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Research report

Intranasal inhalation of oxytocin improves face processing in developmental prosopagnosia

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ABSTRACT

Developmental prosopagnosia (DP) is characterised by a severe lifelong impairment in face recognition. In recent years it has become clear that DP affects a substantial number of people, yet little work has attempted to improve face processing in these individuals. Intriguingly, recent evidence suggests that intranasal inhalation of the hormone oxytocin can improve face processing in unimpaired participants, and we investigated whether similar findings might be noted in DP. Ten adults with DP and 10 matched controls were tested using a randomized placebo-controlled double-blind within-subject experimental design (AB-BA). Each participant took part in two testing sessions separated by a 14–25 day interval. In each session, participants inhaled 24 IU of oxytocin or placebo spray, followed by a 45 min resting period to allow central oxytocin levels to plateau. Participants then completed two face processing tests: one assessing memory for a set of newly encoded faces, and one measuring the ability to match simultaneously presented faces according to identity. Participants completed the Multidimensional Mood Questionnaire (MMQ) at three points in each testing session to assess the possible mood-altering effects of oxytocin and to control for attention and wakefulness. Statistical comparisons revealed an improvement for DP but not control participants on both tests in the oxytocin condition, and analysis of scores on the MMQ indicated that the effect cannot be attributed to changes in mood, attention or wakefulness. This investigation provides the first evidence that oxytocin can improve face processing in DP, and the potential neural underpinnings of the findings are discussed alongside their implications for the treatment of face processing disorders.

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1. Introduction

Face recognition is an important cognitive skill that most people take for granted, yet it depends on a complex set of cognitive and neural processes (Bruce & Young, 1986; Haxby, Hoffman, & Gobbini, 2000). In some individuals this process can be selectively disrupted, resulting in a condition termed "prosopagnosia" or "face-blindness". While prosopagnosia

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can be acquired following brain injury (e.g., Damasio, Damasio, & Van Hoesen, 1982), many more individuals simply fail to develop normal face recognition abilities (e.g., Bate, Haslam, Jansari, & Hodgson, 2009; Bate, Haslam, Tree, & Hodgson, 2008; Behrmann & Avidan, 2005; Bentin, Deouell, & Soroker, 1999; Duchaine, Germine, & Nakayama, 2007; Duchaine & Nakayama, 2006; Jones & Tranel, 2001; Schmalzl, Palermo, Green, Brunsdon, & Coltheart, 2008). The latter form of the disorder has been termed 'developmental prosopagnosia' (DP; but for a discussion of terminology see Susilo & Duchaine, 2013), and has been attributed to a failure to develop the visual recognition mechanisms necessary for successful face recognition, despite intact low-level visual and intellectual functions. Interestingly, there also appears to be a genetic component to the disorder in at least some individuals (Duchaine et al., 2007; Grueter et al., 2007). In the last decade it has become increasingly clear that DP represents a significant clinical disorder, with recent reports suggesting that two percent of the population have the condition (Bowles et al., 2009; Kennerknecht et al., 2006).

Although many studies have investigated the cognitive, neural and genetic basis of DP, little attention has been directed towards improving face recognition in these individuals. While some researchers have attempted to remedy face processing deficits using extensive visual training programmes (e.g., DeGutis, Bentin, Robertson, & D'Esposito, 2007; Schmalzl et al., 2008), recent evidence suggests that an alternative methodology warrants investigation. Specifically, in some circumstances, intranasal inhalation of the hormone oxytocin has been found to improve face processing in both healthy participants (e.g., Rimmele, Hediger, Heinrichs, & Klaver, 2009; Savaskan, Ehrhardt, Schulz, Walter, & Schachinger, 2008) and individuals with autism (Andari et al., 2010).

Oxytocin is a nonapeptide centrally involved in the regulation of basic social and reproductive behaviours, such as cohabitation, gestation, and breastfeeding. It has been found to be crucial for social recognition, grooming, approach behaviour, sexual activity and stress regulation in non-human mammals (e.g., Carter, 1998; Ferguson, Aldag, Insel, & Young, 2001; Lim & Young, 2006). Recent evidence demonstrates that oxytocin also facilitates social cognition and pro-social behaviour in humans (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008; Heinrichs, von Dawans, & Domes, 2009; Mikolajczak et al., 2010; Zak, Stanton, & Ahmadi, 2007). Indeed, studies using healthy participants have shown that intranasal inhalation of oxytocin can strengthen memory for social but not non-social stimuli (Guastella, Mitchell, & Dadds, 2008), including faces (Rimmele et al., 2009; Savaskan et al., 2008). However, the precise influence of oxytocin on face memory remains unclear, as the hormone seems to only improve the recognition of faces displaying particular emotional expressions, and existing studies have reported conflicting findings. For instance, while Rimmele et al. (2009) found oxytocin improved memory for faces displaying both positive and negative expressions, Guastella et al. (2008) observed improved memory for happy but not angry or neutral faces, and Savaskan et al. (2008) reported improved recognition of neutral and angry but not happy faces.

While the precise influence of oxytocin on face memory remains to be unravelled, it is pertinent that the hormone has also been found to influence processing strategy. Indeed, oxytocin has been reported to increase the time spent looking at the eye region of the face (Guastella et al., 2008), an area thought to provide critical information for identification (Ellis, Shepherd, & Davies, 1979; Young, McWeeny, Hay, & Ellis, 1986). It is of note that this shift in processing strategy has also been reported in individuals with autistic spectrum disorder (Andari et al., 2010), who commonly experience face recognition deficits (Schultz, 2005).

The findings discussed above suggest that intranasal inhalation of oxytocin may also facilitate face recognition in DP. The current investigation set out to address this issue, investigating whether oxytocin can improve performance in 10 DPs and 10 matched control participants on a task that assesses the encoding and recognition of new faces. In addition, we also assessed performance on a face matching task that assesses the ability to *perceive* facial identity (thereby placing minimal demands on long-term memory for faces). This issue is particularly relevant to the current study given that some prosopagnosics also have face perception deficits, and sequential models of face processing predict that such impairments inevitably bring about recognition deficits (e.g., Bruce & Young, 1986). This latter task also represents a novel contribution to the literature, given that no studies have examined the influence of oxytocin on face perception skills.

2. Methods

2.1. Design

The study used a randomized, placebo-controlled, double-blind within-subject experimental design (AB-BA) to examine the effects of a one-time 24 IU intranasal dose of oxytocin on face processing performance in 10 individuals with DP and 10 matched control participants. Two face processing tests were used to assess changes in performance: one that measured memory for newly encoded faces, and one that measured the perceptual ability to match faces of the same identity.

2.2. Participants

A group of 10 adults with DP took part in this study [seven male, mean age = 49.2 years, standard deviation (SD) = 14.2]. All participants had contacted our laboratory because they experience severe difficulties with face recognition in everyday life. Prior to the investigation, each participant attended an initial diagnostic testing session where they were interviewed about their neuropsychological history and participated in a set of tests to confirm their prosopagnosia (see Table 1). Indeed, previous work has indicated that both a clinical interview (Grueter, Grueter, & Carbon, 2008) and objective testing (Duchaine, 2008) are necessary for this process. All participants shared personal anecdotes of instances where they failed to recognize close friends and relatives, and reported apparently lifelong and severe difficulties with face recognition. No participant had experienced neurological illness or trauma, and their difficulties were therefore regarded as developmental in origin.

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Table 1 – Demographics of DPs and performance in SD units on tests of face processing, lower-level vision and object recognition. DP scores are compared to published norms for each test.

	Control Mean (SD)	DP1	DP2	DP3	DP4	DP5	DP6	DP7	DP8	DP9	DP10
Age		63	63	64	65	51	47	34	30	44	31
Gender		M	M	M	F	F	M	F	M	M	M
Hand		L	R	R	R	R	L	R	R	R	R
IQ		119	119	119	125	119	113	122	119	119	117
Face processing tests											
CFMT	59.6 (7.6)	−3.76[a]	−4.16[a]	−2.71[a]	−2.32[a]	−3.50[a]	−2.71[a]	−2.97[a]	−2.32[a]	−3.37[a]	−3.11[a]
CFPT	36.7 (12.2)	−2.89[a]	−1.25	−1.25	−1.75	−.76	−.76	−1.91	−2.89[a]	−1.91	−1.25
Famous faces	47.3 (6.2)	−4.76[a]	−3.92[a]	−3.11[a]	−2.15[a]	−2.95[a]	−4.24[a]	−4.73[a]	−3.60[a]	−3.92[a]	−3.92[a]
Mind in eyes	26.2 (3.6)	1.61	−1.44	.22	1.61	1.06	−1.17	1.33	1.33	−1.44	−.06
Lower-level vision											
Length Match	26.9 (1.6)	.69	.06	.69	−1.19	−1.19	.06	−4.94[a]	−1.81	1.31	−3.06[a]
Size Match	27.3 (2.4)	.29	.71	.29	.29	−1.38	−1.79	−.13	−1.38	.71	−.96
Orientation Match	24.8 (2.6)	1.23	.46	1.23	.08	.46	1.23	−.31	.85	1.62	−.69
Position of gap	35.1 (4.0)	.48	−.53	.48	.23	1.23	.48	−.98	.23	.73	−.53
Object Decision test	114.7 (5.7)	1.11	.29	.93	.40	.75	.93	1.28	.93	1.28	−2.05[a]

a Indicates impaired performance.

The neuropsychological testing battery has been used by other researchers to diagnose DP (e.g., Bate et al., 2008; Duchaine et al., 2007; Garrido et al., 2009), and appropriate norms for each test were taken from accompanying research publications or manuals. Face processing skills were assessed using the Cambridge Face Memory Test (CFMT: Duchaine & Nakayama, 2006), a famous faces test (Duchaine et al., 2007), and the Cambridge Face Perception Test (CFPT: Duchaine et al., 2007). While these are well-known tests that have been described extensively elsewhere, it should be noted that some DPs can achieve 'normal' scores on the CFMT by adopting effective compensatory strategies. Nevertheless, we only used participants who scored within the impaired range on both this test and the famous faces test, given any compensatory strategies may obscure the effects of oxytocin on face recognition performance. It should also be noted that poor performance on the CFPT is not necessary for a diagnosis of prosopagnosia. Indeed, only some DPs demonstrate impairments in face perception (in our sample only DP1 and DP8 were impaired on this test), and the condition is therefore regarded as heterogeneous and may be composed of several sub-types (Susilo & Duchaine, 2013). Similarly, while some DPs have difficulties in recognizing facial expression, many others do not struggle with this task (Bate et al., 2009). Expression recognition skills were assessed in the DPs reported here using the Reading the Mind in the Eyes test, and when compared with appropriate published norming data (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), no deficits were observed.

Lower-level vision was also assessed in order to check whether the participants' difficulties in face recognition were underpinned by basic perceptual impairments. Four sub-tests from the Birmingham Object Recognition Battery (BORB: Humphreys & Riddoch, 1993) that have been used in previous investigations (e.g., Bate, Cook, Mole, & Cole, 2013; Garrido et al., 2009) were selected. In the Length Match test, participants are required to judge whether two lines are of the same length; in the Size Match test they judge whether two circles are of the same size; in the Orientation Match test they decide whether two lines are parallel or not; and in the Position of the Gap Match test they decide whether the position of the gap in two circles is in the same place or not. Basic object recognition was tested using the Object Decision test from the BORB. In this test, the participant is presented with a series of line drawings which depict animals or tools. In some trials the drawings represent 'unreal' objects (i.e., the picture shows half of one object combined with half of another object), and the participant is asked to decide whether each of 128 drawings represents a real or unreal object. Appropriate norming data for these tests are presented within the BORB, and while eight of the DP participants did not show any evidence of lower-level perceptual difficulties, DP7 was impaired on the Length Match test and DP10 was impaired on both the Length Match and Object Decision tests. As described above, this may reflect the heterogeneity of the condition and the possibility that different sub-types of DP exist. Because DP7 and DP10 only performed poorly on one or two of the five sub-tests, any lower-level visual impairments were not deemed to be severe and the participants were not removed from our sample.

Ten control participants also participated in this study. They were matched to the DP participants according to age ($M = 46.8$, $SD = 13.2$), gender (seven male) and estimated IQ [using the Wechsler Test of Adult Reading (WTAR): Wechsler, 2001]. All participants reported normal or corrected-to-normal vision. Exclusion criteria were pregnancy, medication, significant medical or psychiatric illness, history of substance abuse, and epilepsy. All participants provided written consent and participated on a voluntary basis. The study was approved by the departmental Ethics Committee at Bournemouth University.

2.3. Measures

Face memory task: Two new versions of the CFMT (Duchaine & Nakayama, 2006) were created for use in this experiment (see Fig. 1A). The CFMT is a measure commonly used to assess facial identity memory (Richler, Cheung, & Gauthier, 2011; Wilmer, Germine, Chabris, et al., 2010) and to diagnose face

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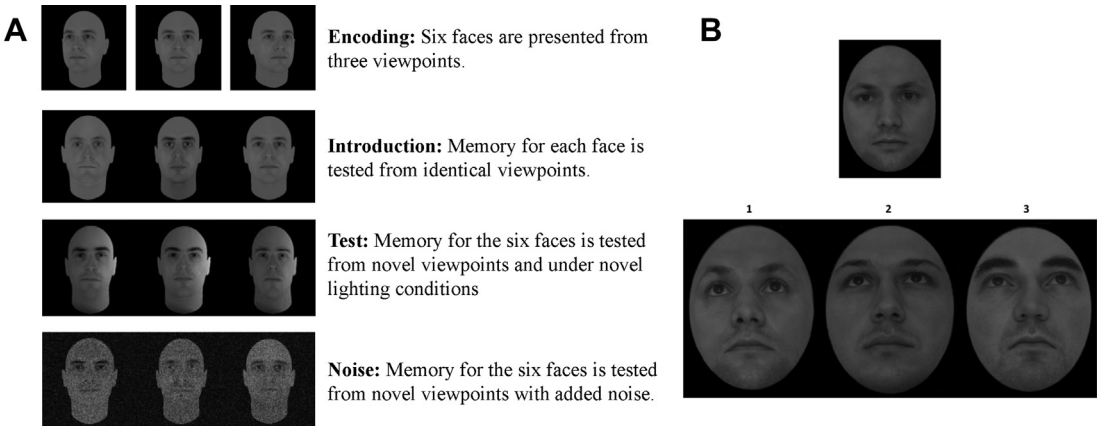

Fig. 1 – Example trials from (A) the new versions of the CFMT and (B) the face matching tests.

recognition impairments in adults (e.g., Avidan, Tanzer, & Behrmann, 2011; Bate et al., 2008, 2009; Bowles et al., 2009; Crookes & McKone, 2009; Furl, Garrido, Dolan, Driver, & Duchaine, 2011; Rivolta, Schmalzl, Coltheart, & Palermo, 2010). The CFMT has demonstrated high reliability (Bowles et al., 2009; Wilmer, Germine, Loken, et al., 2010) and both convergent and divergent validity (Bowles et al., 2009; Dennett et al., 2012; Wilmer, Germine, Chabris, et al., 2010; Wilmer, Germine, Loken, et al., 2010). Alternate versions of the CFMT have similar psychometric properties so the paradigm appears to be an effective means to assess face memory (McKone et al., 2011; Wilmer, Germine, Loken, et al., 2010). In the first part of the CFMT, participants are introduced to six target faces and are then tested with forced-choice items consisting of three faces, one of which is a target. For each target face, three test items contain views identical to those studied in the introduction, five present novel views, and four present novel views with noise. At two points in the test, participants are given the opportunity to review the target faces before proceeding with the next set of trials (for full details see Duchaine & Nakayama, 2006).

Given the effectiveness of the CFMT, we adopted its exact design in preparing our face recognition tests for the current study. However, it was necessary to create two new versions of the test given (a) the within-subjects nature of our investigation, and (b) that all the DP participants had already completed the original version in a previous testing session that confirmed their prosopagnosia (see Table 1). The faces used in the two new versions of the CFMT were generated using FaceGen, a software package that generates life-like faces while permitting the user absolute control over parameters such as head angle, expression, distinguishing characteristics (e.g., freckles, blemishes), and external features that might cue recognition (e.g., ear shape, hairline). An alternate version of the CFMT also used FaceGen faces, and performance on it was highly correlated with performance on the original CFMT (Wilmer, Germine, Loken, et al., 2010).

The two new versions of the CFMT were pilot tested prior to onset of the experiment to ensure they were of equal difficulty. Twenty unimpaired perceivers (10 male, mean age = 20.65 years, SD = 2.85) completed both versions in the same testing session (order of completion was counterbalanced). A 2 (version) × 2 (order) mixed design analysis of variance (ANOVA) confirmed there was no difference in the difficulty of the two versions of the test [version 1: $M = 57.50$, standard error (SE) = 1.94; version 2: $M = 57.05$, SE = 2.25], $F(1,18) = .115$, $p = .739$, $\eta_p^2 = .006$. Further, there was no difference in performance for the test completed first compared to that completed second, irrespective of version, $F(1,18) = .019$, $p = .892$, $\eta_p^2 = .001$. Finally, the order in which the two versions were completed did not interact with test version, $F(1,18) = 1.936$, $p = .181$, $\eta_p^2 = .097$.

Face perception task: To assess the influence of oxytocin on face perception, two versions of a face matching test were created (see Fig. 1B). This test was designed to measure participants' ability to match faces of the same identity, without placing any demands on long-term face memory. Each version of the test contained 40 trials in which a target face was positioned at the top of the screen, and a triad of test images was placed below. Participants were instructed to select the test image that matched the identity of the person displayed in the target image. Forty male and 40 female facial identities were selected from the Bosphorus Face Database (Savran, Sankur, & Bilge, 2012), and different facial identities were used in the two versions of the test (20 male and 20 female in each). All faces displayed neutral expressions and were cropped to exclude any external features that might aid performance. In each trial, the target image was displayed from a frontal perspective, and was reduced in size and darkened in colour from the test images, to prevent participants using low-level visual properties of the images to aid performance. Head direction of the test images was varied across the trials. Specifically, in each version, eight trials displayed faces from each of a frontal, 1/3 left profile, 1/3 right profile, a tilted-upwards and a tilted-downwards perspective. The same participants as described above completed a pilot test to ensure the two versions were of equal difficulty, and no difference in scores was noted (version 1: $M = 31.20$, SE = 1.03; version 2: $M = 30.95$, SE = .77), $F(1,18) = .080$, $p = .781$, $\eta_p^2 = .004$. Again, scores were not influenced by order of completion, $F(1,18) = .119$, $p = .734$, $\eta_p^2 = .007$ and $F(1,18) = .157$, $p = .697$, $\eta_p^2 = .009$.

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2.4. Procedure

Participants were asked to abstain from food and drink other than water for 2 h before the experiment; and from alcohol, smoking and caffeine for 24 h before the experiment. Each participant visited the laboratory on two occasions, separated by a 14–25 ($M = 16.55$, $SD = 5.07$) day interval, dependent on participant availability. The length of the interval between testing sessions did not vary for DP compared to control participants, $F(1,18) = .690$, $p = .417$ $\eta_p^2 = .037$. On each visit, participants received a single intranasal dose of 24 IU oxytocin (Syntocinon Spray, Novartis; three puffs per nostril, each with 4 IU oxytocin) or placebo spray. The placebo spray was prepared by an independent pharmaceutical company, and contained exactly the same ingredients as the experimental spray with the exception of the oxytocin. Preparation of the sprays by an independent company also ensured the experiment was double-blind, and the two sprays were identified by colour rather than their actual identity (i.e., oxytocin or placebo), which was only revealed after data analysis was complete. The order in which participants received the two sprays was randomized, and the 24 IU dose was selected according to previous experimental work that utilised this dosage (e.g., Guastella et al., 2008; Rimmele et al., 2009).

Following inhalation, participants sat quietly for 45 min, the length of time it is believed to take for central oxytocin levels to plateau (Born et al., 2002). Participants were instructed to bring a book or magazine to read during this time. Following the rest period, participants completed the two face processing tasks in the same order (commencing with the face memory task), in order to ensure equality of central oxytocin levels for each test. General affect was measured throughout the experiment using the Multidimensional Mood Questionnaire (MMQ: Steyer, Schwenkmezger, Notz, & Eid, 1997), to assess the possible mood-altering effects of oxytocin, and to control for non-specific effects of attention and wakefulness (the MMQ is composed of three sub-scales: good–bad, awake–tired and calm–nervous). Each participant was required to complete the MMQ at three intervals across the experiment: immediately following inhalation, after the 45 min resting period, and after the two face processing tests had been completed. Finally, the experimenter enquired about adverse side effects during the testing session and again 24 h after test completion.

2.5. Statistical analyses

Statistical analyses were conducted on the MMQ results collected across the testing sessions and on the behavioural data collected from the two face processing tasks. Scores on the MMQ were calculated according to the three sub-scales, and data were entered into a 2 (spray: oxytocin, placebo) × 3 (time of MMQ completion: after inhalation, after rest, end of session) × 2 (group: DP, control) mixed factorial MANOVA. Scores for the two face processing tests were entered into a 2 (spray: oxytocin, placebo) × 2 (group: DP, control) mixed factorial multivariate analysis of variance (MANOVA). The data file for one DP participant was unreadable in the placebo condition of the CFMT, and was therefore not included in the analysis of this test. Additional comparisons were carried out to investigate (a) whether DP performance in the oxytocin condition fell within the same range as control placebo performance, and (b) whether the severity of each individual's prosopagnosia correlated with the extent of their improvement on the two tasks. For the latter analyses, scores obtained on the original version of the CFMT and the CFPT (i.e., the tests run within the original diagnostic session: see Table 1) were correlated against the level of improvement in the oxytocin condition (oxytocin performance minus placebo performance) of the CFMT and matching test, respectively.

3. Results

3.1. Adverse side effects and MMQ

Adverse side effects were only reported by one DP participant following inhalation of either spray. Specifically, this individual reported a slight headache immediately after oxytocin inhalation, but this had disappeared by the 24-h follow-up. A mixed factorial MANOVA revealed no main effect of spray or group, $F(3,16) = .569$, $p = .643$, $\eta_p^2 = .096$ and $F(3,16) = 1.597$, $p = .229$, $\eta_p^2 = .230$, although the interaction between the two factors approached significance, $F(3,16) = 2.904$, $p = .067$, $\eta_p^2 = .353$. This latter effect was driven by the control (but not DP) participants feeling 'better' according to the good–bad scale in the oxytocin condition, while the DP but not the control participants felt calmer in the oxytocin condition. There was a main effect of time, $F(6,13) = 4.271$, $p = .014$, $\eta_p^2 = .663$, and further analyses revealed this was driven by an increase in wakefulness after the 45 min resting period, $F(2,36) = 4.626$, $p = .016$, $\eta_p^2 = .204$. However, this effect did not interact with participant group or spray, $F(2,36) = 1.914$, $p = .162$, $\eta_p^2 = .096$ and $F(2,36) = .225$, $p = .800$, $\eta_p^2 = .012$.

3.2. Face processing tests

A mixed factorial MANOVA revealed a significant improvement in the oxytocin compared to the placebo condition, $F(2,16) = 5.944$, $p = .012$, $\eta_p^2 = .426$. Univariate tests confirmed that performance was better in the oxytocin rather than the placebo condition on both the CFMT (oxytocin: $M = 56.89$, $SE = 1.79$; placebo: $M = 53.93$, $SE = 2.14$) and matching test (oxytocin: $M = 33.11$, $SE = .76$; placebo: $M = 31.10$, $SE = .96$), $F(1,17) = 4.975$, $p = .039$, $\eta_p^2 = .226$ and $F(1,17) = 5.786$, $p = .028$, $\eta_p^2 = .254$. While there was no main effect of group on the multivariate analysis, $F(2,16) = 2.307$, $p = .132$, $\eta_p^2 = .224$, group and spray did interact, $F(2,16) = 4.422$, $p = .030$, $\eta_p^2 = .356$. Univariate analyses confirmed that this interaction was driven by a greater improvement on the CFMT in DPs compared to controls, but the same effect was not significant for the matching test, $F(1,17) = 6.035$, $p = .025$, $\eta_p^2 = .262$ and $F(1,17) = 2.098$, $p = .166$, $\eta_p^2 = .110$ (see Fig. 2). Follow-up comparisons found that while the performance of DPs improved in the oxytocin condition for both the CFMT and matching test, $F(1,8) = 7.667$, $p = .024$, $\eta_p^2 = .489$ and $F(1,9) = 9.238$, $p = .014$, $\eta_p^2 = .507$, the same pattern was not observed in control participants, $F(1,9) = .040$, $p = .847$, $\eta_p^2 = .004$ and $F(1,9) = .482$, $p = .505$, $\eta_p^2 = .051$.

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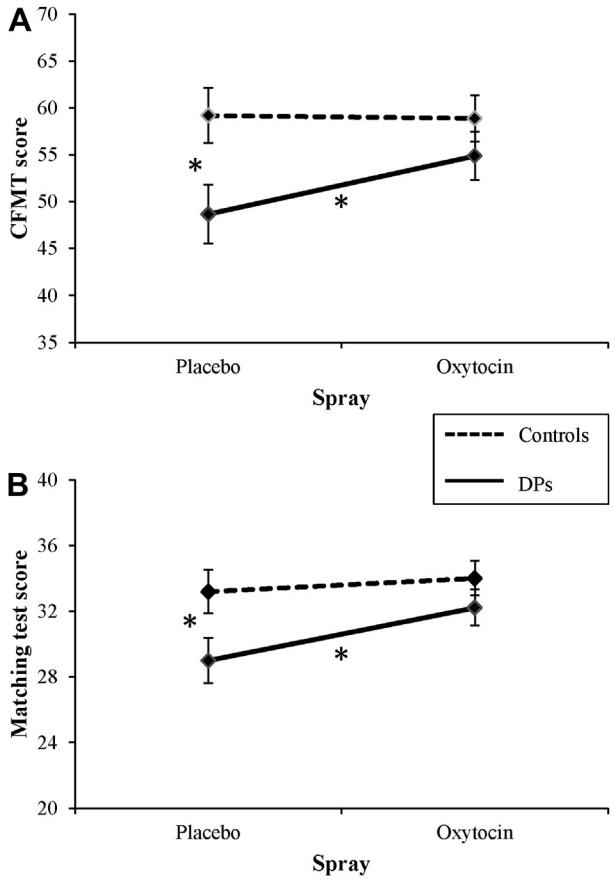

Fig. 2 – Performance of DP and control participants under placebo and oxytocin conditions in (A) the CFMT (maximum score of 72) and (B) the face matching test (maximum score of 40). Asterisks indicate significant between- and within-group differences.

Further analyses focused on the performance of the DP group. While, DP performance in the CFMT placebo condition was significantly lower than that of controls, $F(1,17) = 6.308$, $p = .025$, $\eta_p^2 = .262$, their performance in this condition was greater than their performance on the original diagnostic version of the CFMT (i.e., the version completed within the diagnostic session: see Table 1), $F(1,8) = 8.228$, $p = .021$, $\eta_p^2 = .507$. It is possible that this difference may be attributed to a placebo effect, but potential practice effects and the fundamental differences between the stimuli in the experimental CFMTs compared to the original version make this observation tentative. Strikingly, DP performance in the oxytocin condition did not differ from that of controls, $F(1,18) = 1.257$, $p = .277$, $\eta_p^2 = .065$, and a similar pattern was observed in the matching test. Indeed, while DP performance in the placebo condition remained lower than control placebo performance, $F(1,18) = 6.322$, $p = .022$, $\eta_p^2 = .260$, DP performance in the oxytocin condition did not differ from control oxytocin scores, $F(1,18) = 2.266$, $p = .150$, $\eta_p^2 = .112$.

A final set of analyses investigated whether the severity of each individual's prosopagnosia predicted the extent of their improvement in the oxytocin condition. Performance on the original version of the CFMT (from the diagnostic session) did not correlate with the extent of the improvement in the experimental CFMT, $r = .352$, $n = 9$, $p = .353$. Likewise, performance on the CFPT (a face perception test from the diagnostic session) did not correlate with the extent of improvement on the matching test, $r = .073$, $n = 10$, $p = .842$ (see Fig. 3).

4. Discussion

This investigation aimed to examine whether intranasal inhalation of the hormone oxytocin improves face processing in a group of individuals with DP. Participants were asked to complete two face processing tests after inhaling either oxytocin or placebo nasal spray: a face memory task that required participants to encode and recall a set of six faces, and a face matching task that required participants to match simultaneously presented faces according to their identity. An improvement was noted in both tasks in the oxytocin condition, but only for DP and not control participants. Analysis of responses on the MMQ indicates that these findings cannot be attributed to non-specific changes in attention, mood or wakefulness.

Importantly, there are two novel findings from the DP group. First, we have presented the first evidence that

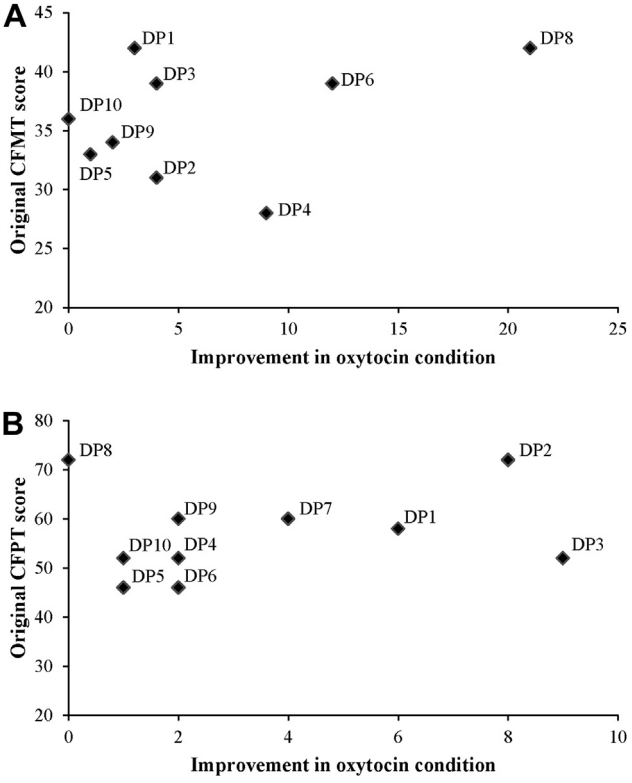

Fig. 3 – (A) Scores on the original version of the CFMT plotted against the level of improvement in the oxytocin condition on the new versions of the CFMT (i.e., the difference between the scores achieved in the oxytocin and placebo conditions), and (B) scores on the CFPT plotted against the level of improvement in the oxytocin condition on the face matching tests.

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oxytocin can temporarily improve face recognition in the condition, as has been observed in some investigations using typical perceivers (e.g., Rimmele et al., 2009; Savaskan et al., 2008; but see below for a discussion of this issue). Findings from recent neuroimaging investigations permit speculation of the potential neural underpinnings of this effect. Indeed, Haxby et al. (2000) identified three structures that are thought to compose a 'core' face neural processing system: an occipital face area (OFA) that has been implicated in the early visual processing of faces (e.g., Pitcher, Walsh, & Duchaine, 2011), the fusiform face area (FFA) that is believed to process facial identity (e.g., Kanwisher, McDermott, & Chun, 1997), and the superior temporal sulcus (STS) which is thought to process changeable social aspects of the face, such as expression and eye gaze direction (e.g., Hoffman & Haxby, 2000). Although no work to date has recorded brain activity while participants attempt to recognize facial identity under oxytocin conditions, there is some indication from emotional expression recognition tasks that the hormone modulates activity in the distributed face processing network. Notably, a modulation in activity in the FFA has been reported while participants recognize emotional expressions under oxytocin conditions (Domes et al., 2007, 2010; Kirsch et al., 2005; Labuschagne et al., 2010; Petrovic, Kalisch, Singer, & Dolan, 2008), and it is likely that increased activity in this region might underpin the heightened recognition performance in the oxytocin condition reported here. In addition, several investigations have provided evidence that the amygdala might have a critical role in the mediation of the socio-cognitive effects of oxytocin (Domes et al., 2007; Kirsch et al., 2005; Petrovic et al., 2008), and it is of note that this neural structure is thought to be part of the extended face processing system that acts in concert with the core system (Haxby et al., 2000).

A second novel finding reported here is that, in the DP participants, oxytocin improved the perception of facial identity in a face matching task. To our knowledge this is the first evidence that oxytocin can improve face perception in any participant group, providing further insight into the locus of the effects of the hormone. However, neuroimaging work examining the influence of oxytocin on face perception is required. Indeed, while it is plausible that enhanced fusiform activity promotes performance on both face memory and face perception tasks, it is currently unknown whether oxytocin can also promote activity in neural structures implicated in earlier stages of the face processing network, such as the OFA (although modulation in occipital areas was noted by Domes et al., 2010). Nevertheless, we can speculate that our findings imply that oxytocin acts upon neural structures that are open to modulation even in DP, despite possible abnormalities in these areas (see Garrido et al., 2009; Hasson, Avidan, Deouell, Bentin, & Malach, 2003; Thomas et al., 2009).

When considering the influence of oxytocin on facial perception, it is pertinent to examine each individual DP's neuropsychological background in relation to their improvement in the oxytocin condition. Indeed, while all DPs have a deficit in face recognition, an impairment in the perception of facial identity (i.e., when no demands are placed on memory) is not necessary for a diagnosis of the condition. This is one example of the heterogeneity of DP, and it is of note that only two participants (DP1 and DP8) in our sample were impaired on the CFPT in the initial diagnostic session. Although no overall correlation was noted between initial CFPT performance and level of improvement on the face matching test, it is relevant that oxytocin brought about one of the largest improvements on this test in DP1, although DP8 did not show any improvement. In addition, DP7 and DP10 presented with some difficulties in lower-level vision on tests of the BORB in the diagnostic session, although their CFPT scores were in the normal range. Unfortunately DP7's data were lost for the CFMT in the placebo condition, but he displayed a small improvment in the matching test in the oxytocin condition. DP10 displayed very little improvement on both tests in the oxytocin condition. Thus, while examination of the participants on an individual basis suggests that those with lower-level visual impairments may be less susceptible to the effects of oxytocin, it is more difficult to make inferences based on the presence or absence of face perception deficits. In part, this can be attributed to the small sample size, and future work needs to further examine these issues in a much larger participant group.

It may also be the case that a 'placebo effect' is at work in some DP participants, and this may obscure other findings in the study. Indeed, standard errors were larger in the placebo compared to the oxytocin condition in the DPs, indicating that some participants were more influenced by the placebo spray than others. This suggestion is supported by the finding that the DPs achieved higher scores on the experimental CFMT in the placebo condition than in the original version administered in the initial diagnostic session. However, some caution must be exercised when interpreting this observation, as it is unclear whether the finding actually reflects a placebo effect. Indeed, it is likely that the higher scores in the placebo condition were brought about by practice effects (the DPs had completed at least one version of the CFMT before participating in the placebo condition and were therefore aware of the nature of the task), and the computer-generated stimuli used in the experimental CFMT may be more vulnerable to compensatory strategies (e.g., the use of feature-matching) than the 'real' faces used in the original version. Unfortunately, the available data from the control participants do not provide further insight into this issue, as these participants did not complete the original version of the CFMT (no initial diagnostic session was required for these individuals). Hence, while it is possible that a placebo effect was at work at least in the DP participants, the design of the current study and available data do not permit firm conclusions to be drawn on this issue.

The lack of significance in the correlations between DP severity and extent of improvement under oxytocin conditions provides some insight into the finding that control performance was not influenced by oxytocin in either task. Indeed, it may be the case that oxytocin has a greater effect in individuals with poorer face processing skills, and at a group-level, the data presented here support this claim. However, it is evident from the discussion above that this is a complex issue, and examination of the DPs on a case-by-case basis suggests the influence of other factors. It is also of note that the pattern of findings observed in the controls speaks to previous work that reports conflicting findings for typical viewers recognizing faces that display different emotional

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expressions. Indeed, only faces displaying neutral expressions were used in the tasks reported here, and the lack of improvement in control participants fits well with the finding reported by Guastella et al. (2008), where oxytocin only improved the recognition of happy and not angry or neutral faces. On the other hand, Savaskan et al. (2008) reported the reverse finding, where oxytocin improved the recognition of neutral and angry but not happy faces, and it is therefore clear that we do not have a firm understanding of the interaction between oxytocin, face memory and emotional expression. If it is the case that emotional expression interferes with the capacity of oxytocin to improve face recognition, our findings raise the possibility that expression interferes to a greater extent for unimpaired perceivers than DPs. Alternatively, it may simply be the case that the impaired face processing system is more amenable to improvement than the normal face processing system. However, these comments are merely speculative, and again further work is required to investigate this issue.

Finally, our findings have implications for the development of intervention strategies in disorders that present with face recognition impairments. While several studies have examined the potential therapeutic role of oxytocin in relieving symptoms in autistic spectrum disorders, obsessive compulsive disorder, post-traumatic stress disorder, personality disorders, anxiety disorders, schizophrenia and depression (for reviews see Ishak, Kahloon, & Fakhry, 2011; Macdonald & Macdonald, 2010), this study is the first to report its effectiveness in DP. This is an important issue given that face processing impairments do not only present in DP, but also following brain injury, degenerative disease, and in socio-developmental disorders such as autism, William's syndrome and Turner's syndrome. Thus, future work might examine whether oxytocin can improve face processing impairments in all conditions regardless of aetiology, or whether it is only effective in certain disorders. Further, while the current study examined the influence of a single dose of oxytocin in bringing about a temporary improvement in face processing in DP, further work might also consider the therapeutic value of repetitive inhalation of oxytocin in this condition and the sustainability of any improvements.

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