Understanding the social meaning of the eyes: is Williams syndrome so different from autism?

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Background: **Understanding the social meaning of the eyes is crucial to normal development. We studied this ability in a neuro-developmental genetic disorder, Williams syndrome (WS) that, among other characteristics, has a distinctive cognitive profile with reported proficiency in language, face processing and social skills, but seriously impaired visuo-spatial and number skills.**

Methods: **Based on our earlier challenges to claim about intact face processing and good social cognition skills in WS, as well as from our work on early social cognition in WS infants, we ran two simple experiments, both with control conditions, to test the hypothesis that the ability to process eye gaze direction and facial emotions would be impaired in WS adults, compared to control groups of typically developing 4- and 6-year-old children and normal adults.**

Results: **We found that adolescents and adults with WS were seriously delayed in the detection of eye gaze direction as well as being specifically impaired at interpreting "sadness" and "anger", even compared to 4-year-old controls.**

Conclusions: **We speculate that the WS problems lie not in their difficulty to process eyes per se, but in their problems with interpreting the social meaning of the eyes, implicating dysfunction of the amygdala circuit. Finally, our results lead us to question a prevailing view that WS and autism are situated at opposite ends of the continuum with respect to social cognition.**

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Introduction

Face processing plays a crucial role in our everyday life. This is because faces are complex social stimuli and contain, particularly in the eye region, a multitude of important information for social interaction. The ability to process faces develops early in normal infancy[1] and continues to be fine-tuned through to adolescence.[2] Indeed, psychological research has yielded a fascinating fact about human newborns: the moment that they emerge from the womb, they start to maintain eye contact with others and follow others' eye gaze—a vital capacity that immediately enhances their introduction to the social world.[3] Later, at around 10-14 months, typically developing infants not only follow eye gaze, but they use it as a reliable indicator of another's focus of attention.[4] This marks the passage from dyadic attention to triadic attention and is a major developmental milestone. Joint attention to a common external object, person or event, is crucial for the subsequent development of social cognition in general,[5-8] as well as for vocabulary acquisition.[9] Triadic attention also provides an important way in which reference is established.[10] And, with increasing age, children become capable of detecting not only in which general direction someone is looking, but also exactly where he or she is focused, with a surprising degree of precision. But what happens if face processing follows an atypical developmental trajectory? How does this affect social cognition in clinical groups? In this paper, we focus on a specific neurodevelopmental disorder, Williams syndrome (WS).

Face processing in Williams syndrome

Williams syndrome is a rare neurodevelopmental disorder, caused by a microdeletion of some 28 genes on the long arm of one copy of chromosome 7.[11,12] It occurs in about 1 in 20 000 live births. Clinical features include a range of physiological abnormalities, including supravalvular aortic stenosis and a dysmorphic face, that are accompanied by mild to moderate mental retardation and a specific personality profile. Despite the wealth of data on face memory and face identification abilities from individuals with Williams syndrome, very few studies have hitherto focused on how people with WS interpret the social meaning of facial expressions. These social aspects of face processing, such as eye gaze direction and the interpretation of facial emotions are the focus of the present paper.

It is now well established that individuals with autism are particularly impaired in processing eye-gaze, emotional cues and speech-related facial movement. This leads to profound deficits in their social understanding and their general communicative skills.[13] In contrast, individuals with WS achieve scores in the normal range on standardized face identity and face memory tasks[14,15] as well as in some experimental studies.[16] The latter studies have claimed that individuals with WS process faces just like healthy controls. By contrast, other behavioral studies have indicated that WS face processing follows an atypical developmental trajectory and relies predominantly on featural or holistic processing rather than configural processing.[17-20] WS face processing also appears to be sustained by different electrophysiological responses in the brain,[21] in which cerebral integration is also atypical.[22] Moreover, experimental studies of early communicative abilities in WS toddlers also point to atypicality.[23,24] This is despite anecdotal reports of the very friendly social nature of children and adults in this clinical population,[25] particularly with respect to their hypersociability towards strangers.[26,27] Thus, despite a wealth of research on WS face processing, experimental findings on the processing of faces as they relate to social cognition remain controversial.[16,20,27,28]

Note that if social perceptual skills were intact in WS[27] and eye gaze detection were just as automatic as in healthy individuals, people with WS should have no problem with a task that requires the simple computation of eye gaze direction. Nevertheless, preliminary observational data by Bertrand et al[29] suggest that toddlers with WS make use of different strategies than eye gaze to establish reference (see also experimental studies on this topic[24]). We therefore predicted (Experiment 1) that, compared to healthy controls, people with WS would be impaired in their ability to make inferences from eye gaze direction alone.

Another aspect of face stimuli that has a profound effect on social development is the processing of facial emotion expression. The current consensus in normal research is that the identification of most facial expressions requires configural processing.[30] But what about clinical groups and their ability to process emotional expressions in faces?

Research by Gagliardi and colleagues,[31] using whole facial images, found that recognition of all six basic facial emotions was worse for the more difficult items in individuals with WS compared to chronological age (CA)-matched controls, but did not differ from that of mental age (MA)-matched controls. The WS negative findings for difficult items on all emotion expressions were interpreted on the basis of the fact that facial emotion expressions alter the overall configuration of the face and that individuals with WS have weak sensitivity to configural differences. By contrast, Elsabbagh and colleagues[32] reported a whole-face emotional labelling study that revealed no significant difference between WS children (mean age 9 years) and chronologically-matched controls across five basic emotion expressions. The reasons for these discrepant results remain to be elucidated.

In an attempt to render the stimuli in the present study less complex than a full face, we used isolated parts of faces (Experiment 2). Although this simplifies the configuration, it does not of course totally remove configural cues, because spacing between the eyebrows, as well as between eyes and eyebrows, does convey some configural information. However, in our view, part faces should simplify the task for participants who focus mainly on featural information. We therefore predicted that there would be no difference in facial emotion recognition between adults with WS and normal controls, if they were able to rely on featural information only.

To address the above issues, two experiments were carried out to compare adolescents and adults with WS, typically developing children and a group of healthy adults. Experiment 1 used a simple task of eye gaze direction, which requires computation of line-of-sight to one of five specific locations. A control condition used the same array of objects but instead of eye gaze direction, arrows pointed to the location of each of the five objects. In Experiment 2, participants were presented with digitized black and white photographs of isolated eye regions of faces, and asked to make a decision as to which of six basic emotions best described what the person in the photograph was experiencing. Participants' responses were again compared with a control condition, in which they were asked to judge emotional expressions from the mouth region only.

We focused more specifically on the eye regions of faces because: (1) extensive research on healthy individuals has shown that when encountering a human face, normal infants, children and adults spontaneously focus on the eye regions and spend the majority of their time on the eyes to extract information, and (2) individuals with autism tend to avoid eye contact with other people and focus on other parts of the face (e.g., the mouth) for face processing. Thus, if individuals with WS are unlike those with autism, the former should have no difficulty in determining the direction of another's eye gaze nor in deciphering basic emotional information conveyed by the eyes alone.

Methods

Experiment 1 and participants

The sample was composed of individuals with WS, typically developing children aged 4 and 6 years matched on MA with the WS group, as well as healthy adults matched chronologically to the clinical group. The WS sample (11 adolescents and adults, mean age 29;2 years) was recruited through the Williams Syndrome Foundation, a UK-based parent support group. All the participants with WS had been diagnosed both clinically and by means of the fluorescence *in situ* hybridization (FISH) genetic test for deletion of the elastin gene on one copy of chromosome 7. Thirty-eight typically developing children (17 four-year-olds; 21 six-year-olds) were recruited through nursery and primary mainstream schools around London. Finally, 12 healthy adolescents and adults (mean age 27;7 years) were also tested.

The British Picture Vocabulary Scale II (BPVS-II)[33] and the British Ability Scales-II (BAS-II)[34] were used to match the groups of typically developing children to the group of participants with WS on the basis of vocabulary development and visuo-spatial abilities, respectively. The standard score (SS) of the BPVS-II and the ability score (AS) of the BAS-II are shown in Tables 1 and 2, respectively.

Design and procedures

All the materials were computer-based and delivered with in-house software on a 14-inch PC-laptop screen. The computer was programed to collect and collate response type (accuracy) per trial. The computerized task was adapted from the report of Elgar et al.[35] Digital photographs of a female sitter were obtained under two conditions, each of which required her to inspect a location just below the plane of sight line of the camera. There were five locations: left 10° displacement from the centre, left 5°, 0°, right 5° and right 10° displacement from the center.

In the first series of captured images, head and eyes were aligned with respect to the direction of eye gaze, while in the second series of images the head was fixed facing the camera, with direction of eye gaze alone indicating sight line. Twenty images, comprising 40 trials, were captured for each of the five angular positions with: (a) head fixed with eye gaze alone providing gaze direction; (b) head direction congruent with eye gaze direction. Each of these images was digitized and a horizontal rule, indicating each of the five positions, shown as Arabic numbers, was added to the display at the bottom of the image.

At the start of each trial, a fixation cross in the center of the screen was replaced by a single full colour face image, approximately 10 cm × 15 cm, appearing in the center of the grey screen, at a viewing distance of about 50 cm. Each of the 20 images was used in a randomised order. Participants were asked to say the number corresponding to the line of gaze, and the experimenter, who was seated next to them, indicated participants' responses by a mouse click to the number position. If a participant with WS or a young 4-year-old were unsure about reading the numbers 1 to 5, they were also allowed to point to the object on the screen. In fact, all participants displayed the small number reading ability with ease. A practice session, including five images of the same sitter that were not used in the

Table 1. BPVS II: mean CA, standard score and mental age equivalent of the participants with WS and typically developing controls

Group	Mean CA in years	Mean standard score	Mean mental age equivalent in years
4-year controls (*n*=17)	4;4	103.52	4;4
6-year controls (*n*=21)	6;7	102.57	6;3
Adult controls	27;7	-	-
WS (*n*=11)	29;2	83	10;9

Table 2. BAS II: mean of the CA, ability score and mental age equivalent of the participants with WS and typically developing controls

Group	Mean CA in years	Mean ability score	Mean mental age equivalent in years
4-year controls (*n*=17)	4;4	80.47	4;3
6-year controls (*n*=21)	6;7	111.52	6;7
Adult controls	27;7	-	-
WS (*n*=11)	29;2	92	5;2

experiment proper, preceded testing. The dependent variable was the number of correct responses for each location.

Results

Means and standard deviations (scores in brackets) are summarised in Table 3 and Fig. 1. Fig. 1 shows that the adult controls were more accurate than the other three groups in both conditions. The figure also illustrates the ability to follow eye gaze in the typically developing children, with a gradual developmental trajectory that extends beyond 6 years, with a more rapid development for the condition of congruent head and eyes condition between 4 and 6 years than for the condition of the eyes alone. By contrast, the WS group had still not reached the level of 6-year-old children for either condition, although they also found the eyes alone condition harder, like the controls.

Repeated measures of ANOVA were computed to test the hypothesis that the WS group differed from the controls in the ability to follow eye gaze (4 and 6 years of age, adolescents/adults with WS, and adult controls) and between factor, and condition (eyes alone or head/eyes congruent) as the within factor. The ANOVA yielded a main condition effect [$F(1,57)=10.721$, $P<0.005$], a main group [$F(3,57)=7.3$, $P<0.001$], and a significant group × condition interaction [$F(3,57)=23.015$, $P<0.001$]. Post hoc analysis (Tukey's test, $P<0.05$) suggested that for both conditions the 6-year-old controls were more accurate at following eye gaze than the 4-year-olds. In addition, for the head plus eyes congruent condition, the WS group and adult controls were more accurate at eye gaze than the 4-year-old controls. For the eyes-only condition, the adult controls were more accurate at eye gaze than all other groups.

To assess within-group differences between the two conditions, paired *t* tests were conducted. The paired *t* test for the 6-year-old controls demonstrated that gaze direction was judged more accurately when head orientation and eye gaze were congruent than in the eyes alone condition (*t* value=3.295; *df*=20; $P<0.005$). A similar pattern emerged for the WS group (*t* value=4.644; *df*=10; $P<0.005$). This contrast was not significant for the 4-year-olds (*t* value=-1.845; *df*=16; $P>0.05$) who were still learning the congruent position, nor for the adult controls (*t* value=0.546; *df*=11, $P>0.05$) who performed well on both conditions.

Table 3. Eyes only vs head-eyes congruent: mean and standard deviation (in brackets) for each group

Group	Eyes only	Head-eyes congruent
4-year-old controls (*n*=17)	5.88 (2.82)	4.76 (2.53)
6-year-old controls (*n*=21)	8.61 (2.94)	10.95 (3.27)
Adults (*n*=12)	12.58 (2.06)	13.00 (3.35)
WS (*n*=11)	7.18 (2.56)	10.36 (2.24)

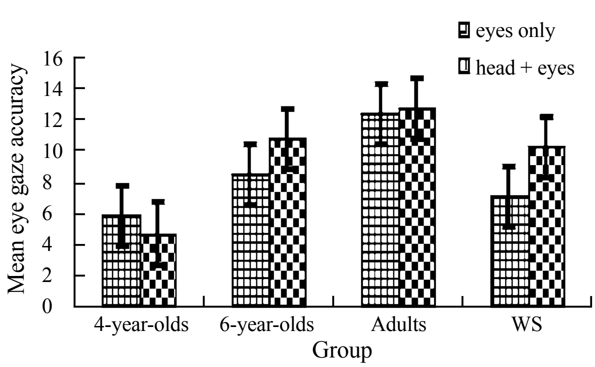

Fig. 1. Mean eye gaze accuracy for each group.

Analysis

Although the WS group did as well as the other groups when eyes and head were congruent, there was a significant decrement in gaze accuracy when the head was fixed and eyes alone indicated the location of eye gaze. Research has shown that, by adulthood, healthy controls make greater use of eye than head orientation in determining the locus of eye gaze.[36] It had previous been claimed that individuals with WS were proficient at social cognition and, if this were the case, then our clinical adolescents and adults should have performed far better than the typically developing 4- and 6-year-olds, since the WS group was much older. But they did not. Our findings suggest a serious delay in the clinical group, which has also been documented in individuals with Turner syndrome[35] and in autism.[37,38]

The present findings also suggest that mastering the social informational value of eye direction alone is a relatively late milestone even in typical development, and is only achieved beyond the age of 6 years. Indeed, while the 6-year-old controls were able to use information from head orientation to detect which object was being looked at, their full mastery in performing this task on the basis of eye direction alone was not complete. Thus, although healthy infants are already sensitive to differences in global direction of eye gaze,[4] it takes several years before they can fully master the use of eye gaze to determine with precision exactly where someone is looking.

The impaired ability of WS adolescents and adults to infer simple locations from the position of eye gaze alone might be thought to stem from their behavioral deficits in visuo-spatial tasks in general.[25,39,40] A second condition for Experiment 1 was therefore designed to test this visuo-spatial hypothesis. This was identical to the first condition, except for the fact that the female face and her different eye gaze directions were replaced by non-social arrows in the centre of the display, pointing to each of the 5 locations of the objects.

All groups including the WS clinical participants were at ceiling on the task, so no further analyses were performed. Ceiling results are of course somewhat difficult to interpret because the task itself may not have been sensitive enough to pinpoint subtle deficits. However, condition 2 was to all intents and purposes identical to condition 1 except for the replacement of eyes by arrows. We therefore contend that the results of condition 2 in which all participants, including those in the clinical group, were at ceiling, thus allow us to argue that the deficits in the WS group in condition 1 can not be simply explained by their poor visuo-spatial abilities. Rather, we believe that their difficulty lies in their lack of fully understanding the social meaning of the eyes. To test this hypothesis, Experiment 2 examined participants' ability to interpret emotional expressions conveyed by the eyes alone.

Experiment 2 and participants

The participants in Experiment 2 were the same as those in Experiment 1. The order of the two experiments was randomized across subjects.

Design and procedures

This task, adapted from Elgar et al,[41] examined accuracy at choosing one of six basic emotions:[42] happiness, surprise, fear, sadness, disgust and anger, based on stimuli representing only part of the face. Digital photographs of images of either men or women were presented through the same 14-inch PC-laptop computer screen as used in Experiment 1. Ten matched pairs of faces comprising 120 trials were seen under two presentation conditions: upper face (eyes) or lower face (mouth). At each trial, either the upper or lower face images, approximately 10 cm × 15 cm, were presented in the centre of a grey screen at a viewing distance of about 50 cm. The presentation of an upper-half was followed by the presentation of a lower half from trial to trial. Participants were asked to select one of the six basic emotion labels listed above, displayed in groups of three on each side of the image. For young control children and any WS participants who could not read, the Experimenter read out all the emotion labels for each trial. Participants reported the emotion that they thought corresponded to each part-facial image, and the experimenter, seated next to each participant, indicated the participant's responses by a mouse click to the emotion label. A practice session including twelve images of the same pairs of faces, which were not used in the experiment proper, preceded testing. The dependent variable was the number of correct responses for each expression.

Results

The mean accuracy and standard deviation (scores in brackets) for upper-face and the lower-face are summarized in Table 4.

A group by condition repeated ANOVA revealed a main effect due to condition [$F(1,72)=23.905$, $P<0.001$], a main effect of group [$F(3,72)=28.763$, $P<0.001$], as well as an interaction effect due to condition × group [$F(3,72)=8.416$, $P<0.001$]. Post hoc analysis (Tukey's test, $P<0.05$) indicated that, for all six emotions grouped, the healthy controls of all ages, even the 4-year-olds, were more accurate at labelling emotion on both the upper-face and the lower-face stimuli than the adolescents and adults with WS.

The mean and the standard deviation (scores in brackets) for each emotion label for each group are given in Table 5. Fig. 2 indicates that in every group "happiness" and "anger" were more successfully identified than "surprise", "fear", and "disgust". Repeated measures of ANOVA were computed to assess whether the recognition of facial emotion expressions differed as a function of group. This analysis pointed to a significant main effect due to facial emotion expression [$F(5,285)=96.749$, $P<0.001$] and to group [$F(3,57)=30.073$, $P<0.001$]. In addition, an interaction effect due to facial emotion expression × group [$F(15,285)=4.238$, $P<0.001$] emerged.

Because of the interaction effect, a series of MANOVAs were carried out. Each expression was examined with respect to group. After applying Bonferroni corrections to control for multiple comparisons, it turned out that although the WS adolescents and adults were best at "happiness" and "anger" compared to the other emotions, they were more specifically impaired at interpreting "sadness" and "anger" when compared with even the 4-year-olds, and also impaired at interpreting "fear" and "disgust"

Table 4. Upper-face and lower-face: mean and standard deviation (in brackets) for each group, for all expressions grouped

Group	Eyes	Mouth
4-year-old controls (*n*=17)	28.76 (5.20)	25.64 (6.37)
6-year-old controls (*n*=21)	30.95 (4.37)	21.04 (4.24)
Adults (*n*=12)	39.83 (3.8)	40.08 (5.19)
WS (*n*=11)	26.53 (7.52)	24.30 (6.59)

when compared with the chronologically-age matched adult controls. Finally, the performance of the adult controls was overall better than that of all the other groups.

Repeated measures of ANOVA were also computed to test the hypothesis that recognition of facial emotion expression would differ as a function of the region (eye vs mouth) for which each emotion label was presented. The results of this analysis showed a significant main effect due to facial region [$F(1,57)=26,354$, $P<0.05$], and to group [$F(3,57)=30,023$, $P<0.05$]. In addition, an interaction effect emerged because of facial region × group [$F(3,57)=8,406$, $P<0.05$]. Post hoc analysis (Tukey's test) showed that adults were generally better at processing facial emotion expressions than the other groups and specifically they were better at processing emotions from the eye region. The mean and the standard deviations (the scores in brackets) for the eye and mouth region for each group are given in Table 5.

Pearson's product moment correlation coefficients were calculated between each emotional expression and each of the two conditions of Experiment 1 in each group. It was found that "fear" in experiment 2, and that expression alone, correlated significantly with WS performance on Experiment 1 when the direction of gaze alone indicated the location. Also, a relation between "happiness", "disgust" and performance when both head and eyes indicated together the location was significant at 0.05 for the 4-year-olds. Other relations between each emotional expression and each of the two conditions of Experiment 1 were not significant. Finally, relations between the ability score on BPVS and performance on Experiment 1 did not reach significance.

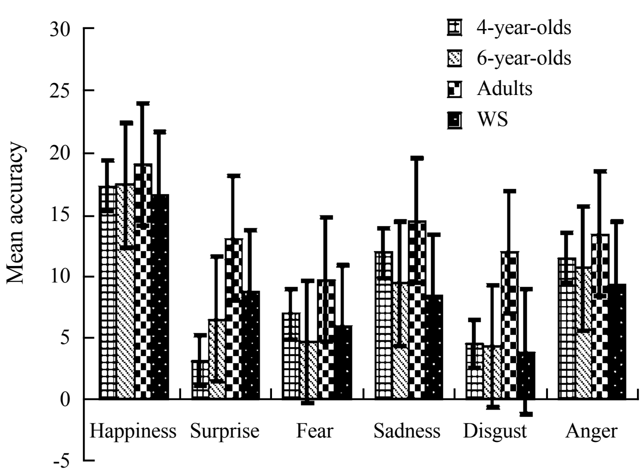

Fig. 2. Mean accuracy for each facial expression.

Analysis

In the emotion part-face labelling task, "sadness", "fear", "disgust" and "surprise" emerged as more difficult than "happiness" and "anger" in all groups. Interestingly, however, the WS group was specifically impaired at interpreting "sadness" and "anger", even compared with the 4-year-olds and, like the child controls, impaired at interpreting "fear" and "disgust", when compared to the adult controls.

The emotions of "happiness" and "anger" may have been easier for all groups including the WS group, because these emotions may be more frequently encountered in everyday life.[32] Despite this frequent occurrence, it is noteworthy that the WS group did significantly more poorly than the 4-year-old controls on "anger". Our present results are not entirely in line with those of a previous study in which the WS group showed impairments on difficult items on all facial emotions.[31] We believe this is because the Gagliardi stimuli may have required more complex configural processing. Indeed, our earlier study using high-density event related potentials[21] yielded atypical brain processes in WS in the perceptual integration of part-wholes into a configural whole. For the present study, we had purposely designed our stimuli so that they reduced the amount of configural information that needed to be integrated, allowing participants to focus on parts rather than the whole face. This might explain why they did somewhat better on some emotions compared to stimuli used by other researchers with whole faces. Our design enabled the WS adolescents and adults to display their abilities in emotions like happiness, but still revealed subtle deficits in the emotions of sadness, fear, surprise and disgust, and

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Table 5. Accuracy for each facial expression: mean and standard deviation (in brackets) for each group, for eyes and mouth grouped

Facial expression	4-year-olds	6-year-olds	Adults (n=12)	WS (n=11)
Happiness	17.17 (1.74)	17.19 (2.42)	18.83 (0.71)	16.45 (3.69)
Surprise	3.00 (3.25)	6.38 (5.73)	12.91 (2.74)	8.54 (4.90)
Fear	6.76 (2.94)	4.52 (3.64)	9.58 (3.34)	5.72 (3.10)
Sadness	11.76 (2.01)	9.23 (3.04)	14.33 (2.34)	8.18 (3.28)
Disgust	4.35 (3.18)	4.19 (2.96)	11.83 (1.69)	3.72 (3.71)
Anger	11.35 (4.51)	10.47 (3.60)	13.25 (2.49)	9.18 (3.65)

even for the easier emotion of anger when compared to the very young controls.

Discussion

Could differences in brain structure help to explain our findings? For example, brain-imaging studies of healthy controls suggest that different facial expressions activate specific brain networks, particularly within the amygdala circuit. However, in WS, the morphology as well as the anatomy of structures such as the amygdala, thalamus, putamen and globus pallidus have been shown to be different from those of healthy controls.[43,44] Furthermore, magnetic resonance imaging[45] has demonstrated that compared to healthy controls, individuals with WS have a reduced overall brain volume, a reduced cortical volume, alongside relative preservation of cerebellar, and superior temporal gyrus volume, and a disproportionately reduced volume of the brainstem. Moreover, while density of gray matter in individuals with WS is relatively similar to that of the controls, WS have a disproportionately reduced volume of cerebral white matter. This could affect the development of emotion recognition over developmental time. However, why this should have a greater effect on some emotions (e.g., surprise) and not on others (e.g., happiness) remains to be explained.

The amygdala, together with the superior temporal gyrus and the orbitofrontal cortex, comprise a neural network claimed to be responsible for "social intelligence".[46] This network, which is implicated in the ability to respond to and follow the direction of another's gaze,[47] has been shown to be abnormal in autism.[48] Moreover, preliminary structural imaging studies in Turner syndrome (TS) suggest that the morphology and the anatomy of the amygdala in women with TS are different from those in control women.[49] On these grounds, we argue that WS, TS and autism, which are all neurodevelopmental disorders with a genetic basis, may all result in the disruption of the functional integrity of the amygdala circuit.

The present study could be thought of as challenging the claim that people with WS are good at processing individual features, since all that Experiment 1 required was a focus on the eyes, and all that Experiment 2 needed was a focus on isolated parts of half-faces for which configural processing was reduced. But this misses the point. Our new findings suggest that it is the ***social meaning*** of eye gaze direction and emotion identification, rather than just featural processing per se, which helps to explain the atypical patterns in our clinical population.

Paradoxically, WS has often been situated at the opposite end of the social disorders continuum from autism. Our current results suggest, by contrast, that it is always important to focus on cross-syndrome associations and not merely dissociations, and that in some respects there is more in common between autism and Williams syndrome in the social domain than previously thought.

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References

1 Johnson MH, Morton J. Biology and cognitive development: the case of face recognition. New York: Blackwell, 1991.
2 Carey S, Diamond R. From piecemeal to configurational representation of faces. Science 1977;195:312-314.
3 Nadel J, Muir D. Emotional development: current and future research directions. Oxford: Oxford University Press, 2005.
4 Corkum V, Moore C. Development of joint visual attention in infants. In: Moore C, Durnham P, eds. Joint attention: its origins and role in development. Erlbaum: Hillsdale NJ, 1994: 61-85.
5 Butterworth GE, Cochran E. Towards a mechanism of joint visual attention in human infancy. Int J Behav Dev

1980;3:253-272.
6 Freire A, Eskritt M, Lee K. Are eyes windows to a deceiver's soul: children's use of another's eye gaze cues in a deceptive situation. Dev Psychol 2004;40:1093-1104.
7 Freire A, Lee K. Face recognition in 4- to 7-year-olds: processing of configural, featrural, and paraphernalia information. J Exp Child Psychol 2001;80:347-371.
8 Freire A, Lee K. Person recognition by young children: configural, featural, and paraphernalia processing. In: Pascalis O, Slater A, eds. The development of face processing in infancy and early childhood: current perspectives. New York: Nova Science Publishers, 2004: 191-205.
9 Werner H, Kaplan B. Symbol formation. New York: Wiley, 1963.
10 Baldwin DA. Infants' contribution to the achievement of joint reference. Child Dev 1991;62:875-890.
11 Morris CA, Demsey SA, Leonard CO, Dilts C, Blackburn BL. Natural history of Williams syndrome: physical characteristics. J Pediatr 1988;113:318-326.
12 Donnai D, Karmiloff-Smith A. Williams syndrome: from genotype through to the cognitive phenotype. Am J Med Genet 2000;97:164-171.
13 Frith U. Autism: explaining the enigma. Oxford: Blackwell, 1989.
14 Bellugi U, Marks S, Bihrle A, Sabo H. Dissociation between language and cognitive functions in Williams syndrome. In: Bishop D, Mogford K, eds. Language development in exceptional circumstances. Edinburgh: Churchill Livingstone, 1988: 177-189.
15 Udwin O, Yule W. A cognitive and behavioural phenotype in Williams syndrome. J Clin Exp Neuropsychol 1991;13: 232-244.
16 Tager-Flusberg H, Plesa-Skwerer D, Faja S, Joseph RM. People with Williams syndrome process faces holistically. Cognition 2003;89:11-24.
17 Deruelle C, Mancini J, Livet M, Casse-Perrot C, de Schonen S. Configural and local processing of faces in children with Williams syndrome. Brain Cogn 1999;41:276-298.
18 Karmiloff-Smith A. Crucial differences between developmental cognitive neuroscience and adult neuropsychology. Dev Neuropsychol 1997;13:513-524.
19 Karmiloff-Smith A. Development itself is the key to understanding developmental disorders. Trends Cogn Sci 1998;2:389-398.
20 Karmiloff-Smith A, Thomas M, Annaz D, Humphreys K, Ewing S, Grice S, et al. Exploring the Williams syndrome face processing debate: the importance of building developmental trajectories. J Child Psychol Psychiatry 2004;45:1258-1274.
21 Grice SJ, Haan MD, Halit H, Johnson MH, Csibra G, Grant J, et al. ERP abnormalities of visual perception in Williams syndrome. Neuroreport 2003;14:1773-1777.
22 Grice S, Spratling MW, Karmiloff-Smith A, Halit H, Csibra G, de Haan M, et al. Disordered visual processing and oscillatory brain activity in autism and Williams syndrome. Neuroreport 2001;12:2697-2700.
23 Jones W, Bellugi U, Lai Z, Chiles M, Reilly J, Lincoln A, et al. Hypersociability in Williams syndrome. J Cogn Neurosci 2000;12(Suppl 1):30-46.
24 Laing E, Butterworth G, Ansari D, Gsodl M, Longhi E, Panagiotaki G, et al. Atypical development of language and social communication in toddlers with Williams syndrome. Dev Sci 2002;5:233-246.
25 Bellugi U, Bihrle A, Jernigan T, Trauner D, Doherty S. Neuropsychological, neurological and neuroanatomical profile of Williams syndrome. Am J Med Genet Suppl 1990;6: 115-125.
26 Doyle T, Bellugi U, Korenberg J, Graham J. Everybody in the world is my friend: hypersociability in children with Williams syndrome. Am J Med Genet 2003;124A:263-273.
27 Tager-Flusberg H, Sullivan K. A componential view of theory of mind: evidence from Williams syndrome. Cognition 2000; 76:59-89.
28 Karmiloff-Smith A, Klima ES, Bellugi U, Grant J, Baron-Cohen S. Is there a social module? Language, face processing, and theory of mind in subjects with Williams syndrome. J Cogn Neurosci 1995;7:196-208.
29 Bertrand J, Mervis C, Rice CE, Adamson L. Development of joint attention by a toddler with Williams syndrome. Paper presented at the Gatlinburg Conference on Research and Theory in Mental Retardation and Developmental Disabilities, Gatlinburg, 1993.
30 Calder AJ, Young AW, Keane J, Dean M. Configural information in facial expression. J Exp Psychol Hum Percept Perform 2000;26:527-551.
31 Gagliardi C, Frigerio E, Burt DM, Cazzaniga I, Perrett DI, Borgatti R. Facial recognition in Williams syndrome. Neuropsychologia 2003;41:733-738.
32 Elsabbagh M, Reilly J, Bellugi U. Facial expression and comprehension in Williams syndrome. Poster presented at the Gatlinburg Conference on Mental Retardation, San Diego, California, 2004.
33 Dunn LM, Dunn LM, Whetton C, Burley J. The British Picture Vocabulary Scale Ringwood, 2nd ed. Hamp: NFER-Nelson, 1997.
34 Elliott CD, Smith P, McCulloch K. British Ability Scales II. Windsor: NFER-Nelson, 1995.
35 Elgar K, Campbell R, Skuse D. Are you looking at me? Accuracy in processing line-of-sight in Turner syndrome. Proc Biol Sci 2002;269:2415-2422.
36 Langton SR, Watt RJ, Bruce II. Do the eyes have it? Cues to the direction of social attention. Trends Cogn Sci 2000; 4:50-59.
37 Leekam S, Baron-Cohen S, Perrett D, Milders M. Eye-direction detection: a dissociation between geometric and joint attention skills in autism. Br J Dev Psychol 1997;15:77-95.
38 Leekam SR, Hunnisett E, Moore C. Targets and cues: gaze-following in children with autism. J Child Psychol Psychiatry 1998;39:951-962.
39 Farran EK, Jarrold C, Gathercole SE. Block design performance in the Williams syndrome phenotype: problem with mental imagery? J Child Psychol Psychiatry 2001;42: 719-728.
40 Brown JH, Johnson MH, Paterson S, Gilmore R, Longhi E, Karmiloff-Smith A. Spatial representation and attention in toddlers with Williams syndrome and Down syndrome. Neuropsychologia 2003;41:1037-1046.
41 Elgar K, Kuntsi J, Coleman M, Campbell R, Skuse D. Face recognition deficits in Turner syndrome: a possible role for X-linked genes in amygdala development. Neuropsychologia, in press.
42 Ekman P, Friesen WV. Pictures of facial affect. Palo Alto: Consulting Psychologists, 1976.
43 Jernigan TL, Bellugi U. Anomalous brain morphology on magnetic images in Williams syndrome and Down syndrome.

Arch Neurology 1990;47:529-533.
44 Jernigan TL, Bellugi U, Sowell E, Doherty S, Hesselink JR. Cerebral morphologic distinctions between Williams and Down syndromes. Arch Neurology 1993;50:186-191.
45 Reiss AL, Eliez S, Schmitt JE, Straus E, Lai Z, Jones W, et al. Neuroanatomy of Williams syndrome: a high-resolution MRI study. J Cogn Neurosci 2000;12(Suppl 1):65-73.
46 Brothers L. The social brain: a project for integrating primate behaviour and neurophysiology in a new domain. Concepts Neurosci 1990;1:27-51.
47 Emery NJ. The eyes have it: the neuroethology, function and evolution of social gaze. Neurosci Biobehav Rev 2000;24: 581-604.
48 Baron-Cohen S, Ring HA, Wheelwright S, Bullmore ET, Brammer MJ, Simmons A, et al. Social intelligence in the normal and autistic brain: an fMRI study. Eur J Neurosci 1999;11:1891-1898.
49 Good C, Elgar K, Kuntsi J, Akers R, Price C, Ashburner J, et al. Gene deletion mapping of the X chromosome. Human Brain Mapping 2001, Brighton. Neuroimage 2001;13:S793.

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