

# Are you looking at me? Accuracy in processing line-of-sight in Turner syndrome

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The behavioural phenotype of women with Turner syndrome (X-monosomy, 45,X) is poorly understood, but includes reports of some social development anomalies. With this in mind, accuracy of direction of gaze detection was investigated in women with Turner syndrome. Two simple experimental tasks were used to test the prediction that the ability to ascertain gaze direction from face photographs showing small lateral angular gaze deviations would be impaired in this syndrome, compared with a control population of men and women. The prediction was confirmed and was found to affect both the detection of egocentric gaze from the eyes ('is the face looking at me?') and the detection of allocentric gaze, where the eyes in a photographed face inspected one of a number of locations of attention ('where is she looking?'). We suggest that dosage-sensitive X-linked genes contribute to the development of gaze-monitoring abilities.

**Keywords:** gaze acuity; Turner syndrome; autism

## 1. INTRODUCTION

Turner syndrome (TS) is a sporadic disorder of human females in which all or part of one X chromosome is deleted (Turner 1938). The karyotype may be described as 45,X compared with the normal female 46,XX or the normal male 46,XY. While TS is of clinical interest, studies of behaviour of women with TS promise more general insights into X-linked genetic mechanisms that influence the normal development of behavioural and cognitive processes. In particular, there may be X-linked genes for which two copies are needed in normal (female) development. Such genes are expressed in insufficient dosage (they are haplo-insufficient) in TS (Ross & Zinn 1999).

Individuals with TS generally have verbal abilities within the normal range, although specific cognitive difficulties, for example in visuo-spatial skills, may exist (Ross *et al.* 1995). They can have problems in forming and maintaining peer relationships, and difficulties in interpreting non-verbal communication (McCauley *et al.* 1987). Creswell & Skuse (2000) reported that autistic features can be associated with TS, and that the risk of autism may be increased 500-fold in women with TS compared with 46,XX females. Such difficulties in the realm of social behaviour, including some autistic features, may therefore reflect haplo-insufficiency of X-linked gene products. Until recently, however, few experimental studies have cast light on socio-perceptual processes in TS in comparison with karyotypically normal groups of men and women. We have recently reported reliable deficits in the recognition of faces, and in the identification of a 'fearful' facial expression, in women with TS (Elgar *et al.* 2002). These particular deficits are reminiscent of those reported for people with autism (e.g. Howard *et al.* 2000). We therefore hypothesized that, in view of their increased risk

of expressing autistic behavioural features, 45,X women may present other anomalies in socio-perceptual processing, similar to those reported for people with autism. The processing of gaze is one such feature. Children with autism, and those at risk for developing autism, show less eye contact and reduced ability to follow the gaze of another (e.g. Hutt & Ounsted 1966; Baron-Cohen 1995; Swettenham *et al.* 1998), especially when the attention of another is directed to an event of social interest (Dawson *et al.* 1998; Ruffman *et al.* 2001). The present study reports adult performance in two simple tasks of gaze processing, one of which requires that the viewer detect whether gaze is engaged ('is she looking at you?'), while the other ('where is she looking?') requires computation of line-of-sight to a location in the picture plane, but does not involve engaged gaze. In people with autism, these skills have been reported to dissociate, so that direct apprehension of gaze can be impaired, but computing line-of-sight when the looker is attending to a location away from the viewer, need not be. One interpretation of this pattern is that usually it is the former task that reflects what the pictured person is thinking, planning or feeling about (especially in relation to the viewer—the camera): in other words, intention is inferred from such images (Baron-Cohen *et al.* 1996; Leekam *et al.* 1997). A similar dissociated pattern has been observed in adult patients with schizophrenia (Rosse *et al.* 1994; Franck *et al.* 1998). Despite this apparent dissociation, studies of gaze direction detection have rarely been comparable. The finding of specific impairment in detecting if gaze is engaged (egocentric gaze) may therefore reflect greater task difficulty for such tasks than for those where line-of-sight to a location or object (allocentric gaze) is assessed.

Adult precision in the detection of line-of-sight of another is generally extremely high. Anstis *et al.* (1969) suggested that a horizontal displacement of the iris of less than 2 mm is detectable at 122 cm viewing distance. Such small displacements can be reliably detected in photo-

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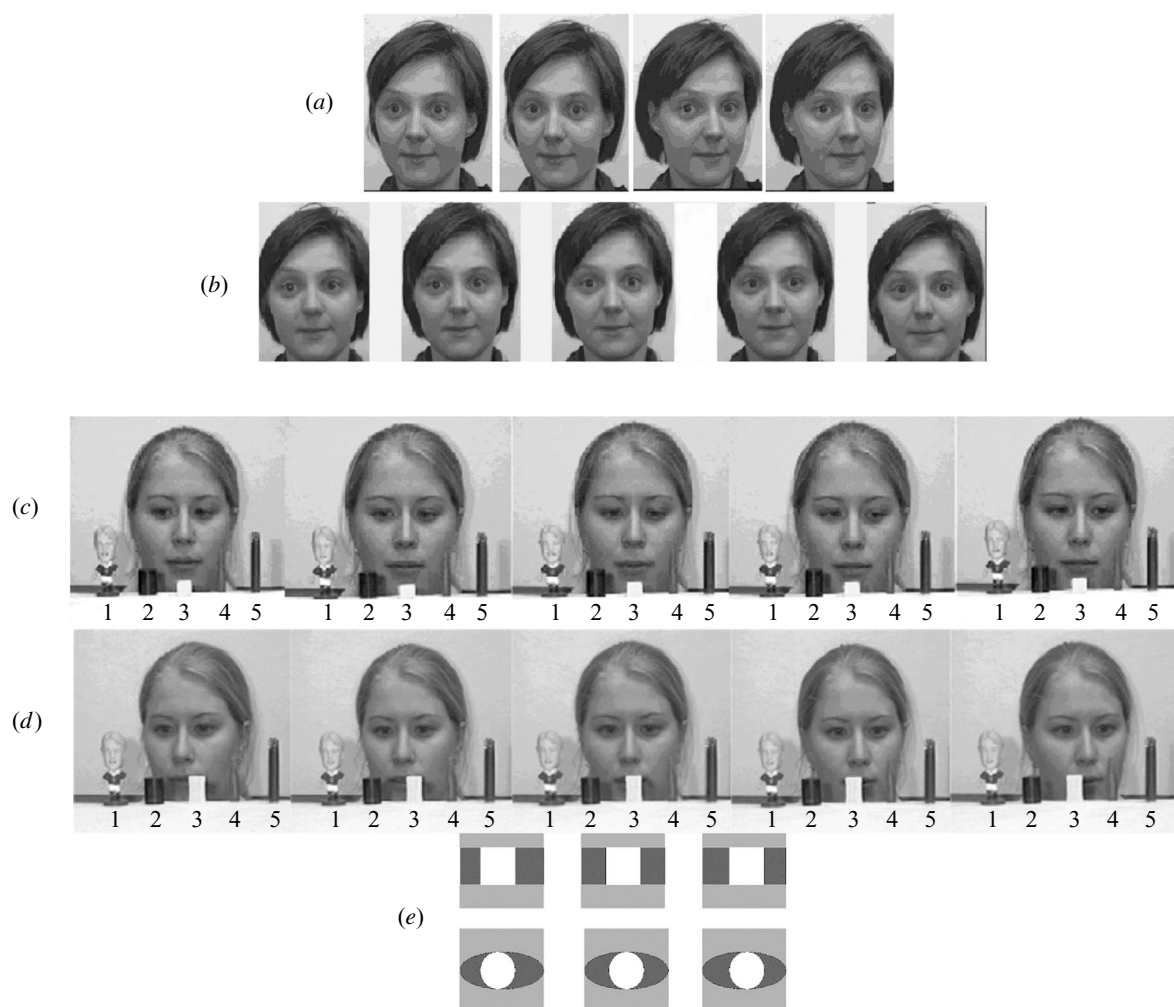


Figure 1. (a) Experiment 1: examples of head averted left and right with gaze averted and gaze to camera. (b) Experiment 1: head fixed, gaze left 10°; left 5°; 0°; right 5° and right 10°. (c) Experiment 2: head fixed, gaze left 10°; left 5°; 0°; right 5° and right 10°. (d) Experiment 2: head and gaze congruent: gaze left 10°; left 5°; 0°; right 5° and right 10°. (e) Experiment 3: examples of stimuli used. The task was to indicate whether the inner object was centrally placed within the outer one.

images of full faces looking at the viewer, as long as the contrast polarity (greyscale values) is preserved (Ricciardelli *et al.* 2000). One purpose of this study was therefore to compare accuracy in explicit detection of line-of-sight of a face under egocentric and allocentric viewing conditions, where the two experimental conditions used similar displays, both requiring fine discrimination of the angle of regard. Figure 1 shows a selection of images from relevant test sequences (not to scale). It should be noted that in both series, the position of the iris within the sclera is visible.

Three experiments were performed in which men and women of normal karyotype (46,XX and 46,XY), and women with TS (45,X) were compared. The first experiment examined accuracy in egocentric gaze. The task required the participant to detect whether a pictured full face engaged gaze ('is she looking at you?'). The second experiment used similar test materials, but tested allocentric gaze. The face inspected different locations in the picture plane, and did not engage gaze with the viewer. A final experiment served as a control task for the ability to calibrate the position of the iris in the sclera, which must be accurately assessed in order to determine line-of-sight. This required participants to detect the central positioning

of one small form embedded within another. The prediction was that women with TS may be impaired in the egocentric gaze task compared with controls. Predictions concerning performance on the allocentric and control tasks were open with respect to TS.

## 2. EXPERIMENT 1

### (a) Introduction

Does simple accuracy in detecting engagement of gaze vary with karyotypic status? Women with TS and control groups of men and women were shown images of a full face whose gaze was either to camera or averted left or right, and were asked to detect when the face engaged gaze ('is it looking at you?'). Similar displays to those used here, when shown to rhesus macaques, generated activity in neurons within the superior temporal regions (Perrett *et al.* 1985), and lesions to these regions specifically impaired gaze detection accuracy in monkeys (Campbell *et al.* 1990; Heywood & Cowey 1992). In humans, patients with right-hemisphere posterior lesions can show impairment in such tasks (Campbell *et al.* 1990), as do people with autism, both in childhood (Leekam *et al.* 1997) and as adults (Howard *et al.* 2000).

Table 1. Participant characteristics in experiments 1–3; means (and standard deviations).

	<i>n</i>	age (years)	WAIS performance	WAIS verbal
women 46,XX	34	24.08 (6.02)	110.5 (14.71)	100.68 (10.52)
men 46,XY	18	22.83 (4.48)	106.78 (11.94)	105.28 (8.47)
Turner syndrome 45,X	41	22.20 (6.76)	92.37 (16.49)	101.44 (11.70)

## (b) Methods

### (i) Participants

Forty-one individuals with TS were recruited through the Child Growth Foundation and through a specialist clinic at the Middlesex Hospital, London, UK. Karyotyping established that they had a single X chromosome. The TS group included women with a single X chromosome that was either maternal (45,X<sup>m</sup>, *n* = 29) or paternal (45,X<sup>p</sup>, *n* = 12). They were aged between 18 and 35 years. All participants were screened, and were included if they had a verbal intelligence quotient (IQ) above 80 and had no known neurological or psychiatric disease, including autism. Fifty-two volunteers (34 of them female), assumed to be of normal karyotype, aged between 19 and 35 years, were recruited from within London. Participants were excluded if they had known neurological or psychiatric disease or if they had lived in the UK for less than 3 years. Participant characteristics are summarized in table 1.

### (ii) Background tests

#### Performance IQ

The picture completion, block design and digit symbol subtests of the WAIS-R (Wechsler 1981) were administered, and scores pro-rated to provide an estimate of performance IQ (PIQ). The rationale for this short measure of PIQ was that these sub-tests provide the best overall correlation with the complete set of non-verbal IQ scores (Ward & Ryan 1996).

#### Verbal IQ

Four sub-tests of the WAIS were used: information, digit span (which is also related to verbal memory), arithmetic and similarities.

#### Experimental task

Head and neck photographs of a female sitter were digitally captured. The sitter inspected five locations in the plane of line-of-sight of the camera. These were: left 10° displacement from centre; left 5° displacement from centre; straight ahead; right 5° displacement from centre; and right 10° displacement from centre. Pilot testing indicated that a fully orthogonal design, systematically changing head and eye position (three head positions—left, right and ahead—and five inspection locations) was too difficult to resolve. For averted heads, therefore, only three inspection locations were digitally captured: ahead; left 10°; and right 10° (six images: two looking left; two looking right; and two looking ahead).

When the head faced forward, five positions were inspected (left 10°, left 5°, ahead, right 5° and right 10°), resulting in five images. The straight-ahead image from this series was duplicated, to give a total of six images, with two looking left, two looking right and two looking ahead. In this way, the number of images with head averted and head forward was matched, as was the number of lateral and straight-ahead gaze images. These were then mirror-reversed to give a total of 24 images used in the experiment proper (see figure 1*a,b*).

At the start of each trial, a fixation cross in the centre of the screen was replaced by a single, full-colour face image, *ca.* 10 cm × 15 cm, appearing in the centre of the grey screen at a viewing distance of *ca.* 50 cm. There were 24 trials in total, which appeared in a randomized order. Participants indicated whether they thought the person was looking at them or away from them by pressing the space-bar or the 'b' key on the keyboard. A practice session with three out-take images from the series, preceded the experiment proper. The dependent variable was accuracy of response (ahead or away).

## (c) Results

### (i) Group statistics

Group statistics are shown in table 1. The groups did not differ significantly in age or verbal IQ, but differed significantly in PIQ. Separate *t*-tests contrasted female controls and TS (*t* = 4.8, d.f. = 73, *p* < 0.01), and male controls and TS (*t* = 2.2, d.f. = 57, *p* < 0.05). This is in line with previous findings indicating relatively reduced spatial intelligence in TS (Temple & Carney 1995; Collaer *et al.* 2002). The strategy of including PIQ as a covariate in all group comparisons was used as the main means of controlling for any independent contribution of this factor to patterns of performance on the experimental tasks. It could be argued that the inclusion of the digit symbol subtest within the short form of the PIQ test loads primarily on perceptual speed, and may therefore 'dilute' any correlations with perceptual processing. However, as the three sub-test measure is believed to correlate most strongly with overall non-verbal intelligence (Ward & Ryan 1996), that is the one reported here. When, instead of the overall PIQ measure, individual sub-test measures of block design and of picture completion were used as covariates in the analyses reported, there were no material changes from the pattern reported here.

### (ii) Task analysis

#### Head orientation

The first analysis examined the effect of head orientation (head averted or forward) on accuracy of direct gaze decisions. This was a repeated measures analysis (SPSS GLM procedure), with karyotype as the between-subjects factor, head orientation as the within-subject factor, and PIQ as the covariate. The effect of the covariate did not reach significance. Means are shown in figure 2*a*. The effect of karyotype was significant ( $F_{2,89} = 13.22$ , *p* < 0.001), and was the only significant effect. There was no effect of head orientation (*F* < 0.5), and no interaction of the factors. The simple contrast analysis showed 45,X < 46,XX = 46,XY (*p* < 0.01).

#### Angular displacement

The women with TS may have been worse at this task because they used a different criterion for accepting or

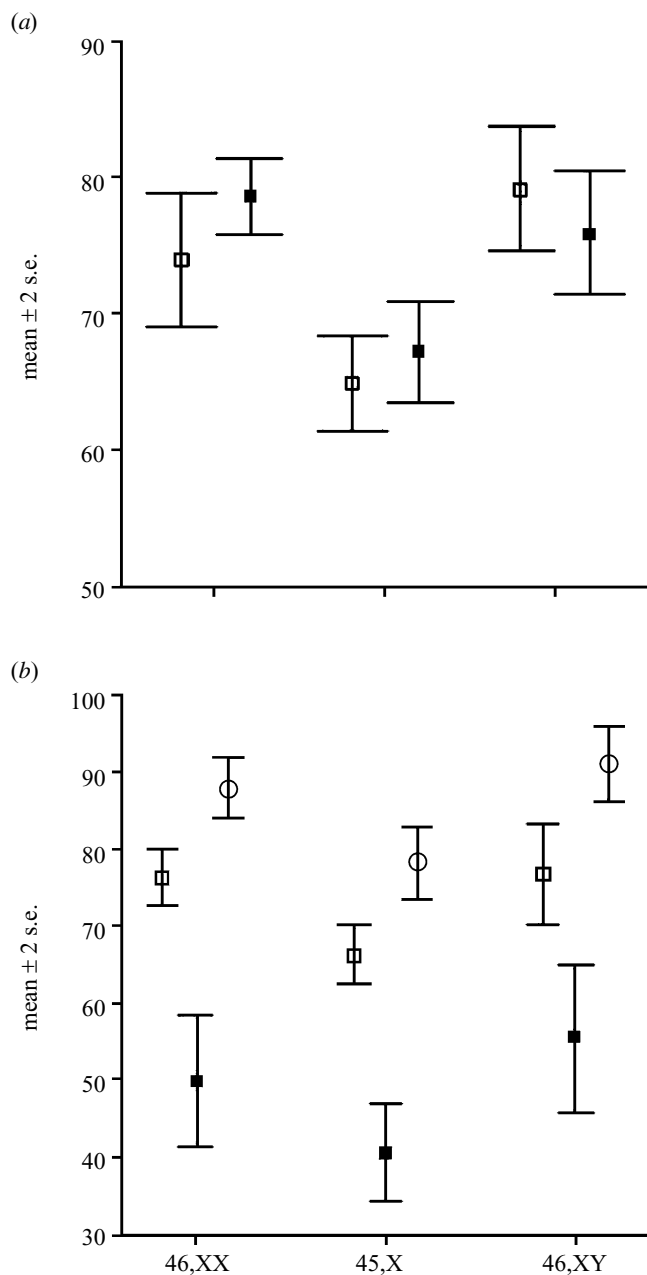


Figure 2. Experiment 1. 'Is she looking at me?' (a) Mean percentage accuracy as a function of head position. Open squares, head forward; closed squares, head averted. (b) Mean percentage accuracy as a function of angular displacement. Open squares, 10° ('no'); closed squares, 5° ('no'); open circles, 0° ('yes').

rejecting a face than controls. If this were the case, a different proportion of 'yes' and 'no' responses should be seen in this group. The data were recast, so that mean accuracy for each of the angular deviations (10°, 5° and 0°) was calculated for each participant. This distinguishes 'yes' (0°) and 'no' (5° and 10°) responses, summed across both head-averted and head-fixed conditions.

The analysis (SPSS-GLM repeated measures) examined angle of view (three levels), with karyotype as the between-subjects factor and PIQ as the covariate. Once again, a significant effect of karyotype was observed ( $F_{2,89} = 11.51$ ,  $p < 0.001$ ) and simple contrasts showed a significant impairment confined to the TS group,

45,X < 46,XX = 46,XY ( $p < 0.01$ ). In addition, there was a significant effect of angle: 5° accuracy was lower than either 10° or 0° ( $F_{1,89} = 4.37$ ,  $p < 0.04$ ). Means are shown in figure 2b.

However, there were no further effects, and importantly, no interactions of karyotype with angle of view. Women with TS did not have different confidence levels than controls, but were less accurate at all angles of regard, whether their responses were negative or positive.

#### (d) Discussion

##### (i) TS affects explicit social gaze accuracy

This experiment explored accuracy in the explicit use of direction of gaze to determine if viewers could accurately indicate when a pictured face was looking directly at the camera ('is she looking at you?'). Unlike more sophisticated readings of gaze, this task is, in principle, performable solely on the basis of the alignment of the eyes, and required no further abilities, such as determining mental or social disposition of the pictured face. This simple ability to use line of regard to detect whether a face engaged gaze was sensitive to karyotype. Unlike men and women in the control group, who did not differ from each other, women with TS were relatively poor at detecting engaged social gaze from a single pictured face. The deficit was not related to specific test conditions: they were equally impaired whether responding 'yes' or 'no', and were sensitive to the angular displacement of the head.

The women with TS had lower PIQ than the control groups. However, the social-gaze deficit survived covarying for PIQ, indicating that these were independent impairments within this syndrome.

### 3. EXPERIMENT 2

#### (a) Introduction

The previous experiment used images of a face that engaged gaze directly with the perceiver, or looked to one of four other horizontally displaced locations. In this second experiment, participants were required to make explicit decisions on the direction of line-of-sight of a pictured face, where it appeared to look down to one of five different locations. These images were similar in angle of view to those in experiment 1, and the face image (size and disposition) was similar to that experiment (figure 1c,d). The main differences from experiment 1 were, first, this task required the choice of one from five responses, whereas the previous response choice was dichotomous, and, second, neither the task ('where is she looking?'), nor the display, had a direct socio-affective component, for the face did not appear to engage gaze with the viewer at any time. The non-social dimension of the task was underlined by the presence in the pictured displays of small objects at each of the positions of regard. The only answer to the question 'where is she looking?' is therefore 'at the short white object' or 'to position number 3'.

If the deficit described in experiment 1 was due to a specific socio-cognitive impairment in egocentric gaze processing, then this task, requiring the calibration of line-of-sight between the looker and the position of attention of gaze may be performed normally by women with TS.

**(b) Methods****(i) Participants**

The same people participated in this experiment as in experiment 1 (table 1). The task was one of a battery of different face processing and psychometric tasks that were given in one session. The order of presentation (experiment 1 or experiment 2 first) was varied randomly across all participants.

**(ii) Experimental task: stimuli and procedure**

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 line-of-sight of the camera. The five locations captured were, as in the previous experiment: left 10° displacement from centre; left 5° displacement from centre; straight ahead, right 5° displacement from centre; and right 10° displacement from centre. In the first series of captured images, the head and eyes were aligned with respect to the direction of gaze. In the second series of images, the head was fixed facing the camera, and direction of gaze, alone, indicated line-of-sight. Thus, 10 images were captured for each of five angular positions, under two conditions of head position. A further 10 images were obtained by lateral reversal (mirror rotation) to create a total of 20 stimuli. 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 (see figure 1*c,d*).

The task was computer-controlled and delivered using in-house software on a 14 inch PC-laptop screen. At the start of each trial, a fixation cross in the centre of the screen was replaced by a single, full-colour face image, *ca.* 10 cm × 15 cm, appearing in the centre of the grey screen, at a viewing distance of *ca.* 50 cm. The experiment used each of the 20 images, twice, in a randomized order. Participants indicated the number corresponding to line of gaze by mouse click to the number position. A practise session, including five images of the same sitter that were not used in the experiment proper, preceded the experiment. The dependent variable was accuracy of response, scored as correct responses for each numbered position.

**(c) Results****(i) Head fixed versus head-eyes congruent**

Stimuli in this task included items where the head was fixed (ahead) and only eye direction varied, as well as items in which head orientation and eye orientation were congruent. Once again, a repeated-measures ANOVA (SPSS-GLM procedure) tested the hypothesis that the groups may differ in sensitivity to this factor. The group factor was karyotype. The within-subjects factor was accuracy as a function of head position (fixed or congruent). PIQ was again entered into the analysis as a covariate. Once again, this did not account for a significant amount of the variance. Relevant means are shown in figure 3. No main effects of group or of task were significant. The interaction of task (head position) and group was significant ( $F_{2,89} = 7.59$ ,  $p = 0.001$ ). One-way ANOVA confirmed that for the head-fixed condition, but not for the head-eyes-congruent condition, women with TS were significantly less accurate than either of the other groups ( $45,X < 46,XX = 46,XY$ , Scheffé tests, significant at  $p < 0.01$ ). Considering women with TS only, gaze direction when head position and eye position were congruent was judged more accurately than eye position when the

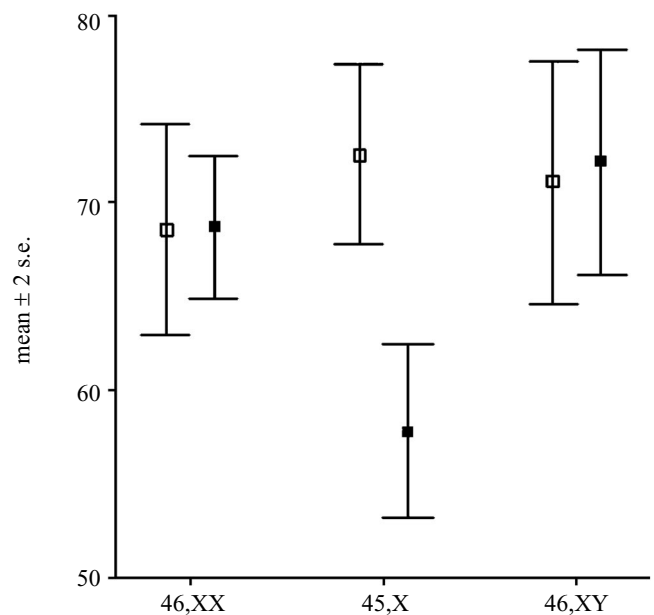


Figure 3. Experiment 2: effects of eye-head congruence 'where is she looking?' Open squares, head-eyes congruent; closed squares, head fixed.

head was fixed ( $t = 4.57$ , d.f. = 40,  $p < 0.001$ ). This contrast was not significant in either of the other groups.

**(d) Discussion**

In this experiment, which required participants to indicate where a face was looking within the picture plane, women with TS were as accurate, overall, as men and women of normal karyotype. This contrasts with their impairment in the egocentric gaze task of experiment 1. Superficially, then, it appears that egocentric gaze is affected by TS, but allocentric gaze is not. However, in women with TS, when the head was fixed, and eyes alone indicated location of gaze, there was a significant decrement in gaze accuracy. People of normal karyotype make relatively greater use of eye than head information in determining the locus of non-social gaze (Langton *et al.* 2000). However, head direction seems to offer a more reliable cue for women with TS.

Why should women with TS show a reduced ability to infer simple locations from the position of the eyes alone? Although performance on this task was analysed taking PIQ into account, it is possible that specific visual-processing difficulties may account for their problems. Visually guided action and mental imagery tasks can be impaired in TS (Ross & Zinn 1999), and we have noted that the resolution of direction of gaze from the eyes requires high levels of acuity. The final experiment was a control experiment to test this possibility.

**4. EXPERIMENT 3****(a) Introduction**

Visuo-spatial processing difficulties can characterize women with TS (e.g. Collaer *et al.* 2002). The analyses of experiments 1 and 2 indicated that covarying for PIQ did not account for the anomalies in gaze detection in the clinical group. However, could further general visual-processing impairments have a specific impact on accuracy

in detecting direction of gaze? If the position of the iris in the sclera is hard to judge for reasons of visual acuity or of spatial processing, then gaze-accuracy detection is likely to be sensitive to difficulty in this domain. In both experiments 1 and 2, women with TS were specifically impaired in tasks that required fine judgement of eye alignment, including the relative position of the pupil in the iris of the eye.

To test the proposal that a visual deficit may be implicated in the performance of women with TS on the gaze task, all participants were presented with a task that required them to judge the eccentricity of an embedded figure, and in which the display characteristics ensured similar visibility (i.e. visual angle) of the embedded form.

## (b) Method

### (i) Participants

Two female control subjects returned incomplete data. Otherwise, these were the participants who had completed experiments 1 and 2 (total  $n = 91$ ). This task was performed after the two gaze tasks.

### (ii) Experimental task

This task assessed the ability to judge the relative centrality of one shape within the other. The stimuli were greyscale rectangular ( $n = 18$ ) or oval ( $n = 18$ ) shapes, each of which was *ca.* 120 mm  $\times$  55 mm, containing a rectangular or circular form of *ca.* 55 mm diameter. The embedded shape was either centrally placed, or displaced by 1, 2 or 3 mm within the larger shape. There were nine forms for each shape presented vertically, and nine presented horizontally. Viewing distance was *ca.* 50 cm. Thus, the visual angle for discrimination was between  $0.02^\circ$  and  $0.06^\circ$ . Samples of the images are shown in figure 1*e*.

There were 36 trials, presented in random order. Participants mouse-clicked a response grid to indicate whether the smaller object was central, to the left, right, higher or lower, within the larger object. A practise trial preceded the experiment with three practise stimuli offered at random.

### (c) Results

Accuracy for each condition was analysed by repeated-measures ANOVA. The group factor was karyotype, and the within-subjects factor was task (four levels of angular displacement of the inner form:  $0^\circ$ ; 1 mm displacement; 2 and 3 mm displacements), with PIQ as covariate. Means are shown in figure 4.

There was a significant main effect of angular displacement ( $F_{3,87} = 4.4$ ,  $p < 0.01$ ). In this analysis, unlike previous ones, the covariate PIQ had a significant effect on outcomes ( $F_{1,87} = 10.49$ ,  $p < 0.01$ ). There were no further main effects and no interactions.<sup>1</sup> In particular, karyotype did not distinguish any of the conditions, either before or after covarying for PIQ.

### (d) Discussion

There is no suggestion from these results that group differences in visual sensitivity to small spatial displacement of embedded forms underlie the main group differences in gaze accuracy. Women with TS were as accurate as controls.

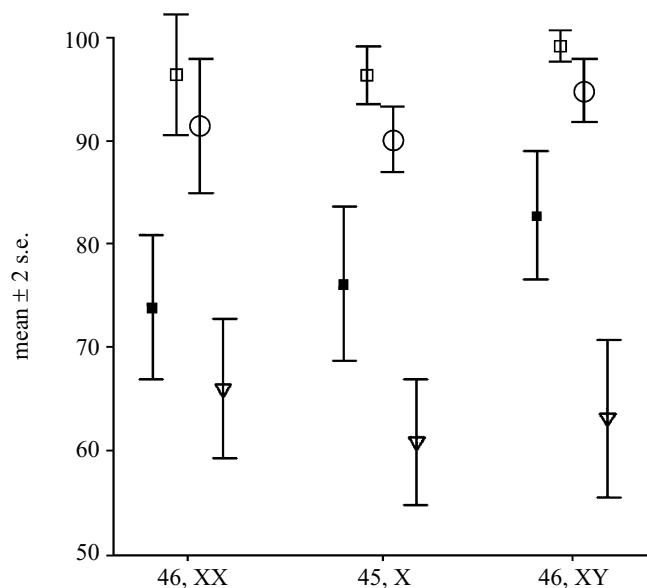


Figure 4. Experiment 3: accuracy in detecting object displacement from centre as a function of actual displacement. Closed squares, centre; open squares, 3 mm; open circles, 2 mm; open triangles, 1 mm.

## 5. GENERAL DISCUSSION

### (a) Direction of gaze accuracy is impaired in Turner syndrome

This investigation was initiated following the observation that women with TS can show social adjustment difficulties, with some autistic-like features of behaviour (Creswell & Skuse 2000).

No women with TS in this large sample fitted the diagnostic criteria for autism, nevertheless they showed general difficulties in analysing direction of gaze, reminiscent of those reported for people with autism. Two experiments to measure accuracy of gaze direction detection explored the extent to which a dissociation between egocentric ('is she looking at me?') and allocentric ('where is she looking?') gaze could be found. Despite the simple task requirements, which did not require that intention be imputed to the face, women with TS were impaired in the egocentric task, as has been reported for people with autism (e.g. Leekam *et al.* 1997), as well as in other groups with socio-cognitive dysfunction (Rosse *et al.* 1994). However, 45,X women were also significantly impaired when required to indicate a location of interest to the gazing face, and only the eyes (rather than the eyes and head together) were informative. It would seem that, when the task simply requires accurate discrimination of hard-to-distinguish angles of view, both a face engaging gaze with the viewer and a face looking at a location with gaze averted are perceived anomalously by women with TS. This may reflect developmental difficulties in ascribing social intention to facial gaze: which then generalize to a more widespread difficulty with gaze direction detection. This hypothesis will require testing with girls and children with TS. Whatever may be its cause, it seems unlikely that this pattern of disability directly reflected difficulty with the specific visual aspects of the task. The control experiment requiring detection of small degrees of eccentricity of an embedded figure was performed equally well by all

groups, and showed a direct effect of PIQ in all groups, which was absent for all the other tasks.

One implication of these findings is that, when tested appropriately, people with autism may show a similar pattern to that demonstrated here for TS.

### (b) *Plausible neural bases for 'gaze-reading'*

Circuitry involving the amygdala, orbito-frontal cortex and superior temporal sulcus constitutes a probable neurological basis for the development of different behavioural phenotypes related to gaze processing. This network has been implicated in the perceptual processing of a range of social behaviours (Brothers 1990), which neuroimaging studies show are preferentially activated in viewing face and especially eye-region actions (e.g. Allison *et al.* 2000; Calder *et al.* 2002).

Abnormalities of this circuit, and of its component parts, have been specifically implicated in people with autism (e.g. Abell *et al.* 1999; Baron-Cohen *et al.* 2000; Howard *et al.* 2000). Structural evidence is accumulating that this circuitry may be affected in TS (Good *et al.* 2001a). The amygdala, in particular, is highly sensitive to direct gaze (Kawashima *et al.* 1999) and is also replete with oestrogen-sensitive receptors (Toran-Allerand *et al.* 1999). Its development is sensitive to sex differentiation (Goldstein *et al.* 2001; Good *et al.* 2001b). Women with TS do not produce endogenous oestrogen, although all in this study received supplementation from puberty.

### (c) *Implications for understanding the influence of X-linked genes on socio-cognitive skills*

There is no indication that autism, the behavioural features of which guided the present study, has a single, specific genetic marker. Nevertheless, genetic endowment does appear to have a part in autism, with strong family linkages for autistic spectrum disorder, and some candidate genes suggested (Monaco & Bailey 2001). One recent claim (Baron-Cohen 2002) is that autism may represent the male end of the sexually dimorphic socio-cognitive behavioural continuum. This speculation itself indicates a role for X-expression in relation to the development of socio-cognitive and socio-perceptual abilities, and possibly, therefore to gaze sensitivity. However, TS may provide stronger evidence for the contribution of X-linked genes to social behaviour and to gaze, specifically. The behavioural phenotype of women with TS largely reflects inadequate dosage of X-linked gene products, expressed from both X chromosomes in normal females.

This study has demonstrated that women with TS are less accurate than men or women of normal karyotype at a simple task of judging accuracy in direction of eye gaze, and this was not related to other visuo-spatial difficulties. The development of social cognition may be indexed by gaze direction accuracy: both to the gazer and to where she is looking. The presence in the normal female karyotype of two complete X chromosomes may be an important factor that aids in the development of the ability to follow the 'talk of those turning eyeballs' (Walt Whitman, 'The Song of the Open Road' 1850).

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### ENDNOTE

<sup>1</sup>In a secondary ANOVA, only the 1 mm and centre conditions were examined. It was thought that the 3 mm and 2 mm conditions, which were performed quite accurately throughout, may have swamped any significant patterns. However, the secondary analysis failed to generate any further significant findings and corroborated the influence of PIQ.

### REFERENCES

- Abell, F., Krams, M., Ashburner, J., Passingham, R., Friston, K., Frackowiak, R., Happe, F., Frith, C. & Frith, U. 1999 The neuroanatomy of autism: a voxel-based whole brain analysis of structural scans. *NeuroReport* **10**, 1647–1651.
- Allison, T., Puce, A. & McCarthy, G. 2000 Social perception from visual cues: role of the STS region. *Trends Cogn. Sci.* **4**, 267–278.
- Anstis, S. M., Mayhew, J. W. & Morley, T. 1969 The perception of where a TV portrait is looking. *Am. J. Psychol.* **82**, 474–489.
- Baron-Cohen, S. 1995 *Mind-blindness: an essay on the psychology of autism*. Cambridge, MA: MIT Press.
- Baron-Cohen, S. 2002 The extreme male brain theory of autism. *Trends Cogn. Sci.* **6**, 248–254.
- Baron-Cohen, S., Campbell, R., Walker, J. & Karmiloff-Smith, A. 1996 Are children with autism blind to the mentalistic significance of the eyes? *Br. J. Dev. Psychol.* **13**, 379–398.
- Baron-Cohen, S., Ring, H. A., Bullmore, E. T., Wheelwright, S., Ashwin, C. & Williams, S. C. 2000 The amygdala theory of autism. *Neurosci. Biobehav. Rev.* **24**, 355–364.
- Brothers, L. 1990 The social brain: a project for integrating primate behaviour and neurophysiology in a new domain. *Concepts Neurosci.* **1**, 27–51.
- Calder, A. J., Lawrence, A. D., Keane, J., Scott, S. K., Owen, A. M., Christoffels, I. & Young, A. W. 2002 Reading the mind from eye gaze. *Neuropsychologia* **40**, 1129–1138.
- Campbell, R., Heywood, C. A., Cowey, A., Regard, M. & Landis, T. 1990 Sensitivity to eye gaze in prosopagnosic patients and monkeys with superior temporal sulcus ablation. *Neuropsychologia* **28**, 1123–1142.
- Collaer, M. L., Geffner, M. E., Kaufman, F. R., Buckingham, B. & Hines, M. 2002 Cognitive and behavioral characteristics of Turner syndrome: exploring a role for ovarian hormones in female sexual differentiation. *Hormones Behav.* **41**, 139–155.
- Creswell, C. & Skuse, D. 2000 Autism in association with Turner syndrome: implications for male vulnerability to pervasive developmental disorders. *Neurocase* **5**, 511–518.
- Dawson, G., Meltzoff, A. N., Osterling, J., Rinaldi, J. & Brown, E. 1998 Children with autism fail to orient to naturally occurring social stimuli. *J. Autism Dev. Disord.* **28**, 479–485.
- Elgar, K., Kuntsi, J., Campbell, R., Coleman, M. & Skuse, D. 2002 Face and emotion recognition deficits in Turner syndrome: a possible role for X-linked genes in amygdala development. *Neuropsychology*. (In the press.)
- Franck, N., Daprati, E., Michel, F., Saoud, M., Dalery, J., MarieCardine, M. & Georgieff, N. 1998 Gaze discrimination is unimpaired in schizophrenia. *Psychol. Res.* **81**, 67–75.
- Goldstein, J. M., Seidman, L. J., Horton, N. J., Makris, N., Kennedy, D. N., Caviness Jr, V. S., Faraone, S. V. & Tsuang, M. T. 2001 Normal sexual dimorphism of the adult

- human brain assessed by *in vivo* magnetic resonance imaging. *Cerebr. Cortex* **11**, 490–497.
- Good, C., Elgar, K., Kuntsi, J., Akers, R., Price, C., Ashburner, J., Friston, K., Frakowiak, R. & Skuse, D. 2001a Gene deletion mapping of the X chromosome. Human brain mapping 2001, Brighton. *NeuroImage* **13**, S793.
- Good, C. D., Johnsrude, L., Ashburner, J., Henson, R. N., Friston, K. J. & Frackowiak, R. S. 2001b Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains. *NeuroImage* **14**, 685–700.
- Heywood, C. & Cowey, A. 1992 The role of the 'face-cell' area in the discrimination and recognition of faces by monkeys. *Phil. Trans. R. Soc. Lond. B* **335**, 31–38.
- Howard, M., Cowell, P., Boucher, J., Broks, P., Mayes, A., Farrant, A. & Roberts, N. 2000 Convergent neuroanatomical and behavioural evidence of an amygdala hypothesis of autism. *NeuroReport* **11**, 2931–2935.
- Hutt, C. & Ounsted, C. 1966 The biological significance of gaze aversion with particular reference to the syndrome of infantile autism. *Behav. Sci.* **11**, 346–356.
- Kawashima, R., Sugiura, M., Kato, T., Nakamura, A., Hatano, K., Ito, K., Fukuda, H., Kojima, S. & Nakamura, K. 1999 The human amygdala plays an important role in gaze monitoring. A PET study. *Brain* **122**, 779–783.
- Langton, S. R. H., Watt, R. J. & Bruce, V. 2000 Do the eyes have it? Cues to the direction of social attention. *Trends Cogn. Sci.* **4**, 50–58.
- Leekam, S., Baron-Cohen, S., Perrett, D. I., Milders, M. & Brown, S. 1997 Eye-direction detection: a dissociation between geometric and joint attention skills in autism. *Br. J. Dev. Psychol.* **15**, 77–95.
- McCauley, E., Kay, T., Ito, J. & Treder, R. 1987 The Turner syndrome: cognitive deficits, affective discrimination, and behavior problems. *Child Dev.* **58**, 464–473.
- Monaco, A. P. & Bailey, A. J. 2001 Autism. The search for susceptibility genes. *Lancet* **358**(Suppl. S3).
- Perrett, D. I., Smith, P. A. J., Potter, D. D., Mistlin, A. J., Head, A. S., Milner, A. D. & Jeeves, M. 1985 Visual cells in the temporal cortex sensitive to face view and gaze direction. *Proc. R. Soc. Lond. B* **223**, 293–317.
- Ricciardelli, P., Baylis, G. & Driver, J. 2000 The positive and negative of human expertise in gaze perception. *Cognition* **77**, B1–B14.
- Ross, J. & Zinn, A. 1999 Turner syndrome: potential hormonal and genetic influences on the neurocognitive profile. In *Neurodevelopmental disorders* (ed. H. Tager-Flusberg), pp. 251–267. Cambridge, MA: MIT Press.
- Ross, J., Stefanos, G., Roeltgen, D., Kushner, H. & Cutler Jr, G. 1995 Ullrich–Turner syndrome: neuro-developmental changes from childhood through adolescence. *Am. J. Med. Genet.* **58**, 74–82.
- Rosse, R. B., Kendrick, K., Wyatt, R. J., Isaac, A. & Deutsch, S. I. 1994 Gaze discrimination in patients with schizophrenia: a preliminary report. *Am. J. Psychiat.* **151**, 919–921.
- Ruffman, T., Garnham, W. & Rideout, P. 2001 Social understanding in autism: eye gaze as a measure of core insights. *J. Child Psychol. Psychiat.* **42**, 1083–1094.
- Swettenham, J., Baron-Cohen, S., Charman, T., Cox, A., Baird, G., Drew, A., Rees, L. & Wheelwright, S. 1998 The frequency and distribution of spontaneous attention shifts between social and nonsocial stimuli in autistic, typically developing, and nonautistic developmentally delayed infants. *J. Child Psychol. Psychiat.* **39**, 747–753.
- Temple, C. M. & Carney, R. A. 1995 Patterns of spatial functioning in Turner syndrome. *Cortex* **31**, 109–118.
- Toran-Allerand, C. D., Singh, M. & Setalo, G. 1999 Novel mechanisms of estrogen action in the brain: new players in an old story. *Frontiers Neuroendocrinol.* **20**, 97–121.
- Turner, H. 1938 A syndrome of infantilism, congenital webbed neck, and cubitus valgus. *Endocrinology* **23**, 566–574.
- Ward, L. C. & Ryan, J. J. 1996 Validity and time saving in the selection of short forms of the Wechsler adult intelligence scale: revised. *Psychol. Assess.* **8**, 69–72.
- Weschler, D. 1981 *Adult intelligence scales (reduced)*. San Antonio, TX: Psychological Corporation.

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