Available online at www.sciencedirect.com
SCIENCE DIRECT®
Schizophrenia Research 67 (2004) 11–21
SCHIZOPHRENIA RESEARCH
www.elsevier.com/locate/schres

# Visual scanpath dysfunction in first-degree relatives of schizophrenia probands: evidence for a vulnerability marker?

Carmel M. Loughland[a,b,*], Leanne M. Williams[a], Anthony W. Harris[a,c]

[a] Cognitive Neuroscience Unit, School of Psychology and The Brain Dynamics Centre, University of Sydney, NSW 2006, Australia
[b] NISAD, Centre for Mental Health Studies, Discipline of Psychiatry, University of Newcastle, Callaghan, NSW 2308, Australia
[c] Prevention, Early Intervention and Recovery Service, Western Sydney Mental Health Service, Parramatta, NSW 2150, Australia

Received 30 November 2001; accepted 14 March 2003

**Abstract**

Previous research demonstrates that people with schizophrenia have abnormally 'restricted' visual scanpaths to face and facial expression stimuli, which appear to be diagnostically specific to schizophrenia [Schizophr. Res. 55 (2002) 159; Biol. Psychiatry 52 (2002) 338]. This study examined the familial transmission of 'restricted' scanpaths in first-degree relatives of schizophrenia subjects. We recorded visual scanpaths for 65 schizophrenia subjects, 37 biological first-degree relatives and 61 nonrelated 'healthy' control subjects in two experiments: 'face recognition' and 'facial affect recognition'. Concurrent behavioral tasks were face matching and expression matching, each under two multiple-choice conditions (seven or three options). As predicted, first-degree relatives generally showed an attenuated form of the markedly 'restricted' scanpaths of schizophrenia subjects across all face stimuli. The notable exception to this pattern was the relatives' extreme avoidance of facial features (compared to both schizophrenia and healthy control groups). Our results offer the first evidence that some components of visual scanpath dysfunction may represent a trait marker in the familial transmission of schizophrenia, but that first-degree relatives may have additional disturbances in social cognition associated with the perception of facial features.


*Keywords:* Visual scanpaths; Schizophrenia; First-degree relatives; Familial; Face; Emotion

## 1. Introduction

Disturbed face processing in schizophrenia is well documented, and is thought to underlie problems in interpersonal communication and social perception (Cramer et al., 1992). Parallel, but less severe, impairments are also observed in first-degree relatives (McCown et al., 1989; Toomey et al., 1999), suggesting that these disturbances may be associated with a familial vulnerability to schizophrenic disorder.

One of the candidate mechanisms for disturbed face perception in schizophrenia is a breakdown in the neurocognitive strategies for visual processing of face stimuli. The visual scanpath (pattern of eye movements and foveal fixations) provides an objective, real-time measure of the neurocognitive strategies individuals employ while viewing face stimuli.

* Corresponding author. Neuroscience Institute of Schizophrenia and Allied Disorders (NISAD), Centre for Mental Health Studies, University of Newcastle and Hunter Mental Health, Newcastle, NSW 2300, Australia. Tel.: +61-4024-6611; fax: +61-4924-6608.
*E-mail address:* cloughla@mail.newcastle.edu.au (C.M. Loughland).

0920-9964/$ - see front matter © 2003 Elsevier Science B.V. All rights reserved.
doi:10.1016/S0920-9964(03)00094-X

Previously, we examined the visual scanpath performance of schizophrenia vs. healthy control subjects. Schizophrenia subjects produced markedly 'restricted' scanpaths (Gordon et al., 1992), which were most apparent for face, compared to geometric and degraded (nonidentifiable) face-like stimuli (Manor et al., 1999; Williams et al., 1999). With regard to facial emotion, restricted scanpaths were most pronounced for positive (happy) and neutral compared to negative (sad) expressions (Loughland et al., 2002a). The replication of restricted scanpaths to face stimuli in other centres (Phillips and David, 1997, 1998; Streit et al., 1997) suggests that it is a robust index of schizophrenia impairments in face perception. Evidence from a comparison of schizophrenia and affective disorder suggests that it might also be specific to the diagnosis of schizophrenia (Loughland et al., 2002b). Scanpath studies of other disorders, albeit in some cases with non-face stimuli, also report disturbances that are quite distinct from those observed in schizophrenia (Bryant et al., 1995; Freeman et al., 2000).

To date, the extent to which visual scanpath disturbances represent a trait-based factor in a familial vulnerability to schizophrenia has not been examined. Evidence for the stability of these disturbances over time and illness progression points to their trait-like nature (Streit et al., 1997). Nevertheless, it has been noted that restricted scanpaths may normalize to some extent with treatment (Phillips et al., 1998).

Other measures of eye movement function suggest that an attenuated form of the restricted visual scanpath might be present in 'at-risk' familial samples. For instance, clinically healthy, biological, first-degree relatives show parallel, though less severe, oculomotor dysfunction (i.e., smooth pursuit eye movements) to their schizophrenia counterparts (Arolt et al., 1996; Crawford et al., 1998). First-degree relatives also show similar deficits in face perception (McCown et al., 1989; Toomey et al., 1999).

We predicted that first-degree relatives would display abnormal visual scanpaths (increased number and duration of fixations, reduced scanpath length), but less severe disturbances than their schizophrenia relatives, particularly in relation to facial affect stimuli. This pattern would be replicated in concurrent recognition tasks.

## 2. Methods

### 2.1. Subjects

A total of 63 schizophrenia subjects were recruited through hospital outpatients and community centres in Sydney, and 37 of their healthy biological first-degree relatives were recruited concurrently. The 61 nonrelated healthy control subjects were volunteers from the general community. Written informed consent (in accordance with NHMRC guidelines) was obtained from all subjects after the procedures were fully explained. Subjects had normal vision (assessed by Snellen chart). Exclusion criteria were a recent substance abuse history, epilepsy or other neurological disorders, mental retardation or head injury [assessed using Section M from Composite International Diagnostic Interview—CIDI (Robins et al., 1988), and the Westmead Hospital Clinical Information Base (WHCIB) questionnaire]. Sections G and P from the CIDI were used to confirm diagnoses of schizophrenia according to DSM-IV criteria (American Psychiatric Association, 1994). First-degree relatives and control subjects were assessed using the General Health Questionnaire (GHQ; Goldberg, 1972) and screened for a history of psychiatric illness or treatment using the WHCIB. The WHCIB was also used to obtain demographic information for participants.

Schizophrenia subjects (43 males, 20 females; mean age, 34.0, S.D. = 7.8 years) had a mean illness duration of 11.8 years (S.D. = 7.5 years). For medicated patients (33 on typical neuroleptics, 24 on atypical), the mean daily chlorpromazine equivalent (van Kammen and Marder, 1995, p. 2008) medication level was 608.7 mg (S.D. = 790.9 mg), and the dosage distribution was markedly positively skewed.

First-degree relatives (11 males, 26 females; mean age of 48.1, S.D. = 13.3 years) comprised 19 parents, 14 adult siblings and 3 adult children of people with schizophrenia. Within the relative and schizophrenia samples, there were 10 family groups (eight relative–schizophrenia pairings, one triad of two relatives and one schizophrenia subject and one quad comprising three relatives and one schizophrenia subject). All first-degree relatives were involved in a primary care role with their schizophrenia relative.

The healthy control group (17 males, 43 females) had a mean age of 25.7 years (S.D. = 10.7 years).

One-way ANOVAs revealed a group effect for age ($F_{(2,156)} = 52.74$, $p < 0.001$) but not years of formal education ($F_{(2,156)} = 0.098$, $p < 0.402$). Post hoc protected *t*-tests showed that first-degree relatives were significantly ($p < 0.05$) older than both schizophrenia and control subjects, and that schizophrenia subjects were also older than controls. There was a significant association between group and gender ($\chi^2_{(2,159)} = 24.8$, $p < 0.001$). Post hoc paired Fisher's exact comparisons showed the schizophrenia group to have a greater proportion of males than either the first-degree relatives (43 vs. 10, $\chi^2_{(1,99)} = 15.0$, $p < 0.001$) or healthy controls (43 vs. 17, $\chi^2_{(1,123)} = 19.6$, $p < 0.001$), reflecting the proportion accessing health services (Loughland et al., 2001). First-degree relative and healthy controls did not differ in gender distribution (10 vs. 17, $\chi^2_{(1,96)} = 0.05$). Both age and gender were, therefore, explicitly controlled for in the primary analyses.

### 2.2. Apparatus and stimuli

The stimuli and apparatus are described in detail elsewhere (Williams et al., 1999; Loughland et al., 2002a). Colour photographs of male and female models depicting 'neutral', 'happy' and 'sad' facial expressions were selected from a standardised series by Mazurski and Bond (1993) on the basis of highest inter-rater agreement for expression category, and equivalent intensity ratings. Degraded versions of 'neutral' face stimuli were constructed using a mosaic filter to produce a 'block portrait'.

Visual scanpaths were recorded using a CEDRIC Mark II eye gaze monitoring system. Retinal and corneal reflections produced by an infrared light were recorded from the right eye every 50 ms to obtain subjects' point of fixation (error of resolution less than 0.5°).

### 2.3. Procedure

Following previous protocols (Williams et al., 1999; Loughland et al., 2002a), a soft head restraint was used to minimize head movements. In each experiment, following calibration, subjects' viewed each face stimulus for 10 s. The experimental software ensured a central fixation before each presentation.

#### 2.3.1. Face recognition experiment

Subjects viewed a series of eight stimuli (two randomised exposures of each male and female nondegraded and degraded neutral face). Following scanpath recordings, accuracy for stimulus recognition was assessed by verbal report under two multiple choice conditions: (1) choice of seven photographs (six similar and one 'correct' face, all nondegraded) and (2) choice of only three photographs (two similar and one 'correct' face).

#### 2.3.2. Facial affect recognition experiment

Twelve stimuli (two randomised exposures of each male and female 'neutral', 'happy' and 'sad' faces) were presented, and affect recognition also assessed under two multiple-choice conditions following recording: (1) choice of correct affect from seven options (neutral, happy, sad, angry, surprise, disgust) and (2) choice from only three options (neutral, happy, sad).

### 2.4. Data analysis

Details of data analysis have been reported elsewhere (Williams et al., 1999; Loughland et al., 2002a).

Following previous procedures, scanpaths were analysed in terms of both temporal parameters (median fixation duration, total fixation duration and total number of fixations), spatial parameters (median distance between fixations, raw and fixation scanpath length) and spatio-temporal 'feature' indices (proportion of fixation number and duration to facial features. Features were defined by eyes ($1.5° \times 1.5°$.), nose ($1.5° \times 2.0°$) and mouth ($1.5° \times 1.0°$). A computerized cluster analysis of fixations to these regions provided feature indices, with values between $-1.00$ and 1.00 (positive values indicating a proportionately greater number of fixations or fixation duration to features, and negative values greater attention to nonfeatures).

Recognition accuracy data for the different expressions was analysed using ANOVA and *t*-tests.

Primary analyses of each scanpath parameter were conducted using mixed-design, repeated measures MANOVAs, with group as the between-subjects factor. The within-subjects factor was either stimulus (nondegraded vs. degraded) or affect (happy vs. neutral or sad vs. neutral). Preliminary analyses of family

status (first-degree relatives related vs. unrelated to a schizophrenia subject) were undertaken to rule out any effect on focal variables of interest. Preliminary MANOVAs with task (three vs. seven options) as a second within-subject factor were also conducted to ensure that the multiple-choice conditions did not have a differential effect on visual scanpaths.

Post hoc comparisons were conducted using protected *t*-tests. MANCOVA, chi-square and univariate analyses were used to examine the possible confounding effects of age, gender and medication on visual scanpaths.

## 3. Results

### 3.1. First-degree relative group

Independent group *t*-tests and chi-square analysis of family status (related vs. unrelated) showed that related first-degree relatives did not differ from unrelated first-degree relatives on age, sex distribution, education level or GHQ scores. MANOVAs for family status and scanpath parameters produced only isolated effects for fixation scanpath length and family status.[1] Family status groups did not differ in their pattern of associations between accuracy (face and facial affect recognition) and scanpath parameters. Schizophrenia relatives and nonrelatives were, therefore, combined into a single 'first-degree relative' group.

### 3.2. Accuracy data: face experiment

Experimental groups differed only in the seven-option accuracy condition for nondegraded neutral faces ($F_{(2,156)} = 11.0$, $p < 0.001$). Schizophrenia subjects were less (percent) accurate in this condition than both the relatives (48% vs. 76%, $t_{(97)} = 3.6$, $p < 0.001$) and controls (48% vs. 73%, $t_{(121)} = 3.9$, $p < 0.001$), who did not differ from each other. Recognition accuracy was consistently and significantly ($p < 0.05$) greater for nondegraded than for degraded faces within the seven-option condition.

[1] First-degree relatives of a schizophrenia subject produced comparatively longer scanpaths to nondegraded, but shorter to degraded neutral faces. They also had generally longer scanpaths across happy and neutral.

### 3.3. Accuracy data: facial affect experiment

Schizophrenia, first-degree relative and control groups differed significantly for facial affect recognition accuracy (happy: 81% vs. 94% vs. 92%; sad: 48% vs. 58% vs. 55%) in the seven-option condition for happy faces only ($F_{(2,156)} = 4.70$, $p < 0.01$). Protected *t*-tests confirmed that only the schizophrenia group were less accurate in this condition (relative: $t_{(97)} = 2.4$, $p < 0.02$; control: $t_{(121)} = 2.3$, $p < 0.02$). Within each group, paired *t*-tests confirmed that happy expressions were consistently associated with significantly ($p < 0.05$) greater recognition accuracy (compared to sad and neutral).

### 3.4. Scanpath data

There were significant but isolated task effects for four scanpath parameters for individual expressions, and a single group by task interaction for proportion of fixation duration to feature areas.[2] Given the general lack of task effects across the eight parameters and four types of face stimuli (with only an isolated interaction for group) we collapsed across the task factor in focal MANOVAs. The power to detect between-group interactions increased from 0.16 in preliminary analyses to 0.99 in focal MANOVAs.

Table 1 presents the means and standard deviations for the eight scanpath parameters for each stimulus across the three groups.

### 3.5. Scanpath data: face experiment

MANOVA results for degraded vs. nondegraded neutral face stimuli are summarized in Table 2.

These results confirmed the within and between-group scanpath patterns indicated in Table 1. Protected *t*-tests showed that the significant group main effects were due to the relatively 'restricted' scanpaths of schizophrenia subjects compared to both relatives and controls, reflected in significantly fewer

[2] There were significant ($p < 0.05$) task main effects for degraded face stimuli (median fixation duration, raw scanpath length), happy (raw and fixation scanpath length) and sad (fixation scanpath length) and a task by affect interaction for sad (raw scanpath length). The isolated group by task interaction ($p < 0.03$) for happy (proportion of fixation duration) was due to shorter duration for schizophrenia in the three-option condition.

Table 1
Group mean (and standard deviation) data for degraded and nondegraded neutral face stimuli, and happy and sad facial affect

| Scanpath parameters | Control group | | | | Schizophrenic group | | | | Relatives group | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Degraded | Neutral | Happy | Sad | Degraded | Neutral | Happy | Sad | Degraded | Neutral | Happy | Sad |
| Total number of fixation | 15.0 (2.8) | 14.8 (2.7) | 12.9 (2.8) | 14.2 (3.2) | 13.5 (2.8) | 12.3 (4.4) | 10.5 (4.5) | 11.3 (4.5) | 14.9 (4.0) | 14.5 (3.1) | 14.7 (3.2) | 14.7 (3.2) |
| Total fixation duration (ms) | 5629.9 (1032.7) | 5243.2 (1172.6) | 4834.0 (1196.6) | 5126.7 (1250.4) | 5818.6 (1128.5) | 5039.3 (1783.1) | 4371.2 (1703.0) | 4643.2 (1677.6) | 5875.2 (1523.1) | 5469.7 (1184.2) | 5591.5 (1197.1) | 5551.3 (1031.6) |
| Median fixation duration (ms) | 334.9 (56.6) | 320.5 (71.2) | 327.2 (69.4) | 321.0 (73.4) | 369.2 (65.7) | 371.0 (79.7) | 378.1 (90.3) | 377.4 (83.4) | 357.5 (71.5) | 329.8 (62.9) | 333.5 (71.0) | 342.8 (69.9) |
| Raw scanpath length[a] | 731.6 (234.0) | 812.2 (287.1) | 838.7 (375.0) | 782.9 (271.2) | 653.3 (428.1) | 615.1 (312.4) | 630.6 (311.5) | 593.3 (256.6) | 661.4 (291.5) | 728.8 (316.4) | 739.5 (419.1) | 713.5 (274.7) |
| Fixation scanpath length[a] | 211.8 (80.3) | 206.5 (62.8) | 177.9 (60.8) | 206.0 (67.2) | 154.0 (85.1) | 155.7 (66.7) | 136.6 (69.4) | 142.4 (71.9) | 232.2 (92.1) | 214.6 (77.4) | 216.9 (76.9) | 213.6 (79.6) |
| Median length between fixations[a] | 12.0 (4.1) | 11.5 (3.2) | 11.2 (3.2) | 11.4 (2.7) | 8.6 (3.7) | 10.4 (10.0) | 8.6 (3.2) | 8.6 (3.8) | 11.9 (4.1) | 11.8 (3.9) | 11.5 (4.1) | 11.2 (4.1) |
| Index of fixations to features vs. nonfeatures | −0.26 (0.22) | 0.26 (0.32) | 0.24 (0.29) | 0.26 (0.30) | −0.23 (0.36) | 0.04 (0.40) | 0.02 (0.36) | 0.16 (0.39) | −0.52 (0.24) | −0.28 (0.25) | −0.24 (0.28) | −0.32 (0.26) |
| Index of fixation duration to features vs. nonfeatures | −0.19 (0.24) | 0.35 (0.32) | 0.33 (0.31) | 0.33 (0.32) | −0.17 (0.39) | 0.13 (0.43) | 0.11 (0.41) | 0.22 (0.43) | −0.51 (0.27) | −0.24 (0.28) | −0.22 (0.30) | −0.29 (0.31) |

[a] CEDRIC coordinate = approximately 0.2° visual angle.

fixations (relative: $p < 0.003$; control: $p < 0.001$), with shorter fixation scanpath length (relative: $p < 0.001$; control: $p < 0.001$), and shorter median distance between fixations (relative: $p < 0.012$; control: $p < 0.002$). Schizophrenia subjects also produced a longer median fixation duration (control: $p < 0.001$), and shorter raw scanpath length (control: $p < 0.006$) than controls. Since schizophrenia subjects did not differ from the other groups on total fixation time, group differences appear due to a restricted scanning strategy rather than to a lack of foveal attention to stimuli.

Scanpaths for the first-degree relative group generally fell midway between those of schizophrenia and control groups. For a few parameters, relatives showed a slightly closer resemblance to controls and, therefore, differed significantly from schizophrenia subjects on fixation number ($p < 0.003$), fixation scanpath length ($p < 0.001$) and median length between fixations ($p < 0.01$). However, this pattern was notably reversed for the feature indices for which relatives showed the most extreme avoidance of features (eyes, nose, mouth) of all three groups. Relatives displayed a significantly reduced number of fixations to features compared to both schizophrenia ($p < 0.001$) and control ($p < 0.001$) groups, as well as comparatively reduced duration of fixations to features (controls: $p < 0.000$; schizophrenia: $p < 0.001$). By contrast, the schizophrenia group showed a reduced number ($p < 0.01$) and duration ($p < 0.02$) of fixations to features compared to controls only.

Significant main effects for stimulus were due to a tendency by all subjects to produce a shorter total (as well as median) fixation duration, and to attend relatively more to features for nondegraded neutral faces (Table 1). Typical scanpaths to degraded and nondegraded faces are depicted in Fig. 1a and b for healthy nonrelative subjects, Fig. 1c and d for schiz-

Table 2
Summary of MANOVA results for nondegraded neutral face vs. degraded face stimuli, happy vs. neutral and sad vs. neutral facial affect (significant effects only)

| Scanpath parameters | Sig. *F* (power) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Neutral vs. degraded faces | | | Happy vs. neutral affect | | | Sad vs. neutral affect | | |
| | Group main effect (G) | Stimulus main effect (S) | G × S interaction | Group main effect (G) | Affect main effect (A) | G × A interaction | Group main effect (G) | Affect main effect (A) | G × A interaction |
| Total number of fixation | 0.00 (0.98) | NS | NS | 0.00 (0.95) | 0.00 (0.99) | 0.00 (0.87) | 0.00 (0.95) | NS | NS |
| Total fixation duration (ms) | NS | 0.00 (0.99) | NS | 0.01 (0.72) | 0.00 (0.95) | 0.01 (0.72) | 0.04 (0.59) | NS | NS |
| Median fixation duration (ms) | 0.00 (0.95) | 0.04 (0.53) | NS | 0.00 (0.97) | NS | NS | 0.00 (0.97) | NS | NS |
| Raw scanpath length[a] | 0.02 (0.69) | NS | NS | 0.00 (0.91) | NS | NS | 0.00 (0.96) | NS | NS |
| Fixation scanpath length[a] | 0.00 (0.97) | NS | NS | 0.00 (0.96) | 0.00 (0.92) | 0.05 (0.58) | 0.00 (0.97) | NS | NS |
| Median length between fixations[a] | 0.00 (0.87) | NS | NS | 0.02 (0.68) | NS | NS | 0.01 (0.71) | NS | NS |
| Index of fixations to features vs. nonfeatures | 0.00 (1.0) | 0.00 (1.0) | 0.00 (0.95) | 0.00 (1.0) | NS | NS | 0.00 (1.0) | NS | 0.02 (0.68) |
| Index of fixation duration to features vs. nonfeatures | 0.00 (1.0) | 0.00 (1.0) | 0.00 (0.90) | 0.00 (1.0) | NS | NS | 0.00 (1.0) | NS | NS |

[a] CEDRIC coordinate = approximately 0.2° visual angle.

ophrenia subjects and Fig. 1e and f for first-degree relatives.

### 3.6. Scanpath data: facial affect experiment

MANOVA results for facial affect are also summarised in Table 2. Similar within- and between-group scanpath patterns emerged for facial affect. Protected *t*-tests confirmed that regardless of facial affect, schizophrenia subjects maintained a relatively more 'restricted' scanpath compared to the relatives and controls, characterized by significantly fewer fixations (happy: relative: $p < 0.001$, control: $p < 0.001$; sad: relative: $p < 0.001$; control: $p < 0.001$), of longer median duration (happy: relative: $p < 0.008$, control: $p < 0.001$; sad: relative: $p < 0.004$, control: $p < 0.001$), with a shorter fixation scanpath length (happy: relative: $p < 0.001$, control: $p < 0.001$; sad: relative: $p < 0.001$; control: $p < 0.001$) and median length between fixation (happy: relative: $p < 0.03$, control: $p < 0.01$; sad: relative: $p < 0.03$; control: $p < 0.01$). Schizophrenia subjects also produced a shorter raw scanpath length than controls (happy: control: $p < 0.001$; sad: control: $p < 0.001$), and a shorter fixation duration than relatives (happy: relative: $p < 0.002$; sad: relative: $p < 0.001$).

Scanpaths for the first-degree relatives again fell midway between that of schizophrenia and control

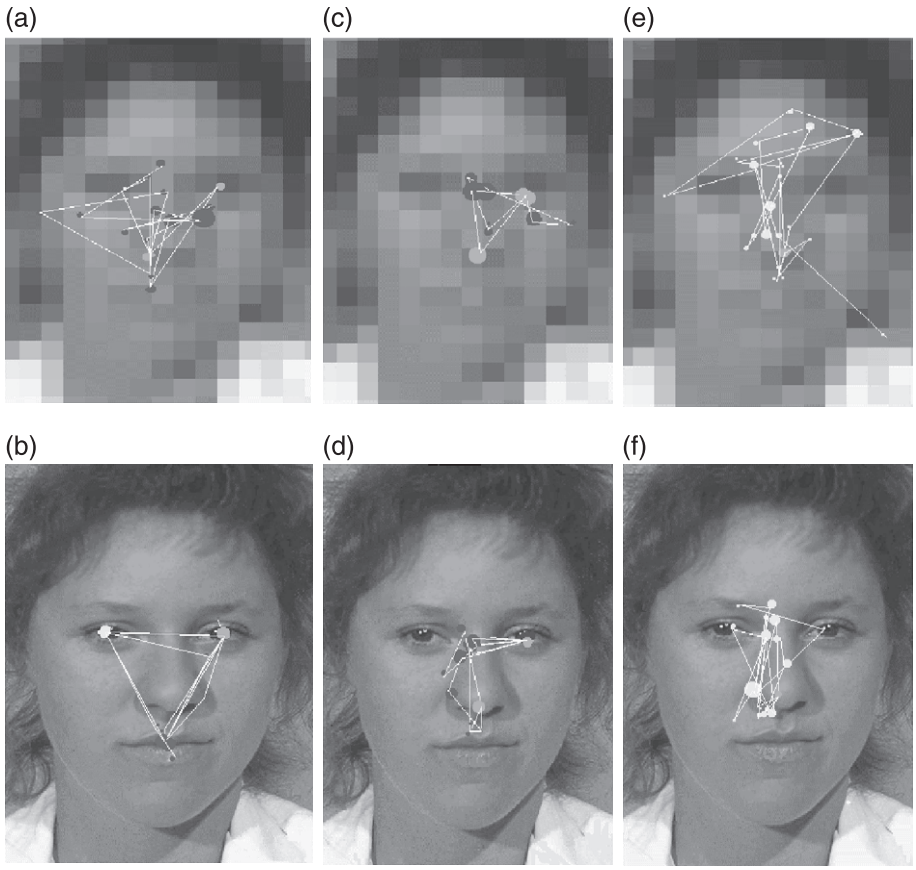


Fig. 1. Scanpaths to degraded (a) and nondegraded (b) face stimuli for a control subject. Scanpaths to degraded (c) and nondegraded (d) face stimuli for a schizophrenia subject. Scanpaths to degraded (e) and nondegraded (f) face stimuli for a control subject. Dot size indicates number of fixations.

subjects, and differed significantly from the schizophrenia group for both happy and sad faces on fixation number (happy: $p<0.001$; sad: $p<0.001$), fixation duration (happy: $p<0.002$; sad: $p<0.004$), median fixation duration (happy: $p<0.008$; sad: $p<0.01$), fixation scanpath length (happy: $p<0.001$; sad: $p<0.001$) and median length between fixations (happy: $p<0.001$; sad: $p<0.03$), and from the controls only on fixation duration for happy ($p<0.02$). For feature indices, relatives again exhibited the most pronounced avoidance of facial features, displaying a significantly reduced fixation number and duration to features for happy and sad (schizophrenia: $p<0.001$; control: $p<0.001$). Schizophrenia subjects again showed a reduced number (happy: $p<0.001$; sad: $p<0.004$) and duration (happy: $p<0.001$; sad: $p<0.008$) of fixations to salient features compared to the control group only.

Significant main effects for happy vs. neutral affect show that both schizophrenia and control subjects exhibited 'briefer' scanpaths characterized by fewer fixations ($p<0.001$), of shorter fixation duration (schizophrenia: $p<0.001$; control: $p<0.002$) and shorter fixation scanpath length (schizophrenia: $p<0.009$; control: $p<0.001$). Relatives, on the other hand, showed a slight increase in fixation number ($p<0.03$), fixation scanpath length ($p<0.000$) and fixation duration ($p<0.045$). Typical scanpaths to neutral, happy and sad faces are depicted in Fig. 2a and b for control subjects, Fig. 2c and d for schizophrenic subjects and Fig. 2e and f for first-degree relative subjects.

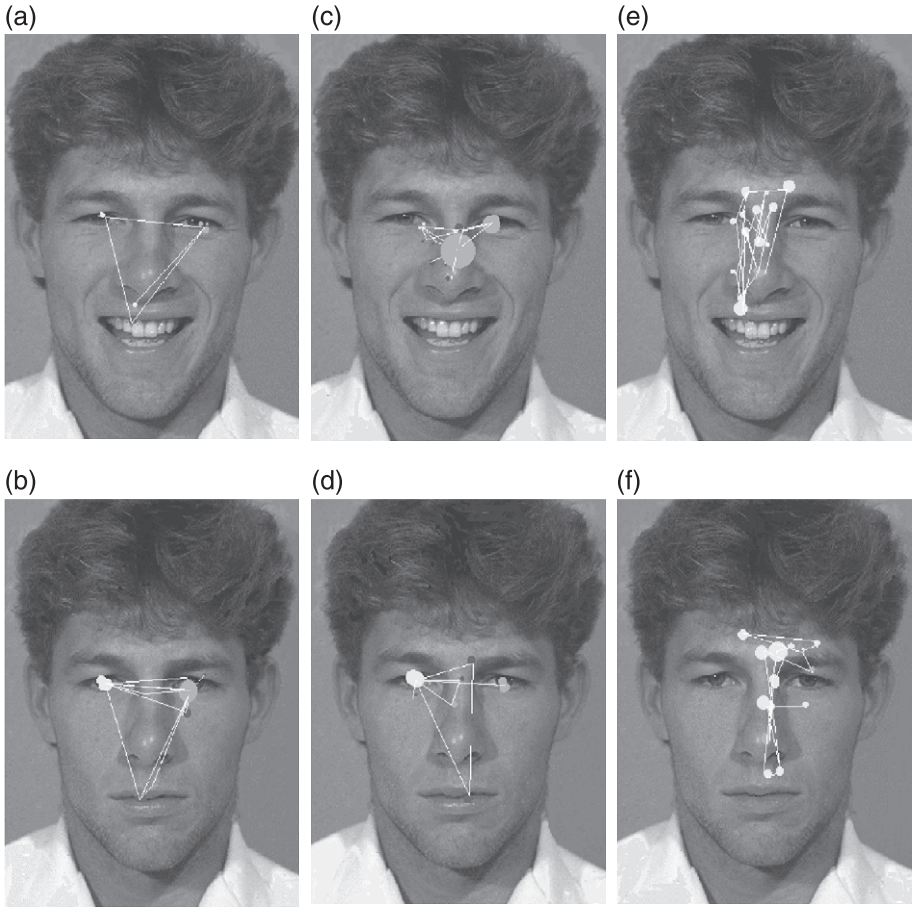


Fig. 2. Scanpaths to happy (a) and sad (b) face stimuli for a control subject. Scanpaths to happy (c) and sad (d) face stimuli for a schizophrenia subject. Scanpaths to happy (e) and sad (f) face stimuli for a first-degree relative subject. Dot size indicates number of fixations.

### *3.7. Analysis of possible confounding variables*

Given differences in the age and gender distribution across the three samples, MANCOVA analyses were conducted to examine the possible confounding effects of these variables on within- and between-group differences in scanpath parameters. Both age and gender covaried significantly with total number of fixations for degraded ($F_{(1,152)} = 4.09$, $p < 05$; $F_{(1,152)} = 6.99$, $p < 0.009$) compared to nondegraded, but only gender covaried significantly with this scanpath parameter for happy ($F_{(1,152)} = 4.09$, $p < 05$) and sad ($F_{(1,152)} = 4.09$, $p < 05$) faces compared to neutral. Gender also covaried significantly with fixation scanpath length for degraded ($F_{(1,151)} = 4.99$, $p < 0.03$) compared to nondegraded, and for happy ($F_{(1,150)} = 7.63$, $p < 0.006$) and sad ($F_{(1,152)} = 7.73$, $p < 0.006$) compared to neutral. However, in these analyses, the strongly significant effects for group, affect and the interactions between group and affect remained.

To further ensure that gender did not account for significant between group differences in scanpath performance, we conducted an additional set of MANOVAs with gender as the second grouping factor. In these analyses, there were no significant interactions between group and gender for any of the eight scanpath parameters across the four stimuli (degraded, nondegraded neutral, happy, sad), indicating that the initial between group findings were robust despite the differential gender distributions.

Chi-square analyses showed there were no significant associations between medication type and all eight scanpath parameters for degraded vs. nondegraded, happy vs. neutral and sad vs. neutral for the schizophrenia group.

## 4. Discussion

The study examined the familial transmission of scanpath aberrations to faces in schizophrenia by including a group of first-degree relatives of schizophrenia subjects as well as nonrelative healthy controls. The first experiment examined face-specific impairments by comparing scanpaths to degraded vs. nondegraded neutral faces, while the second experiment examined the effect of facial expressions of emotion.

For neutral face stimuli, the healthy subjects concentrated their fixations primarily on salient facial feature areas and displayed characteristically 'inverted triangular' scanpath patterns (see Figs. 1a and b) similar to those described by Noton and Stark (1971). Consistent with previous observations, schizophrenia subjects produced comparatively 'restricted' visual scanpaths (fewer fixations of longer median duration, shorter raw and fixation scanpath length and reduced distance between fixations) and a reduced attention to facial features (Williams et al., 1999; Loughland et al., 2002a). By contrast, relatives showed comparatively few disturbances in the general visual scanning of faces. However, relatives showed a striking and unexpectedly extreme avoidance of facial features, particularly for degraded faces, that was even more marked than that in schizophrenia subjects.

First-degree relatives showed a similarly extreme avoidance of salient features to facial expressions of emotion and to sad expression in particular. This pattern was in contrast to schizophrenia subjects who tended to focus more on the features of sad expressions despite a replication of the comparatively restricted scanpath style across facial expressions in general (Loughland et al., 2002a). Despite the lack of attention to facial feature areas, recognition accuracy remained generally unimpaired in first-degree relatives. Schizophrenia subjects, on the other hand, showed significant impairment in accuracy for all stimuli, particularly for the more difficult task. For facial emotion, relatives showed an additional distinctive pattern of increased fixation duration to happy expressions. Like healthy controls, schizophrenia subjects produced shorter (and fewer) fixations to happy vs. neutral and sad faces, consistent with the generally more holistic processing of happy expression (Kirita and Endo, 1995).

The differentiation of schizophrenia subjects and their first-degree relatives in terms of scanpath parameters clearly warrants replication before conclusive interpretations might be reached. However, one might speculate that the greater avoidance of features observed in relatives might reflect a trait factor of schizophrenia that is exacerbated in untreated first-degree relatives. That is, inattention to facial features in first-degree relatives might reflect the true extent of a trait problem in face processing, whereas this dysfunction may be somewhat attenuated (albeit still notably apparent) in schizophrenia due to ongoing treatment. There is substantial evidence that neuroleptic therapy can enhance concentration and attention in schizophrenia subjects (Green and King, 1998; Sweeney et al., 1994). While the present results indicate there are no effect on scanpath parameters from variation in medication dose, comparison of medicated with unmedicated samples in a future study would elucidate the effect of medication on visual scanpaths.

One speculation as to why foveal avoidance of features was particularly marked for sad expressions in first-degree relatives is that these individuals have learnt to avoid engagement in negative interactions. Relatives may learn, for instance, that engagement in such interaction could unnecessarily trigger symptoms (such as paranoia) in their affected family member.

Similarly, greater fixation on happy expressions in first-degree relatives might also reflect the social context effects of being a primary carer. That is, relatives may experience fewer interactions involving pleasant emotions, and thus tend to process happy expression in a more sequential manner than is usually the case (McKelvie, 1995).

Alternatively, specific scanpath abnormalities in first-degree relatives might also be a differential index of vulnerability to impairments in social cognition; particularly those associated with interpersonal com-

munication. Substantial evidence exists that communication (e.g., expressed emotion) is deviant in families of schizophrenia subjects (Hall and Docherty, 2000) although the extent to which these disturbances are the result of psychosis-proneness in family members or the consequence of relating to a mentally ill relative is unclear. Future studies of both relatives and nonrelative primary carers might help to determine if scanpath disturbances to faces are specific to first-degree relatives of schizophrenia probands or the secondary consequence of being the primary carer of a person with a severe mental illness.

This is the first study to document the visual scanpath performance of first-degree relatives of schizophrenia subjects. The observation that first-degree relatives tend to show an attenuated version of schizophrenia disturbances is consistent with the notion that scanpath abnormalities are associated with an underlying biological vulnerability to schizophrenia, particularly schizophrenia disturbances in social cognition. The additional observation of a particularly extreme avoidance of facial features in relatives suggests that these individuals experience further difficulties in social engagement, that might be a consequence of caring for a relative with schizophrenia.

## Acknowledgements

The authors would like to thank Chris Lisle and Dean Davidson, both from the School of Psychology, University of New England, Armidale, for their help with stimulus development and development of the face analysis program, respectively. We also thank those people who gave freely of their time to participate in this study. This research was supported by the Australian Research Council (ARC) and Rebecca Cooper Medical Research Foundation funding.

## References

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV). American Psychiatric Association, Washington, DC.

Arolt, V., Lencer, R., Nolte, A., Pinnow, M., Schwinger, E., 1996. Eye tracking dysfunction in families with multiple cases of schizophrenia. Eur. Arch. Psychiatry Clin. Neurosci. 246 (4), 175–181.

Bryant, R.A., Harvey, A.G., Gordon, E., Barry, R.J., 1995. Eye movement and electrodermal responses to threat stimuli in post-traumatic stress disorder. Int. J. Psychophysiol. 20, 209–213.

Cramer, P., Bowen, J., O'Niell, M., 1992. Schizophrenics and social judgement. Why do schizophrenics get it wrong? Br. J. Psychiatry 160, 481–487.

Crawford, T.J., Sharma, T., Puri, B.K., Murray, R.M., Berridge, D.M., Lewis, S.W., 1998. Saccadic eye movements in families multiply affected with schizophrenia: the Maudsley family study. Am. J. Psychiatry 155 (2), 1703–1710.

Freeman, D., Garety, P.A., Phillips, M.L., 2000. An examination of hypervigilance for external threat in individuals with generalized anxiety disorder and individuals with persecutory delusions using visual scanpaths. Q. J. Exp. Psychol., A 53 (2), 549–567.

Goldberg, D.P., 1972. The Detection of Psychiatric Illness by Questionnaire. Oxford Univ. Press, London.

Gordon, E., Coyle, S., Anderson, J., Healey, P., Corsaro, J., Latimer, C., Mearse, R., 1992. Eye movement response to facial stimulus in schizophrenia. Biol. Psychiatry 31, 626–629.

Green, J., King, D., 1998. The effects of chlorpromazine and lorazepam on abnormal antisaccade and no-saccade distractibility. Biol. Psychiatry 44, 709–715.

Hall, M., Docherty, N., 2000. Parent coping styles and schizophrenia patient behavior as predictors of expressed emotion. Fam. Proc. 39, 435–444.

Kirita, T., Endo, M., 1995. Happy face advantage in recognizing facial expressions. Acta Psychol. 89, 149–163.

Loughland, C.M., Carr, V., Lewin, T.J., 2001. The NISAD schizophrenia research register: why do we need a database of schizophrenia volunteers? Aust. N. Z. J. Psychiatry 35, 660–667.

Loughland, C.M., Williams, L.M., Gordon, E., 2002a. Visual scanpaths to positive and negative facial emotion in an outpatient schizophrenic sample. Schizophr. Res. 55, 159–170.

Loughland, C.M., Williams, L.M., Gordon, E., 2002b. Schizophrenia and affective disorder show different visual scanning behaviour for faces: a trait verse state-based distinction? Biol. Psychiatry 52, 338–348.

Manor, B.R., Gordon, E., Williams, L.M., Rennie, C.J., Bahramali, H., Latimer, C.R., Barry, R.J., Meares, R.A., 1999. Eye movements in schizophrenia and non-psychiatric controls, processing geometric and neutral face stimuli. Biol. Psychiatry 46, 963–969.

Mazurski, E.J., Bond, N.W., 1993. A new series of slides depicting facial expressions of affect: a comparison with the pictures of facial affect series. Aust. J. Psychol. 45, 41–47.

McCown, W., Johnson, J., Austin, S., Shefsky, M., 1989. Deficits in ability to decode facial affects in families of schizophrenics. Psychother. Priv. Pract. 6 (4), 93–101.

McKelvie, S., 1995. Emotional expression in upside-down faces: evidence for configurational and componential processing. Br. J. Soc. Psychol. 34, 325–334.

Noton, D., Stark, L., 1971. Eye movements and visual perception. Sci. Am. 224, 35–43.

Phillips, M.L., David, A.S., 1997. Visual scan paths are abnormal in deluded schizophrenics. Neuropsychologia 35 (1), 99–105.

Phillips, M.L., David, A.S., 1998. Abnormal visual scan paths: a psychophysiological marker of delusions in schizophrenia. Schizophr. Bull. 29, 235–245.

Phillips, M.L., Bullmore, E., Howard, R., Woodruff, P.W., Wright, I.C., Williams, S.C., Simmons, A., Andrew, C., Brammer, M., Davis, A.S., 1998. Investigation of facial recognition memory and happy and sad facial expression perception: an fMRI study. Psychiatry Res. 28, 127–138.

Robins, L.N., Wing, J., Wittchen, H.U., Helzer, J.E., Babor, T.F., Burke, J., Farmer, A., Jablenski, A., Pickens, R., Reiger, D.A., Sartorius, N., Towle, L.H., 1988. The composite international diagnostic interview. Arch. Gen. Psychiatry 45, 1069–1077.

Streit, M., Wölwer, W., Gaebel, W., 1997. Facial affect recognition and visual scanning behaviour in the course of schizophrenia. Schizophr. Res. 24, 311–317.

Sweeney, J.A., Haas, G.L., Li, S., Weiden, P.J., 1994. Selective effects of antipsychotic medication on eye-tracking performance in schizophrenia. Psychiatry Res. 54, 185–198.

Toomey, R., Seidman, L., Lyons, M., Faraone, S., Tsuang, M., 1999. Poor perception of nonverbal social–emotional cues in relatives of schizophrenic patients. Schizophr. Res. 40 (2), 121–130.

van Kammen, D.P., Marder, S.R., 1995. Dopamine receptor antagonists. In: Kaplan, H.I., Sadock, B.J. (Eds.), Comprehensive Textbook of Psychiatry, 6th ed., vol. 2. Williams and Wilkins, Baltimore.

Williams, L.M., Loughland, C.M., Gordon, E., Davidson, D., 1999. Visual scanpaths in schizophrenia: is there a deficit in face recognition? Schizophr. Res. 36, 189–199.