify their face processing abilities and systematically examine the representation of facial geometry across viewpoints. D1 showed deficits in perceiving geometric information from the face at a given view. D2's impairments seem to arise in later face processing stages involving transferring view-dependent descriptions into a view-invariant representation. FA performed poorly on face learning and recognition relative to the age-appropriate controls. These cases provide evidence for familial transmission of high-level visual recognition deficits with normal intermediate-level form vision.

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1. Introduction

The present study provides a detailed investigation of three cases of developmental prosopagnosia (DP) from one family. Prosopagnosia is a neurological condition characterized by an impairment in face recognition. While acquired prosopagnosia is caused by a brain damage, DP is manifested in the absence of any discernible brain lesion and neuro-developmental disorders (e.g., Asperger syndrome) (Behrmann and Avidan, 2005; Kress and Daum, 2003). Recently, multiple cases of DP in the same family have been reported (Duchaine et al., 2007a; Grueter et al., 2007; Schmalzl et al., 2008), suggesting the heritability of this syndrome (McConachie, 1976). However, little is known about the perceptual basis of these apparently inherited cases of prosopagnosia. In the present study, three of five family members across two generations showed significant deficits in face processing despite normal visual sensory and intellectual function. The affected individuals were then tested with a series of psychophysical experiments that were designed to identify the perceptual locus of the face processing deficits.

Face processing consists of a number of hierarchical stages and parallel processes in a distributed cortical network (Bruce and Young, 1986; Haxby et al., 2000) (see Fig. 1). Thus, the present study used psychophysical tests that systematically assessed different face processing stages. To date, most research with familial prosopagnosics has only assessed early vision and higher-level processes. However, face processing deficits could result from a problem in any part of the network including mid-level visual processes. To evaluate the possibility of general perceptual deficits at the level of intermediate form processing, perception of closed curvature in the DP participants was examined using radial frequency (RF) patterns (Wilkinson et al., 1998). In earlier studies, most DP individuals have performed normally with intermediate form vision tasks involving concentric Glass patterns (Le Grand et al., 2006) or Navon letters (Duchaine et al., 2007a, 2007b; but also see Behrmann et al., 2005; Bentin et al., 2007). Glass pattern detection measures sensitivity to structure in global form, requiring integration of local elements into a global configuration (Gallant et al., 1996; Wilson et al., 1997). The Navon task assesses global-local perception using compound letter stimuli (Navon, 1977). However, neither task involves closed contour curvature, likely a direct input to face processing mechanisms (Wilkinson et al., 2000; Wilson et al., 2000). RF patterns used in the present study are comprised of curvatures and circles that are key attributes of faces and may most effectively probe intermediate form vision important to face and object perception (Wilkinson et al., 1998, 2000). In a functional magnetic resonance imaging (fMRI) study, concentric patterns produced activation similar to the level elicited by faces in V4 and half as much activation as faces in the fusiform face area (FFA) (Wilkinson et al., 2000). In addition, evidence from psychophysical and fMRI data suggests that analysis of concentric patterns in V4 contributes to face processing (Wilkinson et al., 2000; Wilson et al., 2000).

We also used psychophysical tests to examine what types of face processing operations are deficient in the three DPs. Face processing deficits could result from a difficulty in

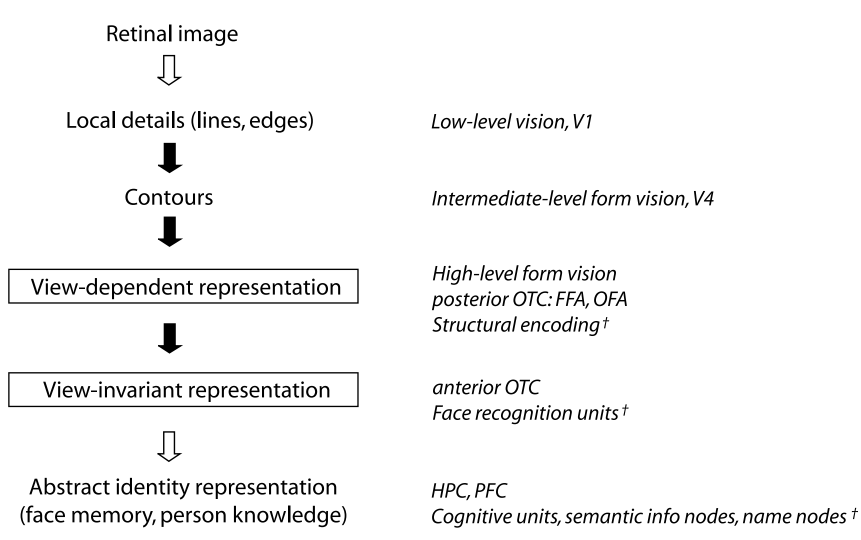

Fig. 1 – A schematic diagram of face processing stages in the brain. Visual representation of faces involves multiple cortical regions along the hierarchy of the ventral visual pathway. Fine representation of individual faces at a particular view would be formed in the (FFA, Kanwisher et al., 1997) and occipital face area (OFA, Gauthier et al., 2000) (Andrews and Ewbank, 2004; Grill-Spector and Malach, 2001). View-invariant representation of facial identity, across a large change in viewpoint, would be achieved in later brain regions (Eger et al., 2005; Pourtois et al., 2005a, 2005b) by associating disparate view representations (Riesenhuber and Poggio, 1999; Wallis and Bülthoff, 2001). Face learning and memory would involve the hippocampus (HPC) and prefrontal cortex (PFC) (Haxby et al., 1996; Quiroga et al., 2005). In real life, faces are hardly ever encountered from identical vantage points. But in an experimental situation where faces are learned and recognized in the same view, view-invariant representation stage could be bypassed. There is not only the feed-forward processing but also top-down modulation to support view-invariant representation and learning (Riesenhuber and Poggio, 1999). The data from DP individuals suggest that connectivity among functional systems is a vital component of face analysis (e.g., Thomas et al., 2009). †face processing stages in Bruce and Young (1986). OTC = occipito-temporal cortex.

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forming view-dependent representation or later stages involving invariant representation (Fig. 1). Previous fMRI studies have suggested that the anatomical regions for viewpoint-dependent and invariant face representations are distinct (Eger et al., 2005; Pourtois et al., 2005a, 2005b). Behaviourally, it has been observed that some prosopagnosic individuals may have an intact percept of faces and perform well on matching faces shown in the same view while being impaired in matching faces that differed in viewpoint (e.g., a DP case in Laeng and Caviness, 2001; acquired cases in Lee et al., 2003 and Marotta et al., 2002). Thus, it is important to distinguish performance with and without a viewpoint change in assessment of face processing deficits.

In the current study, we provide a comprehensive evaluation of three family members affected with DP. Neuropsychological tests used photographic images to assess DP individuals' difficulty during an encounter with natural faces. Psychophysical methods reduced the facial information to contour curvature (RF patterns) and facial geometry (synthetic faces, Wilson et al., 2002) to systematically tap into different aspects of face processing.

2. Prosopagnosic participants: case history

Three healthy DP individuals from one family participated. Testing was conducted over several sessions with each DP individual. When the present study commenced in November 2005, the father FA was 67 years old, one daughter D1 was 39 years old, and a second daughter D2 was 34 years old. FA is a retired professor in visual arts with 20 years of formal education. D1 is an artist and professor in visual arts with a Master's degree. D2 is a professor with a Ph.D. in biology. They have no history of any neurological or psychiatric disorder, head injury, early visual problems such as infantile cataract, or birth complications. All are in good health. They have normal or corrected-to-normal visual acuity (on Snellen acuity chart) and normal contrast sensitivity (on the Pelli-Robson contrast sensitivity test). The family includes two other members, FA's wife (MO) and another daughter (D3), who are not prosopagnosic.

The individuals with DP filled out a questionnaire as an initial screening for prosopagnosia: the questionnaire is based on the questions posted on the author's website (www.faceblind.org) and those in Kennerknecht et al. (2006). Their self-reports revealed the characteristic symptoms prevalent in DP (e.g., Kennerknecht et al., 2006). All reported trouble recognizing familiar people (particularly when encountered out of context) and famous people, and difficulties in learning or remembering new faces. For example, D1 rarely recognizes students from her classes if she sees them even in school outside of class. D2 could not recognize her cousin at a camp when the cousin walked up to her, and for the remainder of the week at camp, she could not pick her cousin out of a crowd. Most recently, she mistook another child for her own son at daycare. This incident made her realize the severity of her face recognition problems and led her to contact our lab. D1 and D2 experience challenges in watching some movies: D1 reports that she often has trouble telling characters apart. Intriguingly, D1 seems to have an intact representation of generic faces despite her problems in recognizing individual faces. She frequently portrays human faces with great detail in her sculptures. D1 and FA's particular difficulties with faces are even more remarkable considering that they are visual artists who have reported excellent visual imagery for non-face objects.

Furthermore, their self-reports on the questionnaire revealed difficulties on other types of visual tasks. FA and D2 experience difficulties in imagining familiar faces. FA sometimes has difficulties recognizing emotional facial expressions and determining eye gaze direction. D1 and D2 have reported trouble distinguishing between cars or between houses (but not other items such as shoes or coats asked in the questionnaire), and a poor sense of direction and problems with navigation. However, none of these individuals reported problems in judging age, gender, and attractiveness from faces. Despite the difficulties that their prosopagnosia causes, these affected individuals are socially well integrated and successful in their professions. None shows signs of autism or Asperger syndrome.

3. Neuropsychological assessment

To investigate their face processing abilities, a series of neuropsychological tests were administered.[1] Each DP's result was individually compared to those of age-appropriate controls using the modified *t*-test for single cases (Crawford and Howell, 1998).

3.1. *Face recognition: famous faces (e.g., Duchaine et al., 2007a)*

The famous faces test involved 60 celebrity faces that were closely cropped so that little hair or clothing was visible. Each image was presented for 5 sec. Participants were asked to name the face presented or provide uniquely identifying information (e.g., movie roles or political office). After the test, the names of the faces that they missed were read to the participant and they answered whether they had seen that person's face many times. Nineteen US and Canadian controls (mean age = 40.9, range = 35–45) correctly identified 52.5 faces (Standard deviation – SD = 6.6) and reported knowing 57.7 faces (90.43% correct).

As expected, MO and D3 did not demonstrate problems with the famous faces test (see Table 1). MO correctly identified only 38 of the faces, but she was familiar with only 46 of the 60 faces. In contrast, D2 and FA recognized 17 and 19 faces out of 47 known faces, respectively. Given her reported familiarity score, D1's results (78.6%) are difficult to interpret, but her two sisters' knowledge of 47 or 60 faces suggests a possibility that she may have underestimated the number of famous faces that she had seen repeatedly.

[1] We did not use the Benton Facial Recognition Test (Benton and Van Allen, 1968), which had been commonly used to reveal face recognition deficits in brain-damaged patients. The Benton test was originally developed to detect more general brain damage (e.g., to distinguish right and left hemisphere damage) and it was shown that normal scores are not always indicative of normal face perception (Duchaine and Nakayama, 2004; Duchaine and Weidenfeld, 2003).

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Table 1 – Results of face recognition tests.

Participant	Famous faces			CFMT				CFPT (errors)	
	Identified	Exposed	%	Intro	Novel	Noise	Total	Upright	Inverted
D1	22**	28	78.6	13**	15**	11	39**	50	76
D2	17**	47	36.2**	17*	8**	12	37**	94**	94**
FA	19**	47	40.4**	16	11	4**	31*	60	76
D3	46	60	76.7	17*	24	15	56	32	64
MO	38*	46	82.6	18	25	17	60	64	72
Young controls	52.5 (6.6)	57.7	90.43	17.9 (.4)	24.5 (3.4)	17.3 (4.9)	59.6 (7.6)	36.7 (12.2)	65.0 (9.8)
Older controls	–	–	–	17.3 (1.0)	19 (5.0)	13 (3.0)	49.3 (7.5)	52.8 (15.7)	77.6 (12.5)

DP participants are indicated in bold. Significant deficits are marked by * ($p < .05$) and ** ($p < .01$). Each individual score was compared to that of the age-appropriate controls using the modified *t*-test (Crawford and Howell, 1998). The number in brackets shows 1 SD of the control group.

3.2. *Cambridge face memory test (CFMT, Duchaine and Nakayama, 2006)*

The results of the famous faces test indicate that FA and D2 and possibly D1 have recognition problems with familiar faces whereas MO and D3 do not. The CFMT examined their memory for unfamiliar faces.

The CFMT required recognition of six target faces in three stages. In the first stage, each target face was introduced to participants in three views (left 3/4 profile, frontal, right 3/4 profile) for 3 sec each. Immediately after viewing the study images for a particular target face, participants were tested with three forced choice items including one image identical to a study image and two distractor faces in the same pose. This study and test cycle was repeated for all six target faces, so the introduction consisted of 18 items (6 faces × 3 test items per face). In the second stage, participants were presented with a review screen simultaneously displaying the six target faces in frontal view and given 20 sec to study the faces again. Then they were tested with 30 trials, each consisting of novel images of one of the six target faces along with two distractor faces. Novel images of the targets differed from the study images in perspective or lighting. The final stage was similar to the second except that Gaussian noise was added on top of novel images (24 test items). Different levels of Gaussian noise were created using filters in the Photoshop editing program (Adobe Systems Inc.). The scores were summed across all three stages.

The results of all participants are placed in Table 1. Young controls, age-appropriate for D1 and D2, included 20 participants (mean age = 45.1). The controls for FA were 17 healthy older adults (mean age = 68.5) with undergraduate or postgraduate level of education. D1, D2 and FA were impaired at the test, and these scores are comparable to those of prosopagnosic cases previously reported (Duchaine and Nakayama, 2006; Duchaine et al., 2007a, 2007b; Garrido et al., 2008). MO and D3 scored normally on the CFMT. Because they exhibited no signs of prosopagnosia, we additionally examined them on only two of the subsequent tests.

3.3. *Cambridge face perception test (CFPT, Duchaine et al., 2007b)*

The CFPT examined whether the impaired face memory seen in FA, D1, and D2 were accompanied by deficits in perception of facial similarity. In the CFPT, faces were presented simultaneously to lessen memory demands. On each trial, participants were presented with a 3/4 profile view of a target face above frontal views of six men's faces. Participants were given 1 min to arrange the test faces in order of similarity to the target face. Each test face was a morph between a frontal view of the target and a frontal view of a different individual's face. For each trial, the six test faces were pulled from six different morph continua: each test face was morphed to contain 28%, 40%, 52%, 64%, 76%, or 88% of the target face. Eight different sets of six test faces were created for the eight trials in each orientation: each was presented once upright and once inverted. Upright and inverted trials were randomly intermixed. Scores for each item were computed by summing the deviations from the correct position for each face. For example, if a face was placed three positions away from its correct location, that was recorded as three errors. Scores for each item of a particular orientation were added to determine a total number of upright or inverted errors. Chance performance with items of one orientation would result in 94 errors.

Table 1 displays upright and inverted errors for all family members and controls (young controls: $n = 21$, mean age = 46.5; older controls: $n = 17$, mean age = 68.5). Controls showed a robust inversion effect. D1's score was not significantly impaired but only two participants from the control group scored more poorly. D2's score of 94 errors with both the upright and inverted items is at chance. FA did not show a significant deficit compared to that of the age-appropriate controls. In previous studies, not all DPs were impaired at this test (Duchaine et al., 2007b; Garrido et al., 2008). D1 and FA's large inversion effects indicate that, like controls, they process upright faces in a qualitatively different manner than inverted faces.

3.4. *Facial expression recognition*

Despite severe impairments with facial identity recognition, some DP individuals recognize facial expressions normally (Bentin et al., 1999; Duchaine et al., 2003; Humphreys et al., 2007; Nunn et al., 2001). To assess the extent of the family members' face processing impairments, the Eyes Test (Baron-Cohen et al., 2001) and an emotion matching task were administered.

In the Eyes Test, each trial presented an eye region along with words describing four emotional states. The emotion state words included expressions other than the six basic emotions of Ekman and Friesen (1976), such as aghast, confident, interested and skeptical. Participants had to choose which of the four words best described the eye region. In Baron-Cohen et al. (2001), which tested 122 members of the general population, the mean score was 26.2 (SD = 3.6) given a total of 36 items. The scores for the DP participants were normal (D1 = 29, D2 = 29, FA = 23).

In the emotion matching experiment (Duchaine et al., 2006), participants were briefly shown a sample face portraying one of four target emotions, happy, disgusted, surprised or neutral. Following the sample, three test faces were displayed simultaneously, each of which portrayed a different emotion. The identities of the sample and three test faces were all different. The participant's task was to choose the face depicting the same emotion as that of the sample face (32 trials in total). All three DPs were good at matching facial expressions (D1 = 29, D2 = 31, FA = 29; controls 29.9, SD = 1.9). The results from these two tests suggest that problems with faces in FA, D1 and D2 do not extend to facial expressions.

3.5. *Face detection (Garrido et al., 2008)*

In a recent investigation of face detection in DP (Garrido et al., 2008), most DP individuals showed some deficits in detecting the presence of a face in a visual scene. Here we used the most sensitive task from that study to assess face detection in the three DPs.

Participants were presented with a stimulus which contained a 3/4 profile face on 75% of trials and no face on 25% (see Garrido et al., 2008, for more details). As in Fig. 2, the images were black and white, and the portions of the field which did not contain the face configuration were populated by face parts. Participants were instructed to press a letter key when a face was present and make no response when absent. There were a total of 48 trials (36 face present and 12 absent).

A′, an unbiased measure of discrimination that varies between .5 and 1.0 (Macmillan and Creelman, 2004), was calculated for each participant. The average of 14 controls (mean age = 28.1) was nearly perfect at .997 (SD = .004) and the average reaction time was 1221 msec (SD = 314). D1 and FA made no errors (A′ = 1), while D2's A′ was .993. Their RTs were a bit slower than those of the younger controls but were not significant in the modified *t*-test: D1 = 1558 msec, [$t(13) = 1.04$, $p = .16$]; D2 = 1713 msec, [$t(13) = 1.5$, $p = .08$]; FA = 1309 msec, [$t(13) = .27$, $p = .4$]. The results indicate that the DP individuals do not have problems with face detection.

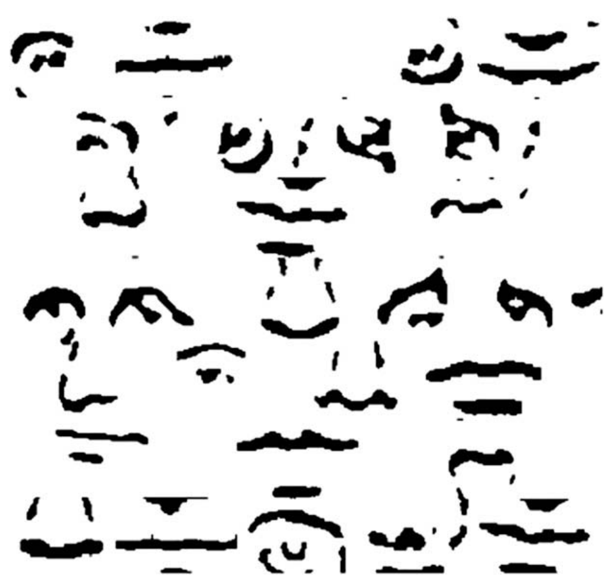

Fig. 2 – Stimuli used in face detection tasks.

3.6. *Within-class object recognition (Duchaine and Nakayama, 2005)*

The three family members' poor performance on several face processing tasks raises the question of whether they also have deficits in object recognition. Some DP individuals exhibit deficits in within-class object recognition (Behrmann et al., 2005; Duchaine and Nakayama, 2005; Duchaine et al., 2007a; Garrido et al., 2008), while others do not (Duchaine et al., 2004, 2006; Duchaine and Nakayama, 2005; Yovel and Duchaine, 2006; Nunn et al., 2001).

The object tasks require old–new recognition of items from seven categories: faces, cars, guns, houses, scenes, sunglasses and tools (Duchaine and Nakayama, 2005; Duchaine et al., 2006). During the study phase of each test, participants saw pictures of ten target items twice, one item at a time for 3 sec, and were asked to memorize them. In the test phase, participants were presented with the target items and 30 additional distractors and were required to indicate whether the items were from the target set or not.

Table 2 shows A′ scores for each object categories. Scores of D1 and D2 were compared to those of 17 graduate students with mean age of 27.8 (range = 24–34). D1 and D2 demonstrated an impairment in face recognition. With objects, D1 was only significantly impaired in recognition of tools and houses, and D2 showed no deficit. FA was not impaired with any of the tests, including the face test, compared to the age-appropriate controls ($n = 17$, mean age = 68.5, all had undergraduate or graduate level of education). When compared to young controls, FA showed superior scores with all object classes except faces, whereas the aging controls performed poorly across all categories demonstrating general memory loss not specific to faces. Inter-individual variability on cognitive tasks is large among older adults (Christensen et al., 1999): some older adults maintain cognitive functions better than others. FA is a high-functioning man who shows no memory deficit in any of the object tests. Accordingly, young adults may be a proper control group for him. The results suggest that D2's and FA's visual recognition deficits are largely restricted to faces, whereas D1's recognition problem extends to non-face object categories.

4. Tests of intermediate-level form vision

The results of neuropsychological tests have established that the three family members, FA, D1 and D2, do have face processing deficits. The first part of the psychophysical study investigated whether their problems with face processing were caused by general deficits in simple shape perception. The three family members' shape perception was assessed in

Table 2 – Performance (in A′) on old–new object recognition tests.

Participant	Faces	Cars	Guns	Houses	Scenes	Sunglasses	Tools
D1	.83**	.92	.98	.82**	.99	.96	.89*
D2	.88**	.93	.95	.98	1.00	.98	.94
FA	.92	.98	.98	.99	.98	.92	.95
D3	.99	–	–	.98	–	–	–
MO	.98	–	–	.97	–	–	–
Young controls	.96 (.02)	.94 (.04)	.91 (.04)	.96 (.03)	.97 (.03)	.91 (.04)	.95 (.03)
Older controls	.91 (.06)	.85 (.07)	–	–	–	.82 (.09)	.87 (.07)

Significant deficits are indicated as * ($p < .05$) and ** ($p < .01$). Each individual score was compared to that of the age-appropriate controls using the modified t-test (Crawford and Howell, 1998). DP participants are indicated in bold. The number in brackets shows 1 SD of the control group.

two experiments using RF patterns (see Appendices A and B for methods).

The first experiment measured discrimination thresholds for a RF of 5.0 cycles (RF5) with a mean radius of 1.0° (see Fig. 3 for an illustration of stimuli and procedure). All DP individuals exhibited normal RF5 pattern discrimination (Fig. 3). Both D1 and D2 performed better than the control group ($p < .0001$ and $p < .005$, respectively). FA's threshold was comparable to that of controls [$t(17) = 1.07$, $p = .15$].

The second experiment examined discrimination of bilateral symmetry using RF contours, which resembled a human

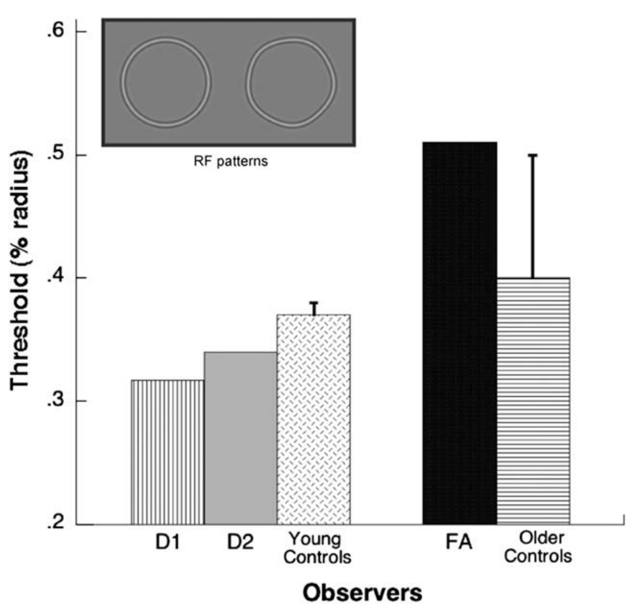

Fig. 3 – RF5 discrimination thresholds. The RF patterns depict a pure circle with no modulation (left), RF0, and an example of a RF5 contour (right). In each trial, one pattern was displayed for 110 msec, followed by a mean luminance blank screen of 200 msec, and a second pattern was displayed for 110 msec. The signal interval presented a RF5 contour and the other interval had a pure circle. The participant's task was to select the interval that contained the deformed circular contour. The threshold was measured in terms of the percentage change in the radius of the mean circle (RF0) that was discriminated at 75% correct performance. DP individuals' performance was similar to that of controls: young adults, $n = 19$, age range 20–30; older adults, $n = 18$, age range 59–76, mean age 65.2, SD 4.3 (the control data from Habak et al., submitted). Error bars: +1 SD of each control group.

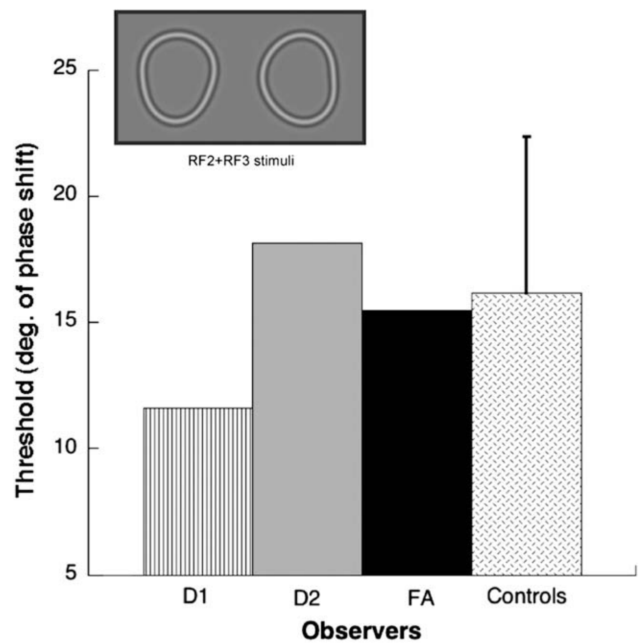

Fig. 4 – Discrimination thresholds for bilateral symmetry shapes. The example shows a symmetric pattern (left) and an asymmetric pattern (right). The stimuli were defined by sums of RF2 and RF3 with a mean radius of .5°. Asymmetric patterns were created by rotating the phase of RF3 relative to RF2. The temporal 2AFC experiment consisted of two stimulus intervals (130 msec each) with one interval containing a symmetric pattern and the other an asymmetric pattern. Both symmetric and asymmetric patterns were randomly rotated 6° left or right of vertical. This was a control for asymmetric patterns whose vertical axis appeared tilted due to phase shift. The participants were required to determine which of two intervals contained the asymmetric pattern. The threshold is in terms of degrees of phase rotation of the RF3 component. DP individuals showed thresholds comparable to those of the control ($n = 4$, age range = 30–40). Error bars: +1 SD of each control group.

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head shape (see Fig. 4; also Wilson and Wilkinson, 2002 for detailed methods). All DP individuals showed normal performance compared to young controls (Fig. 4).

All DP individuals showed normal discrimination of RF shapes. This suggests that their face processing difficulties do not result from impairments in cortical areas from V1 through V4 inclusive.

5. Synthetic face tasks

The following experiments used synthetic faces (Wilson et al., 2002) to assess the DP individuals' face discrimination thresholds across viewpoint changes. Synthetic faces have been useful for quantifying the amount of geometric facial information necessary for face discrimination (e.g., Habak et al., 2008; Lee et al., 2006; Wilson et al., 2002; Wilson and Diaconescu, 2006) and imaging experiments show that they activate the same brain areas as photographed faces (Loffler et al., 2005a, 2005b; Betts and Wilson, 2007). The synthetic face tasks evaluated the extent to which the ability to discriminate and recognize faces transferred to a novel view. Construction of synthetic faces is described in Appendix C (see Fig. 5 for an example).

5.1. *Simultaneous face matching*

This face matching task examined whether the DP individuals could match unfamiliar faces simultaneously presented under different viewpoint conditions. This task tested participants' ability to derive accurate geometric information from photographic faces and match to simplified synthetic versions.

5.1.1. *Stimuli and procedure*

In a 4 alternative forced choice (AFC) procedure, an original photograph (target) was presented at the center of the screen along with four synthetic faces (comparisons) (Fig. 6A). Participants selected which of the four synthetic faces matched the target by clicking on the match with the mouse. There were four viewpoint conditions: the target and comparison faces both in front view (Front–Front), both at 20° side view (Side–Side), 20° side view of target and front view of comparisons and vice versa (Cross views). Performance was measured as percent correct responses. There was no time limit.

As age- and education-appropriate controls for FA, four participants (all males, age range 64–70, mean 67.3, SD 2.5 years) were tested. They had healthy eyes (examined by an optometrist) with normal or corrected-to-normal visual acuity. They had no neurological disorder or medication that could affect their vision or brain function. Younger adult controls' data ($n = 5$) are from Wilson et al. (2002).

5.1.2. *Results and discussion*

In all viewpoint conditions, D2 and FA performed as well as their control groups (see Fig. 6B). D1, however, exhibited an impairment in the front view condition [$t(4) = -3.48$, $p < .013$]. Her score was not significantly impaired in the cross view condition compared to that of the young controls, but similar to that of the older controls.

In summary, D1 was impaired at front view matching that allowed for a feature-to-feature matching strategy although she performed slightly better with the conditions involving side view faces. D1's results suggest that she has a difficulty perceiving geometric information of faces. D2 and FA may be able to transfer a face representation to a novel view across a small viewpoint change, given a target photograph along with comparison synthetic versions and enough time to study faces.

5.2. *Face discrimination*

The simultaneous matching task allowed a direct visual comparison of local features, which prosopagnosic people would often utilize to compensate for their deficit. The next experiment assessed discrimination of unfamiliar faces on

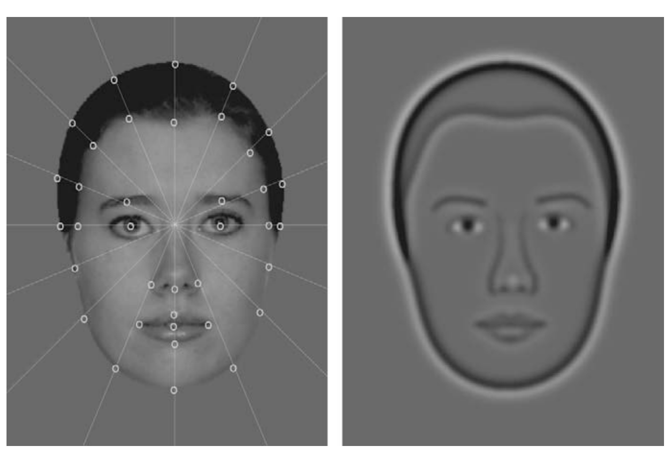

Fig. 5 – An original digital photograph and its synthetic face. Synthetic faces are schematic representations of faces based on digital photographs of individual faces (40 male and 40 female faces in both frontal and 20° side views). They contain 37 measurements of geometric information in the face (head shape, hair line, feature location, feature length and width), while eliminating the fine detailed texture and colour of hair and skin. Face contours were digitized in polar coordinates with respect to the bridge of the nose, and locations of eyes, nose and mouth were also digitized.

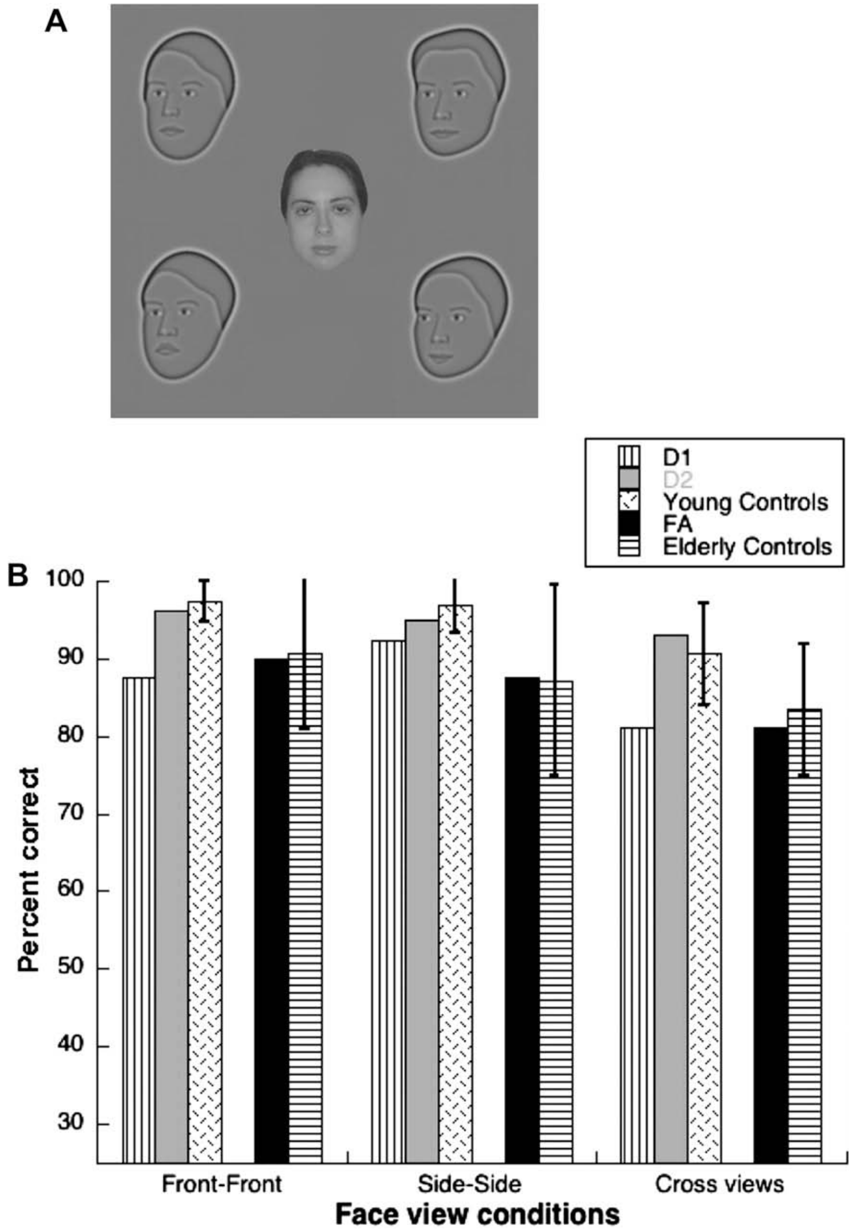

Fig. 6 – 4AFC simultaneous matching. (A) Task. A target photograph and synthetic faces as comparisons were presented simultaneously during each trial. Face views between the target and comparisons were manipulated (same view or 20° view change). The example shows matching of a front view photograph to side view synthetic faces. An experimental run consisted of a total of 80 trials, including 16 different individual female faces, each of which was shown five times as a target in random order. The distractors were selected from the remaining 15 faces not used as the target in an individual trial. (B) Results of three viewpoint conditions. The cross view condition shows an average of Front–Side and Side–Front conditions. The percent correct scores were plotted from the chance level (25%). In all viewpoint conditions, D2 and FA performed as well as their control groups, whereas D1 performed poorly in the front view condition. Error bars: ±1 SD of each control group.

a 2AFC match-to-sample task where synthetic faces were displayed in sequence with a brief target presentation duration.

5.2.1. *Stimuli and procedure*

The present experiment used 0° frontal or 20° side views, and all faces were chosen from 4D face cubes described in Appendix C (see Fig. 7A for examples). The construction of different views of synthetic face stimuli followed the same methods described previously (see Lee et al., 2006 for details). The experiments used the method of constant stimuli. In each trial, a target face was displayed for 130 msec, followed by a wide field noise mask for 200 msec. Immediately after the mask, two comparison faces were displayed side by side and

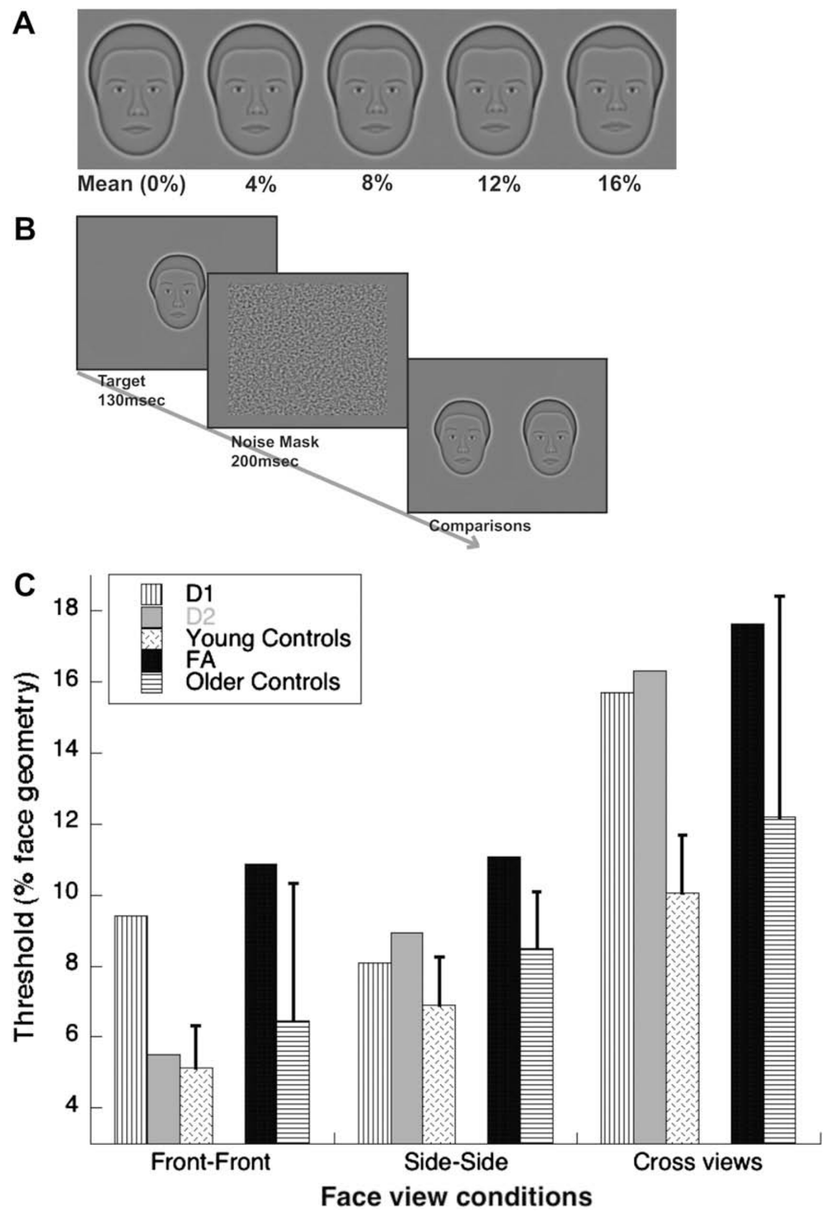

Fig. 7 – 2AFC face discrimination. (A) A male mean face (0%) and synthetic face cubes (4, 8, 12, 16% distanced from the mean face). These face cubes share the same identity but differ in distinctiveness. (B) Procedure in each trial. The example illustrates the Front–Front condition where both the target and comparisons are frontal faces. (C) Results. The discrimination threshold shows the extent of geometric variation between faces that the participants required to perform at the 75% correct level. A smaller threshold value means better performance with fine discrimination of smaller geometric variations between two faces. D1's and D2's threshold increased remarkably in the cross view condition. FA's threshold is comparable to his age-appropriate controls in all view conditions. Error bars: +1 SD of the control group mean.

remained on the screen until the participant clicked on the face that appeared to be identical to the flashed target (Fig. 7B). The target and comparison faces had the same view (Front–Front, Side–Side) or different views (Front–Side, Side–Front). The 130 msec target duration is sufficient for face discrimination (Lehky, 2000; Loffler et al., 2005a, 2005b) but brief enough to prevent eye movements. The position of the target face was randomly jittered by .72° from the center of the screen to prevent continuous fixation on any one feature of the face. The noise was a random dot pattern band-pass filtered with the same Difference of Gaussian (DOG) filter and characteristics as the synthetic faces.

Each run used only one view condition with one face gender and consisted of 120 trials. Testing was repeated alternating the face gender. The threshold for each condition was averaged across at least four runs. The testing order of view conditions was counterbalanced within and across participants. A novel set of synthetic face cubes was created for each run to lessen learning effects. Control data were taken from previous studies.[2] Older controls ($n = 4$) were all healthy males with normal or corrected-to-normal vision and aged 64–70 years (mean 66.75, SD 2.75). Three of them were the same participants from Section 5.1.

5.2.2. Results and discussion

Fig. 7C summarizes the results. With front view faces, D2 and FA did not show a deficit. However, D1 had a higher threshold than young controls [$t(4) = 3.28$, $p < .015$]. In the side view condition, all DP individuals performed similarly to controls.

With view change, both D1 and D2 were impaired: D1 [$t(4) = 3.16$, $p < .017$], D2 [$t(4) = 3.49$, $p < .013$].[3] FA's performance at the cross view condition was not different from that of the older controls. In Habak et al. (2008), the average threshold of older adults ($n = 21$) was approximately 14% when a target duration was 200 msec at this condition. Thus, FA's deficit due to prosopagnosia was within the range of the normal age-related decline in facial identity discrimination. It is unclear how much his performance was affected by age.

Additionally, FA was tested with a longer target exposure duration (1000 msec) in a follow-up experiment. His performance was significantly improved in the same view conditions (to the level of young controls) but not in the cross view condition. In Habak et al. (2008), older participants' performance on cross view discrimination improved with additional presentation time (500 or 1000 msec) compared to the performance with a duration of 200 msec although it did not reach the level of younger participants.

In summary, D1's and D2's performance declined remarkably with changing face viewpoint. D1 performed within the normal range in the side view condition but was poor in the cross view conditions. D2 was good at discrimination of faces presented in the same view and simultaneous matching across viewpoints, but she exhibited a dramatic increase in threshold at discriminating across viewpoints. These data suggest that they have difficulty in transforming a face representation in working memory to a novel view. In addition, D1 has a deficit with the front views, implying that her problems may have resulted from a poor representation of facial geometry.

[2] Previous studies used the same stimuli and procedures except for a shorter target exposure duration (110 msec). The data for five younger adults were taken from Lee et al. (2006). The data for four older control participants were collected by Habak et al. (2008) but were not published in Habak et al.

[3] The DP individuals' difficulty with view change was also observed during testing. Their performance was often close to chance even for the easiest trials. This resulted in a flat psychometric function, which did not allow estimation of thresholds. Hence, the DP individuals had to repeat the experiment more than controls. In those runs that could not yield a threshold (D1: 7 runs out of 9; FA: 7 out of 11), the 16% geometric variation, which was the maximum increment in our experiments, was designated as the nominal threshold. Hence, the thresholds for the cross view conditions of these DP individuals were underestimated in Fig. 7C.

5.3. Face learning and recognition

The 2AFC face discrimination task assessed perceptual face processing involving working memory. The current experiment evaluated long-term memory for faces by incorporating a recognition task in which participants memorized the identity of synthetic faces (Wilson and Diaconescu, 2006).

5.3.1. Stimuli and procedure

Memory faces were presented at 0° frontal or 20° side view. In one testing session, which involved learning two memory faces, 24 distractor faces were created (i.e., 12 distractors for each memory face). Construction of the two memory and 24 distractor faces was previously described in Wilson and Diaconescu (2006) (also see Appendix C). One testing session used only one view condition and one face gender. The memory faces were novel for each testing session.

In one testing session, the participants learned two distinct memory faces (learning phase), and after a 15-min break, they were required to recognize the previously learned face that was shown in the same or different view (recognition phase) (see Fig. 8A). The 2AFC recognition task consisted of 120 trials for DP individuals (5 repetitions of each distractor) and 72 trials for controls (3 repetitions of each distractor). Thresholds for the two memory faces were averaged in each testing session. To lessen the effects of using particular memory faces, DP individuals were tested with both genders (two sessions) in each view condition and data were collapsed across gender. Control participants received only one session with either gender in each condition and the gender of faces was alternated across view conditions.

Control participants were matched in age and education. The same four older men from Section 5.1 (age range 64–70) participated. All the older participants had a graduate degree. Five women (age range 30–40 with a graduate degree) participated as controls for D1 and D2. They had normal or corrected-to-normal visual acuity and no neurological or psychiatric disorder.

5.3.2. Results and discussion

Fig. 8B shows the results. In the front view condition, D1 and D2 performed worse than the control group: D1 [$t(4) = 4.88$, $p < .004$], D2 [$t(4) = 2.21$, $p < .046$]. FA's threshold (12.87%) was statistically non-significant [$t(3) = 1.94$, $p < .074$] probably due to a small number of controls but had a z-score of −2.17 suggesting a deficit (older controls, 5.90%, SD 3.21%).

With the side view condition, D1 had a higher threshold (11.55%, z-score −2.34) than her controls (mean 6.75%, SD 2.05%): [$t(4) = 2.14$, $p < .05$]. However, D2 and FA performed similarly to their controls. The DP individuals seemed to use different strategies in recognizing faces than controls (e.g., Schwarzer et al., 2007). D2 reported that she heavily relied on the face outline and sometimes used a prominent feature (e.g., a wide mouth or square jaw). In the side view condition, she mentioned that the irregular outline (''squiggle'') of the side view was especially important. This is reflected in her improved performance with side views compared to the front view condition. In contrast, the younger group had an increased threshold with side views compared to the front

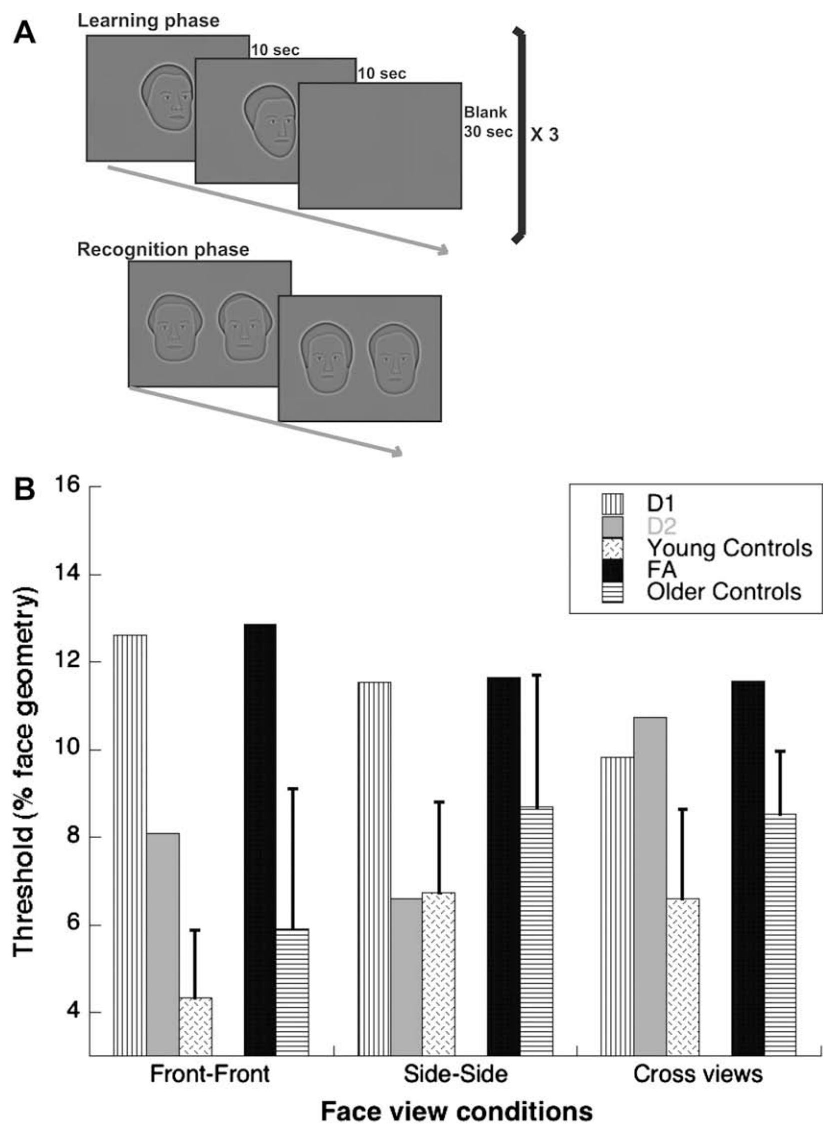

Fig. 8 – Face learning and recognition. (A) Experimental procedure. A learning phase consisted of a blank screen for 30 sec, followed by two memory faces displayed sequentially in random order for 10 sec each. This presentation of a blank screen and two memory faces was consecutively repeated two more times. Thus, each memory face was displayed three times for a total of 30 sec, and the entire learning phase including the blank screen periods lasted a total of 2.5 min. During a recognition phase, a test face was shown beside a randomly selected distractor on the screen, and given unlimited time, the participant had to click on the face that they previously learned. In the example, memory faces have frontal views and test views have 20° side views. (B) Face recognition threshold in terms of the percent geometric distance between the memory face and distractors that was discriminated at 75% correct performance. All DP individuals were worse than controls in most conditions. FA's face recognition deficit was distinguishable from the normal decline shown in the older controls. Error bars: +1 SD of the control mean.

view condition, showing the advantage with symmetric frontal faces: [$t(4) = -2.88$, $p < .04$] in a paired t-test (2-tailed).

When there was a view change between learning and recognition, D2 and FA performed poorly (D2 10.75%, z-score −2.04; young controls: mean 6.60%, SD 2.03%; FA 11.57%, z-score −2.12; older controls: mean 8.54%, SD 1.43%) although their threshold was not statistically different from that of the matched controls in the single case t-test (Crawford and Howell, 1998). In this condition, D2's strategy of relying on distinct features or the head outline would be ineffective since these aspects of the faces would change across viewpoints.

In summary, DP individuals showed deficits in recognition of learned synthetic faces. FA's face recognition deficit was worse than the normal decline observed in the aging controls, particularly in the front view and cross view conditions. However, the DP individuals seem to have some face recognition ability by relying on facial features: they were still able to learn faces and recognize them across viewpoints up to 20°.

6. General discussion

Only a few studies have reported multiple DP cases in the same family (Duchaine et al., 2007a; Grueter et al., 2007; Schmalzl et al., 2008) and little is known about the locus of the deficits in familial cases since previous studies have focused on describing the cases and the pattern of inheritance. The goals of the present study were to determine the nature of recognition problems in familial DP cases and to estimate psychophysically the cortical processing level of their deficits in face processing. The three family members (D1, D2, FA) across two generations reported life-long problems in face recognition and memory. These individuals were assessed with both neuropsychological and psychophysical tests. The neuropsychological tests indicated that the DPs have problems with facial identity perception and facial identity memory. Psychophysical tests assessing intermediate-level form processing and well-controlled face tasks then allowed us to better identify their deficits with facial identity.

6.1. *Neuropsychological results*

In neuropsychological tests, the three members showed deficits in famous face recognition and unfamiliar face memory. Additionally, D1's recognition deficits extended to object categories. D2 and FA, however, performed well on the object recognition test. All three DP individuals demonstrated normal face detection and expression recognition. We will further discuss these results in subsequent sections together with their psychophysical data.

6.2. *Intermediate-level form vision*

All three DP individuals exhibited normal performance in all tests examining intermediate-level visual processing. Our results are consistent with DP cases assessed using Glass patterns or Navon letters (Duchaine et al., 2007a, 2007b; Le Grand et al., 2006). The current experiments employed RF patterns, which would provide critical information on intermediate-level form vision preceding face perception. Evidence from fMRI studies has indicated that the RF stimuli probe the neural representation of curvature and closed shapes in area V4 and the FFA (Betts and Wilson, 2007; Wilkinson et al., 2000), and a patient with unilateral damage in ventral V4 showed a profound deficit in discrimination of RF patterns (Gallant et al., 2000). The current results indicate that the DP individuals' difficulties with faces are higher in the cortical form vision hierarchy than the locus of contour shape processing as assessed with RF patterns (Duchaine et al., 2006; but see Laeng and Caviness, 2001). The results therefore indicate that face processing impairments in these familial cases arise from deficits limited to high-level recognition mechanisms.

6.3. *Locus of face processing deficits*

Having shown that the face recognition problems in the three DPs lie in face processing mechanisms, we used synthetic face experiments to assess processing of face geometry and manipulated viewpoints to more specifically identify their deficits with faces. D1 performed poorly even on front view matching tasks. Similarly, she showed a severe impairment even in the introduction stage of the CFMT, in which she was presented with test images identical to the study views immediately after learning. It appears that she has difficulty in building a fine-grained representation from geometric information in synthetic faces, in which hair and skin texture, surface reflectance, and idiosyncratic facial features are eliminated. It suggests that her relatively better performance on the CFPT and the famous face recognition task may be attributable to the use of local facial cues contained in photographic images. Thus, D1 has difficulty in forming a robust view-dependent representation (Fig. 1). This would further hinder view transformations, which would require more geometric facial information than discrimination of same view faces (Habak et al., 2008).

The other daughter, D2, performed at an equivalent level to the controls in all viewpoint conditions of simultaneous face matching and the same view conditions of sequential face discrimination. Despite intact perception of faces at the level of view-dependent representation (Fig. 1), she was impaired in sequential discrimination of synthetic faces differing by only 20° in view, showing difficulty in transforming a face representation in working memory to novel viewpoints. Moreover, D2 was poor at recognition of learned faces presented in frontal views or across views in synthetic face recognition and a face part of old–new object recognition tests. Consistently, she was impaired in the CFPT and CFMT where viewpoint differed from presentation and testing. D2's poor memory for frontal faces, which could bypass a view-invariant representation stage (see Fig. 1 legend), suggests that her deficits with faces might be due to a problem in transferring view-dependent representation to view-invariant representation and to long-term memory. This is in accordance with recent findings showing that neural connectivity from the FFA to more anterior cortical regions is disrupted in several cases of DP (Thomas et al., 2009). It indicates that connectivity among functional systems is a vital component of face analysis.

FA showed performance equivalent to that of the age-appropriate controls on synthetic face matching and the CFPT, in which target and test faces were presented simultaneously. However, prosopagnosia in FA was evident in his poor performance on face tasks requiring memory. In within-class object recognition, his performance was superior to that of young controls with all object categories but not with faces. He was impaired in recognition of synthetic faces and the CFMT. In contrast, older controls' performance in synthetic face recognition was only slightly worse than that of younger participants, and the average score on the CFMT was within 1.4 SD of the young controls. It is difficult to determine whether FA has a deficit in perceptual stages or only in face recognition memory because of his age. However, the results suggest that assessment of face recognition memory can be used for differential diagnosis of DP in older adults from normal aging.

It is worth noting that some of the individuals' subjective reports about their deficits were not supported by the behavioural tests. D2 performed well on the object recognition tasks although she reported challenges in distinguishing between cars and between houses. FA's score in emotion recognition was within the normal range despite his complaints of occasional problems in recognizing emotions. Our tests might have not captured the deficits as experienced by DPs, but these discrepancies raise concerns for studies that solely relied on participants' self-reports (e.g., Kennerknecht et al., 2006).

6.4. *Familial transmission*

As our DP participants are first-degree relatives, it is likely that genetic factors have caused their face processing deficits. This common basis makes comparison of their cognitive deficits an interesting issue. The pattern of their impairments suggests that various phenotypes of DP exist and they manifest in different forms of deficits. D1's prosopagnosia may be due to a difficulty in forming fine-grained face representations regardless of viewpoint, whereas D2's problem may arise from later face processing stages involving view-invariant representation and recognition memory. Similarly, an earlier study of other familial cases found that face processing impairments were heterogeneous among family members affected with DP (Schmalzl et al., 2008).

While the phenotypes of DP can be distinguished among DP individuals from the same family, different patterns of deficits are also observed between families affected with DP. Duchaine et al. (2007a) examined ten DP individuals from one family. The results of that study can be compared to those of the current study as these two studies employed many of the same neuropsychological tests. In both families, DP was transmitted across generations and all DPs are highly functioning individuals with intact low- and mid-level vision and normal cognitive abilities. The two families share a behavioural characteristic: all performed well on expression recognition tasks despite impairments in face perception and recognition. Nonetheless, there were two significant differences. First, two of the DPs in the current study did well on the object recognition tasks, whereas the other family showed consistent impairments with object recognition (Duchaine et al., 2007a). In addition, all three DPs of our study were normal at face detection, whereas some of the DPs in Duchaine et al. (2007a) showed deficits in face detection (tested in Garrido et al., 2008). Hence, the DP participants (D2, FA) of the current study appear to have more face-specific and higher-level impairments compared to the DPs in Duchaine et al.

Our results add support for a role of genetic factors that selectively affect high-level visual recognition (Duchaine et al., 2007a; Grueter et al., 2007; Schmalzl et al., 2008). Grueter et al. (2007) have observed from self-report data that the pattern of inheritance is consistent with a simple autosomal dominant mode of transmission. In the present three DP cases, the recurrence risk was high in this family as two out of the three daughters were affected by DP. Systematic investigation is needed to elucidate the heritability of this syndrome (e.g., data from molecular genetics) and the developmental trajectory of this condition.

6.5. *Summary and conclusion*

The three DP individuals showed no evidence of general visual deficits or social dysfunctions. However, they exhibited a selective deficit in high-level visual recognition, which spared face detection and expression recognition. D1's deficits appear to encompass both face and object categories. In particular, D1 showed difficulty in perceiving geometric information of the face at a given view. D2's (and probably FA's) problems with faces seem to originate in face processing mechanisms which affect their ability to transform view-dependent representation to a 3D view-invariant representation, and/or its transfer to long-term memory. The present study has demonstrated familial transmission of face recognition deficits with normal intermediate form vision.

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Appendix A. Psychophysical experiments: apparatus, calibration, data analysis

Stimuli for all psychophysical experiments were generated in Matlab and displayed using routines from the Psychophysics and Video Toolbox (Brainard, 1997; Pelli, 1997). All experiments with RF patterns and synthetic faces were conducted on a Macintosh G3 computer in a dimly lit room. The monitor had a resolution of 1028×764 pixels, a refresh rate of 75 Hz and 8 bit/pixel grey scale. The viewing distance was 1.31 m and each pixel subtended 47.0 arc sec. Mean luminance was 38 cd/m^2. The data were fit with a Quick (1974) or Weibull (1951) function using maximum likelihood estimation, and the 75% correct point from the psychometric function was chosen as threshold. Each DP's performance was compared to that of controls with the modified *t*-test by Crawford and Howell (1998).

Appendix B. RF patterns

RF patterns are circular contours defined by sinusoidal modulation of a circle's mean radius in polar coordinates (see Wilkinson et al., 1998, for details). As the radial amplitude increases, deformations from circularity increase. The cross-sectional luminance profile of the contour was defined by the radial fourth derivative of a Gaussian, in which peak spatial frequency was 8.0 cpd and full spatial frequency bandwidth at half amplitude was 1.24 octaves. All experiments testing RF shape discrimination used the method of constant stimuli and a temporal 2AFC procedure. Each participant's data were averaged across three runs (105 trials each).

Appendix C. Synthetic face methods

Synthetic faces

Synthetic faces are constructed by digitizing 37 measurements of geometric information in the face (see Fig. 5). The head shape was converted into sums of seven RF components, and the hair line was fitted with a sum of four RFs. For individual features, generic eye, nose, and mouth templates were used. Images were band-pass filtered with a DOG filter centered at 10.0 cycles per face width (2.0 octave bandwidths at half amplitude), which was equivalent to 8.0 cpd at the viewing distance used. This spatial frequency band provides spatial frequency information crucial for face perception (Gold et al., 1999; Näsänen, 1999). Mean faces for frontal and 20° side view of each gender are based on average values of the 37 parameters from 40 individual faces.

Synthetic face cubes

Discrimination of synthetic faces was assessed in a 4D perceptual space consisting of a set of examplar faces (hypercubes). In this face space, a mean face serves as the origin of a local coordinate system, and four other faces randomly chosen from the database define the four axes. These face cubes are normalized to the same total geometric variation after subtracting a mean face and are made mutually orthogonal by removing cross-correlations between axes. Along each axis (a total of 5 axes including a diagonal) three more faces are created with the same incremental step between the mean face and the face having a maximum variation located at the end of the axis (see Fig. 7A): for example, if the maximum geometric variation is 16%, the four faces along each axis differed by 4, 8, 12, 16% from the mean.

For the learning and recognition tasks used in Section 5.3, memory faces had a distance of 16% from a mean face. Distractor faces were created from a 3D face cube centered at the memory face. They were generated at increments of 4%, 8%, 12%, and 16% from the memory face along each of the three orthogonal axes.

Methodological advantages and limitations

Despite the reduction of facial information, neurologically intact individuals performed extremely well on matching synthetic faces to original photographic faces (Wilson et al., 2002). Recent evidence has suggested that the mathematically orthogonal synthetic faces are perceptually orthogonal as well (Yotsumoto et al., 2007). There are several advantages of using synthetic faces. Synthetic faces are amenable to mathematical transformations (e.g., principal components analysis). The simplicity of synthetic faces may assist linking specific manipulation of facial geometry with its underlying neural mechanism. The use of generic features allows us to focus on geometric aspects of face processing. For these reasons, synthetic faces can complement existing neuropsychological tests in studying prosopagnosia. For example, they can be used to control face properties that have been attributed to configural face processing: the location and relationship of internal generic facial features can be precisely manipulated. Most innovatively, the magnitude of deficit in processing facial geometry information can be quantified. However, the synthetic face methods also impose some limitations. Since face information is represented in only 37 measurements of face geometry, performance should be interpreted within this limited context. Moreover, the use of generic facial features does not permit us to study salient facial features that prosopagnosic people might use.

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