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ORIGINAL PAPER

Social Escape Behaviors in Children with Fragile X Syndrome

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Abstract Social escape behavior is a common behavioral feature of individuals with fragile X syndrome (fraX). In this observational study, we examined the effect of antecedent social and performance demands on problem behaviors in four conditions: face-to-face interview, silent reading, oral reading and a singing task. Results showed that problem behaviors were significantly more likely to occur during the interview and singing conditions. Higher levels of salivary cortisol were predictive of higher levels of fidgeting behavior and lower levels of eye contact in male participants. There were no associations between level of FMRP expression and social escape behaviors. These data suggest that specific antecedent biological and environmental factors evoke social escape behaviors in fragile X syndrome.

Keywords Social escape · Eye contact · Fragile X syndrome · Cortisol

Introduction

Over the past decade, studies examining the determinants of problem behaviors in children with developmental disabilities have begun to focus on the analysis of gene–brain-behavior relations (Kennedy, Caruso, & Thompson, 2001; Reiss & Dant, 2003; Schroeder et al., 2001). This interest has been spawned by the observation that individuals diagnosed with particular genetic syndromes appear to show higher levels of problem behaviors than would be expected in individuals matched for developmental age but without a diagnosis of a syndrome (Bodfish & Lewis, 2002). For example, self-biting in individuals with Lesch-Nyhan syndrome (Christie et al., 1982), stereotypic hand-wringing in Rett syndrome (Hagberg, Aicardi, Dicas, & Ramos, 1983), skin-picking in Prader-Willi syndrome (Thornton & Dawson, 1990), self-hugging in Smith-Magenis syndrome (Finucane, Konar, Haas-Givler, Kurtz, & Scott, 1994), gaze aversion in individuals with Fragile X syndrome (Cohen et al., 1988) and excessive laughing and smiling in Angelman syndrome (Summers, Allison, Lynch, & Sandler, 1995) have all been considered almost inevitable behavioral manifestations of these syndromes. Studies concerned with these ‘‘behavioral phenotypes’’ appear to implicate specific genes in the genesis of these behaviors.

Alongside this development, a large body of literature has emerged documenting the influence of environmental factors on behavior disorders shown by individuals with developmental disabilities (Carr & Durand, 1985; Durand & Carr, 1987; Hanley, Iwata, & McCord, 2003; Iwata et al., 1994). These studies have shown that many behavior disorders are influenced by antecedent and consequent social-environmental events (e.g. antecedent task demands, contingent removal of task demands) and that manipulation of these environmental events can dramatically reduce the occurrence of these problem behaviors (Call, Wacker, Ringdahl, Cooper-Brown, & Boelter, 2004; Pelios,

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Morren, Tesch, & Axelrod, 1999; Taylor & Carr, 1992). In a large sample of 152 individuals with developmental disabilities who showed self-injurious behavior (SIB), for example, Iwata and colleagues (Iwata et al., 1994) found that in 64% of cases, problem behaviors were maintained by social-environmental reinforcement contingencies (e.g. removal of task demands, delivery of attention), and that in a further 25% of cases, SIB was evoked by antecedent non-social environmental events (e.g. low levels of environmental stimulation). Similar results were obtained in a group of 79 individuals with developmental disabilities who showed SIB, aggression and stereotypic behavior (Derby et al., 1992).

Given these data, it is perhaps surprising that so few studies have directly manipulated social-environmental events in individuals with specific genetic syndromes to examine the possible environmental determinants of behaviors common to those syndromes. In one study involving a young girl with Rett syndrome, Oliver and colleagues (Oliver, Murphy, Crayton, & Corbett, 1993) systematically manipulated levels of antecedent social and task demands to examine the effect of these events on the girl's mouth-flicking and mouth-hitting behavior. Observations showed that the girl's mouth flicks were evoked by low levels of environmental stimulation whereas the girl's mouth-hits were evoked by the level of antecedent social demands that the girl received from the experimenter. These data suggested that, in the past, the girls' mouth-flicking behaviors may have been shaped into mouth-hitting behavior by the process of negative reinforcement. Anderson, Dancis, and Alpert (1978) found that in Lesch-Nyhan syndrome, self-biting increased in frequency when the behavior resulted in the delivery of contingent parental attention and decreased when the behavior was ignored or when attention was delivered contingent on the absence of SIB, suggesting that the self-biting may have been maintained by the process of positive reinforcement. These data are supported by the results of a follow-up study of three young boys with Lesch-Nyhan syndrome, in which Hall and colleagues (Hall, Oliver, & Murphy, 2001) found that hand-biting was significantly more likely to occur when parental attention was occurring at low levels. Taken together, these preliminary data suggest that genetic predisposition for particular behavior problems in children may be shaped and maintained by environmental events in the same manner as those individuals without a genetic disorder.

To date, few studies have documented the influence of social-environmental events on the occurrence of problem behaviors shown by individuals with fraX. FraX is the most common known inherited cause of developmental disability affecting approximately 1 in 4000 males and 1 in 8000 females in the general population (Crawford et al., 1999). The syndrome is caused by a mutation to the *FMR1* gene on the long arm of the X chromosome at Xq27.3 (Verkerk et al., 1991). The gene contains a sequence of CGG nucleotides that repeats approximately 5–45 times in unaffected individuals but can expand to over 1000 repeats in length in persons affected by the disorder. If the sequence expands to between 55 and 200 repeats, individuals display few or no symptoms of the disorder, but are considered to be carriers of the premutation form of the gene and are at risk for passing the mutation on to their offspring. If the sequence expands to over 200 repeats, however, individuals have the full mutation of the disorder and hyper-methylation of the promoter region of the gene is highly probable. Methylation of the gene switches off the production of the "fragile X mental retardation protein" (FMRP), the protein product of the *FMR1* gene. FMRP is thought to actively participate in the translational machinery that converts messenger RNA into protein. Thus, it is the lack of FMRP that appears to increase risk for the physical, cognitive and behavioral manifestations of the disorder (Taylor et al., 1994). In addition, it has been also suggested that the hypothalamo-pituitary-adrenal (HPA) axis may be dysfunctional in individuals with fraX (Hessl et al., 2002) which may explain why some individuals with fraX appear to show high levels of anxiety during social situations. Investigation of the biological and environmental determinants of problem behaviors shown by children affected with fraX may therefore offer a unique opportunity to examine the interaction of these factors in the determinants of these behaviors.

Several studies have shown that a common behavioral feature of individuals with fraX is their propensity to engage in social escape behaviors. To examine the social determinants of escape behaviors in fraX, Cohen and colleagues (1988) devised antecedent conditions in which 12 young males were observed while interacting with their mothers for 10 min and then while interacting with a stranger for 10 min. Observations conducted of the children turning their body away from the adult, running away from the adult, looking away from an assigned task and/or not looking at the adult showed that children with fraX engaged in significantly higher levels of these escape behaviors compared to individuals with Down syndrome, autism and typically developing children. Interestingly, children with fraX showed significantly higher levels of escape behaviors while interacting with the stranger, in comparison to a group of individuals with autism who showed comparable levels of escape behaviors in both conditions.

In a more recent study of social escape behavior involving 21 females with fraX, Lesniak-Karpiak, Mazzocco, and Ross (2003) devised several antecedent conditions, one of which involved participants initiating a conversation with an unfamiliar experimenter for 2 min. These authors coded eye contact avoidance, body posture, hand wringing, facial movements, and fidgeting using a 15-s partial interval recording system. Results showed that individuals with fraX took longer to initiate the conversation with the experimenter and that hand wringing and facial movements occurred at higher levels than in a comparison group of typically developing females.

Given the paucity of observational studies examining the environmental determinants of problem behaviors in children with fraX, in the present study, we manipulated levels of antecedent social and performance demands to examine the effect of these environmental events on observed levels of social escape behaviors in both males and females with fraX. For the purposes of the present study, we defined social escape behavior as any participant response that appeared to be evoked by antecedent social stimuli and that these responses would usually have been followed by the removal of these stimuli. Immediately prior to these environmental manipulations, we also measured levels of salivary cortisol in order to determine whether higher cortisol levels (a measure of HPA axis dysfunction) would be predictive of subsequent social escape behavior. We also measured blood levels of FMRP in all children. We hypothesized that situations involving high levels of social and performance demands would evoke specific escape behaviors in both males and female children with fraX. We also hypothesized that the level of social escape behaviors would depend on the children's level of salivary cortisol and/or level of FMRP. Finally, we sought to determine whether repeated prompts for eye contact would generate increased levels of eye contact in these children. Uncovering the biological and environmental determinants of behavior problems in fraX could have significant implications for understanding the causes of behavior problems in fraX and could lead to improvements in the design of interventions for the reduction and elimination of these behaviors.

Method

Participants

Participants were 114 children with fraX (74 males and 40 females) aged between 6 and 17 years of age (males: $M = 11.06$, SD = 2.68; females: $M = 10.42$, SD = 3.10). The ethnic distribution of the study sample was 91.2% Caucasian, 2.6% Hispanic, 2.6% African-American, 1.8% Asian, .9% Pacific Islander and .9% Multi-ethnic. Seventy-two (60%) participants were taking medication at the time of the assessment. Medications primarily included: stimulants (40% of the sample), antidepressants (27%), antihypertensives (4%), and antipsychotics (3%). Eighteen percent of the participants were taking more than one class of medication. Fragile X diagnoses of all children were confirmed by Southern Blot DNA analysis as detailed by Taylor et al. (1994). Seventeen (23%) males and four (10%) females were mosaic for fraX. Fragile X Mental Retardation Protein (FMRP) analyses were conducted on all blood samples using the method devised by Willemsen et al. (1997). Mean percentage FMRP for male and females participants was 12.34% (SD = 11.81, range = 1.5–74%) and 51.03% (SD = 18.57, range = 14.0–77.7%), respectively. On the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cicchetti, 1984), a widely used measure of adaptive skills, the mean standard score for male and female participants was 42.12, (SD = 13.32) and 69.20 (SD = 20.16), respectively. Participants were recruited from across the United States (West: 28.9%, South: 26.3%, Northcentral 24.6%, NorthEast: 15.8%) and Canada (4.4%). Written informed consent was obtained from the parents of all participants and assent was obtained when the children understood the procedure.

Procedure

Two researchers arrived at each participant's home at 8 am, and conducted a series of cognitive and behavioral evaluations throughout the day with the child with fraX, their unaffected sibling and the child's parents. Data for the current study pertains to a videotaped session that was conducted with the child with fraX. All sessions were conducted in an appropriate room in the child's home at approximately 3 pm. Each child was asked to sit down on a chair or sofa and to remain seated until the session had finished. Sessions lasted approximately 15–20 min during which the experimenter (who had engaged in minimal social interaction with the participant before), the camera operator (who had administered the cognitive test battery to the child in the morning) and the child's parents were present in the room. The experimenter sat in a chair 1–3 feet away from the participant and the camera operator stood several feet away from the interviewer, remaining as unobtrusive as possible. All sessions were videotaped and transferred to DVD for later analysis. In order to measure cortisol levels, immediately prior to each session, a sample of the child's saliva was collected using a salivette device (Sarstedt, Inc). Participants were asked to place a 1.5 inch cotton roll into their mouth for 1–2 min and to think of their favorite food. After the sample had been taken, the salivette was placed in the household freezer and subsequently mailed via overnight mail to the research office. Salivettes were centrifuged at 4000 rpm for 5–7 min and the recovered samples were then placed in a freezer until shipped to the assay laboratory (Fairview Unversity, MN, USA). The saliva was processed using the Magic Cortisol radioimmunoassay kit (Bayer, Tarrytown, NY, USA). All cortisol levels were measured in micrograms/deciliter (μg/dl) (Hessl et al., 2002).

Each child was exposed to four experimental conditions presented in the same order; Interview, Silent Reading, Oral Reading, and Singing. In the *Interview* condition, the experimenter said: "The first thing we are going to do is have a conversation, or talk to each other. The main thing I would like you to do is to maintain eye contact, or look into my eyes as much as possible." After a brief pause to ensure that the camera operator was ready, the experimenter began the interview by shaking hands with the participant and then asking a question such as, "How are you doing today?", "Have you seen any movies lately?", "Do you have any hobbies?" and if appropriate for the child's age, questions such as "Where are you from?", "How old are you?". If the participant did not respond, the interviewer asked another question. Throughout the interview condition, the experimenter reminded the participant to maintain eye contact using prompts such as "Remember to look at me" or "You need to look at my eyes". The experimenter also sometimes requested eye contact when the child was already looking at the experimenter. Recording began when the experimenter introduced him/herself.

In the *Silent Reading* condition, the experimenter told the participant, "The next thing I want you to do is to read letters or words silently to yourself." Following a brief pause, the interviewer handed the child a piece of paper containing the reading material and asked him/her to begin reading. Depending on the reading level of the child, the material either consisted of a series of letters from the alphabet, three-letter words, simple short-sentences (words no longer than four letters), or a passage taken from a novel. The reading level of each child was estimated from the cognitive tests that had been administered to the child in the morning of the evaluation day. Males with fraX were given single letters, words or short sentences to read (e.g. "the girl says no") whilst females with fraX were given either short sentences or passages to read (e.g. "One sunny day, the animals were talking..."). If the child appeared to be having difficulty with the material, the experimenter exchanged it for material at an easier level. The experimenter reminded the child to let him/her know when he/she was finished reading the material. Recording began when the experimenter handed the participant the reading material.

In the *Oral Reading* condition, the experimenter told the participant, "The next thing you are going to do is I'm going to give you different reading material, and I want you to read it out loud so that I can hear you." The experimenter handed the child a different version of the reading material appropriate to the participant's reading level. While reading, if the child could not be heard, the interviewer asked the child to speak louder, occasionally pointing to the words if the child had difficulty focusing or pronouncing. Recording began when the experimenter handed the participant the reading material.

In the *Singing* condition, the experimenter told the participant, "The next thing I want you to do is to sing me a song ... any song you would like to sing." After a short pause, the experimenter then asked, "Do you know a song you would like to sing?" If the participant could not think of a song or refused to sing, the experimenter asked, "Would you like me to give you a song to sing? How about *Mary Had a Little Lamb?*" If the participant sang a song of his/her choice, the participant was then asked to sing either *Mary Had a Little Lamb*, or *Twinkle Twinkle Little Star.* All participants were then asked to sing the *Happy Birthday Song*. The experimenter asked the subject to pretend it was the camera operator's birthday and to sing the song to him/her. Throughout the condition, the interviewer would encourage the participant to sing either by initiating the song, or joining in. Singing of the song was stressed, especially if the participant was talking the words of the song. Recording began when the experimenter introduced the condition.

The directions given by the experimenter were always worded the same, rather than paraphrased to the developmental level of the child. This was done so that all participants received the same level of social demands at the beginning of each task. Whilst we were unable to ensure that all of the children understood the requirements of each task, if they appeared not to understand the task, additional prompts and reminders were given during the task. Sessions were conducted by a male experimenter in 33 of the 74 (44.6%) sessions for the male participants and in 19 of the 40 (47.5%) sessions for the female participants[1].

Response Definitions, Recording Technique, and Interobserver Agreement

Following a review of the videotapes, eight participant responses were defined. *Eye contact* was defined as looking directly at the interviewer's face, including looking when prompted; *talking/singing* was defined as any verbal speech or singing appropriate to the context, non-verbal gestures, and nodding in response to questions; *fidgeting* was defined as any repetitive, non-rhythmic, non-functional motor movements; *face-hiding* was defined as any covering of the face, mouth, eyes or ears with hands, body parts or other objects, including rolling over, turning torso away, curling up, completely lying down, burying face in object, or pretending to be asleep; *eye-rubbing* was defined as any pressure to eye area with any object including finger, fist, palm of hand, arm or foot; *hand-biting* was defined as any closure of the mouth on any part of the skin from forearm to fingertips, not including nail biting/thumb sucking; *leaving chair* was defined as any movement of the body away from the interviewer by leaving the chair or sofa for any reason; *refusals* were defined as any vocalization to terminate the task or leave the situation e.g. " I have to go", I don't want to", "no", "go away", "bye bye".

Three experimenter behaviors were also recorded; *social demands* were defined as any vocalizations from the experimenter directed toward the participant such as giving instructions, asking questions, giving general prompts and engaging in singing; *eye contact prompts* were defined as the experimenter asking for eye contact, and other reminders about maintaining eye contact such as "keep looking," "look at me," or "let me see your eyes"; *song prompts* (Singing condition only) were defined as the experimenter prompting the subject to sing a song by singing the first few lines of the song.

Observations were recorded from DVD by the second author using software that allowed multiple behaviors to be simultaneously recorded in real time (Martin, Oliver, & Hall, 1998). All responses except eye contact prompts and refusals were recorded as durations (i.e. the observer was required to press a specific key on the keyboard to indicate its onset and again to indicate its offset). Prompts for eye contact and refusals were recorded as events (i.e. the observer was required to press a specific key only once to indicate its occurrence). The percentage of time during which each behavior occurred in each condition was calculated by dividing the number of seconds of occurrence of each target behavior in the condition by the duration of the condition and multiplying by 100%. The frequency per minute of eye contact prompts and refusals was calculated by dividing the number of times the behavior occurred in each condition by the duration of the condition and multiplying by 60. All observational data were saved in Sequential Data Interchange Standard (SDS) format for later analysis using the GSEQ software program (Bakeman & Quera, 1995). During 25% of the sessions, a second observer (SH) also collected data. Agreement was calculated on a 10-s interval-by-interval basis using Cohen's Kappa (Hartmann, 1977). The mean level of agreement across topographies of child behavior was .79 (range, .48 to .90). The mean level of agreement across topographies of experimenter behavior was .82 (range, .65 to .95).

Parent Perceptions of Child Behavior Problems

The Child Behavior Checklist (CBCL) (Achenbach, 1991) is a 118-item rating scale of behavior problems for children aged 4 to 18 years. Parents rate each item as "not true" (scored 0), "somewhat or sometimes true" (scored 1), or "very true or often true" (scored 2), taking the child's behavior over the past 6 months into account. The Total *T* score was employed as the dependent measure. *T* scores range from 30 to 80, with scores greater than 60 being considered within the "clinical" range. Inter-rater reliability is .76 and test-retest reliability is .93 over a one-week period. The child's mother was the respondent.

Data Analysis

Preliminary analysis of the data showed that the level of eye contact prompts and social demands delivered by the experimenter differed between male and female groups. The mean frequency per minute of eye contact prompts delivered to male participants in the Interview condition was 2.29 (SD = 1.40) while for female participants the mean frequency per minute of eye contact prompts was only 0.85 (SD = 1.15), a statistically significant difference, ($t(94.2) = 5.92$, $P < 0.001$)[2]. In

[1] Three male participants did not participate in the silent and oral reading conditions because they were either uncooperative or were unable to read. Ten male participants did not participate in the silent reading condition because they read aloud despite being prompted to read silently to themselves. One male participant was unable to complete any of the tasks and was therefore excluded from the study.

[2] Eye contact prompts were not delivered in the Silent Reading, Oral Reading or Singing conditions.

the Interview, Silent Reading, Oral Reading and Singing conditions, male participants received social demands for 77.85, 38.37, 52.48 and 52.74% of the time, respectively. The corresponding data for female participants was 48.26, 17.11, 15.27 and 36.9% of the time, respectively. In the Singing condition, the experimenter engaged in singing with the child for 22.11 and 11.16% of the time for male and female participants, respectively. Finally, the mean duration of each condition also differed between males and females. Independent *t*-test comparisons indicated that condition duration differed significantly in the Interview ($t(112) = 3.32$, $P < 0.01$), Silent Reading ($t(49.7) = 3.65$, $P < 0.01$), and Oral Reading ($t(50.4) = 3.85$, $P < 0.001$) conditions, with females receiving longer condition durations. Given these differences in procedural integrity between male and female groups, the results for each group were subjected to separate analyses.

In order to determine whether a particular behavior was more likely to occur in a particular condition, a conditional probability analysis was conducted. Specifically, the conditional probability of a behavior occurring in each condition was calculated by dividing the number of seconds in which the behavior occurred in that condition by the total duration of the condition. To determine the significance of the conditional probability, the Yule's *Q* statistic was employed (Bakeman & Quera, 1995). Yule's *Q*, a transformation of the odds ratio, measures the extent to which a conditional probability deviates from its unconditional probability and ranges from +1 to −1. Yule's *Q* is a preferable measure to the traditional z-score because it is unaffected by the number of tallies in the data (Yoder & Feurer, 2000). Yule's *Q* was thus particularly useful given that condition duration also varied within each group. A Yule's *Q* value of .5 (equivalent to an odds ratio of 3) or greater indicated that a particular behavior occurred at levels in a condition that were significantly higher than its unconditional probability whereas a Yule's *Q* value of −0.5 or lower would indicate that the behavior occurred at levels in a condition that were significantly lower than its unconditional probability (Hall, Thorns, & Oliver, 2003).

In order to examine the effect of experimenter eye contact prompts on child eye contact, a time-based lag sequential analysis procedure was employed (Sackett, 1987). Each occurrence of experimenter eye contact prompts was examined in turn and two time windows were imposed on the data; a 10-s time period preceding each prompt for eye contact and a 10-s time period following each prompt for eye contact. The probability of child eye contact occurring at each second in each time window was then calculated. The unconditional probability of eye contact occurring in these time windows was also calculated. This analysis would allow us to determine whether individuals were responsive to requests for eye contact, i.e. whether the conditional probability of eye contact exceeded its unconditional probability, once a prompt for eye contact had been delivered by the experimenter.

Results

Tables 1 and 2 show the number of participants showing each recorded behavior and the mean percentage of time during which the behaviors were observed in each condition for male and female participants, respectively.

For male participants, the most prevalent problem behaviors observed were face-hiding (74.3%), fidgeting (74.3%), refusals (48.7%), eye-rubbing (46.0%), leaving chair (33.8%) and hand-biting (25.7%). For female participants, the most prevalent problem behaviors were face-hiding (52.5%), fidgeting (37.6%), refusals (32.5%), and eye rubbing (30.0%). Male participants established eye contact with the experimenter for approximately 18% of the time in the Interview condition[3] and for approximately 13% of the time in the Singing condition whereas female participants established eye contact for approximately 40% of the time in the Interview condition and for approximately 24% of the time in the Singing condition. Nine (12.2%) male participants failed to establish eye contact with the experimenter throughout the Interview and Singing conditions. Male participants spent 42.1% of the time responding to questions in the Interview condition whereas females spent 57.3% of the time responding to questions.

Fig. 1 shows the number of different forms of problem behaviors that individuals showed in each group. Twenty-five percent of females with fragile X did not show any form of problem behavior, whereas only one male participant did not show any form of problem behavior. Nearly 30% of male participants showed four forms of problem behavior.

Given the differing condition durations and base rates for each behavior, comparisons between conditions were conducted using a statistical measure of association that controlled for condition duration and base rate, i.e. the Yule's *Q* statistic (see above). Fig. 2

[3] It should be noted that 87.3% of the male participants and 97.1% of the female participants reciprocated the handshake greeting with the experimenter. Of those who reciprocated the handshake, 34.6% of the male participants and 70.6% of the female participants established eye contact when shaking hands.

Table 1 Mean percentage duration of child behaviors observed in each condition—male participants (N = 74)

Child behaviors	Number showing behavior	Condition			
		Interview	Silent reading	Oral reading	Singing
Eye contact	65	17.47	3.52	4.92	12.54
Talking/singing	73	42.10	38.70	53.71	31.33
Refusals[a]	36	0.34	0.17	0.19	2.71
Face-hiding	55	11.86	4.57	7.03	28.18
Eye rubbing	34	4.56	2.32	0.41	3.37
Hand biting	19	6.03	1.17	0.50	1.80
Fidgeting	55	31.10	4.02	8.25	17.27
Leaving chair	25	2.12	0.39	0.14	5.70
Mean condition duration (s)		202.00	51.67	75.79	172.23

[a]Frequency per minute

Table 2 Mean percentage duration of child behaviors observed in each condition—female participants (N = 40)

Child behaviors	Number showing behavior	Condition			
		Interview	Silent reading	Oral reading	Singing
Eye contact	40	39.47	2.88	2.49	23.98
Talking/singing	40	57.29	13.95	77.07	41.74
Refusals[a]	13	0.18	0.08	0.09	1.59
Face-hiding	21	1.06	0.54	0.33	6.43
Eye rubbing	12	0.93	0.02	0	2.32
Hand biting	6	1.49	0.65	0.21	1.84
Fidgeting	15	6.68	0.19	0.78	6.19
Leaving chair	4	2.12	0.83	0	2.37
Mean condition duration (s)		242.75	87.80	128.49	159.13

[a]Frequency per minute

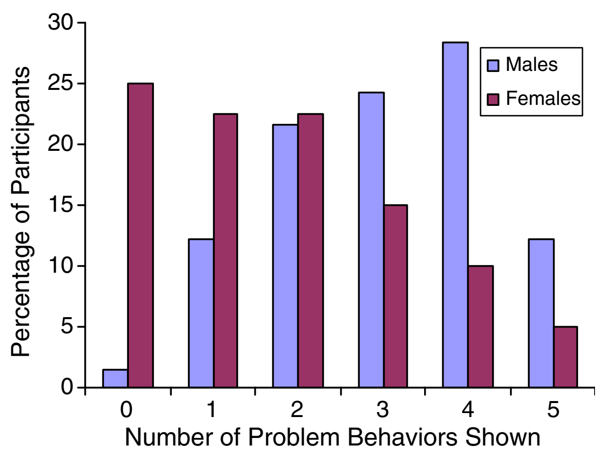

Fig. 1 Number of problem behaviors shown by male and female participants

shows Yule's Q statistics indexing the extent to which each behavior occurred in each condition for male (top panel) and female (bottom panel) participants, respectively.

For male participants, the figure shows that refusals, face-hiding and leaving the chair were more likely to occur in the Singing condition (Yule's Q's of 0.83, 0.54 and 0.71, respectively), whereas hand-biting was more likely to occur in the Interview condition (Yule's Q's = 0.62). Almost all behaviors were less likely to occur in the Silent Reading and Oral Reading conditions (mean Yule's Q computed across behaviors were −.53 and −.63, respectively).

A slightly different pattern of results emerged for female participants (see Fig. 2). Here, refusals, hiding and eye-rubbing were more likely to occur in the Singing condition while none of the behaviors were significantly more likely to occur in the Interview condition. As before, almost all behaviors were significantly less likely to occur in the Silent Reading and Oral Reading conditions (mean Yule's Q's across behaviors of −.75 and −.93, respectively). Taken together, these data suggest that problem behaviors were evoked by antecedent social demands delivered in the Interview and Singing conditions. Problem behaviors did not occur in the Silent and Oral Reading conditions where lower levels of social demands were generally delivered.

Associations between Problem Behaviors

To determine whether problem behaviors occurred together in individuals, ϕ correlation coefficients were computed between pairs of behaviors. Tables 3 and 4 show the resulting correlation matrices for male and female participants, respectively.

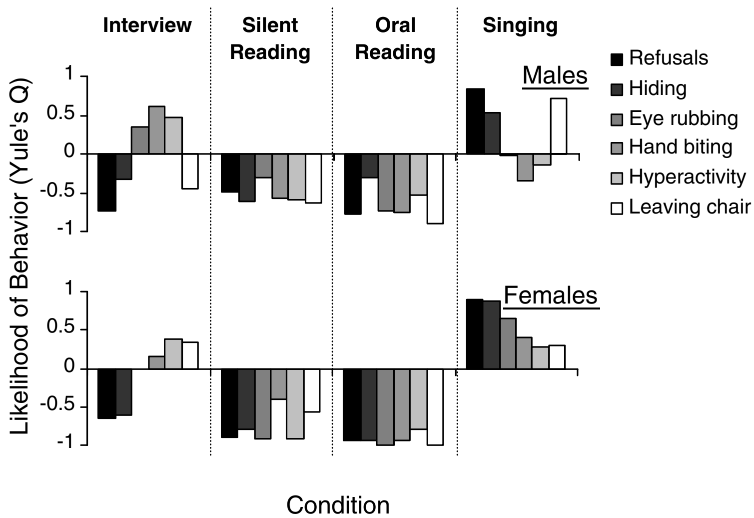

Fig. 2 Yule's Q values indexing the extent to which each behavior occurred in each condition. Values greater than 0.5 indicate that the behavior was significantly more likely to occur in a particular condition. Values less than −0.5 indicate that the behavior was significantly less likely to occur in a particular condition

In both male and female participants, refusals, face-hiding and eye rubbing were significantly associated to one another (ϕ coefficients ranging from .24 to .45). In female participants, hand biting was also associated with eye rubbing (ϕ coefficient of .37). These data suggested that in both male and female individuals with fraX, eye rubbing, face-hiding, and refusals were functionally equivalent behaviors. There were no associations between fidgeting and leaving the chair and any of the other problem behaviors in either group.

Association between biological factors and observed levels of social escape behavior

Mean levels of salivary cortisol in males and females with fraX were 0.22 μg/dl (SD = 0.22) and 0.14 μg/dl (SD = 0.09), respectively. We conducted Spearman Rank Order correlations between the duration of social escape behaviors observed, and cortisol levels, FMRP levels, and medication status. There were no associations between FMRP levels and the number of forms of problem behavior observed or the percentage of time during the behaviors occurred in either group. In males with fraX, however, higher levels of cortisol were associated with decreased levels of eye contact with the experimenter $r(65) = -.31$, $P < 0.05$, and with increased levels of fidgeting, $r(65) = .28$, $P < 0.05$. There were no other associations between social escape behaviors and cortisol levels. Associations between medication status and social escape behaviors indicated that individuals who took medications were less likely to engage in eye contact with the experimenter in both males, [$r(74) = -.431$, $P < 0.01$], and females, [$r(40) = -.353$, $P < 0.05$]. These data suggest that individuals with fewer social skills may be more likely to be prescribed medications. There were no other associations between medication status and social escape behaviors.

Association between parent perceptions of problem behaviors, adaptive behaviors, age, and observed levels of social escape behavior

Mean CBCL T scores in males and females with fraX were 60.58 (SD = 8.71) and 56.63 (SD = 11.06), respectively. We conducted Spearman Rank Order correlations between the duration of social escape behaviors observed, and CBCL scores, Vineland scores, and age. Higher CBCL scores were associated with increased levels of hiding behavior in boys with fraX, $r(74) = .36$, $P < 0.01$, and with increased levels

Table 3 Intercorrelations between behaviors—males (N = 74)

	2	3	4	5	6
1. Refusal	**.26***	**.24***	−.08	−.17	.11
2. Face-hiding		**.36****	.06	.01	.09
3. Eye rubbing			.02	.05	−.09
4. Hand biting				−.22	−.03
5. Fidgeting					.03
6. Leaving chair					

* $P < 0.05$; ** $P < 0.01$

Table 4 Intercorrelations between behaviors—females (N = 40)

	2	3	4	5	6
1. Refusal	**.45****	**.36***	.16	.12	.13
2. Face-hiding		**.40****	.12	.01	.15
3. Eye rubbing			**.34***	.06	.15
4. Hand biting				.11	.09
5. Fidgeting					.09
6. Leaving chair					

* $P < 0.05$; ** $P < 0.01$

of refusals in girls with fraX, $r(40) = .32$, $P < 0.05$. Lower Vineland scores were significantly associated with lower levels of eye contact in both males [$r(74) = .32$, $P < 0.01$] and females [$r(40) = .31$, $P < 0.05$] with fraX. There were no other associations between social escape behaviors and CBCL or Vineland scores and there were no associations between social escape behaviors and age.

Association between experimenter prompts and child eye contact

Figure 3 shows the results of a time-based lag sequential analysis conducted on the data for child eye contact and experimenter prompts in male (top panel) and female (bottom panel) groups.

The figure shows the mean probability of child eye contact at each second preceding and following experimenter eye contact prompts, pooled across participants. In the figure, data are presented at each second for the 10-s period prior to the experimenter delivering a prompt, and for the 10-s period following the experimenter delivering a prompt. The unconditional probability of eye contact is shown by the dotted line. The top panel of the figure shows that for males, in the 5-s time period preceding the experimenter delivering a prompt, the probability of eye contact decreased to low levels (~0.05), below its unconditional probability. Once the experimenter delivered a prompt for eye contact (lag 0), the conditional probability of eye contact increased to above its unconditional probability (~0.2) and declined thereafter to its unconditional probability. A similar pattern of results emerged for female participants (bottom panel). Here, however, the conditional probability of eye contact increased four-fold (from .1 to .4), once the experimenter had delivered a prompt for eye contact. Thereafter, the conditional probability of eye contact decreased rapidly to its unconditional probability. These data suggest that while both males and females were responsive to prompts for eye contact, eye contact was maintained, on average, for only 1 or 2 s once a prompt had been delivered by the experimenter. In addition, it appeared that females with fraX were more responsive to eye contact prompts than males.

Discussion

Social escape behavior has been described as a common behavioral feature or phenotype of fraX. In this study, we wanted to measure the behavioral components of social escape, namely eye contact aversion and other problem behaviors commonly seen in children with fraX. To do this, we systematically manipulated levels of antecedent social-environmental events using tasks with varied levels of social and performance demands (i.e. interview, silent reading, oral reading and singing a song). Under these conditions, the most prevalent form of problem behavior observed in both groups was face-hiding (i.e. shielding eyes with hands). This behavior occurred in 74% of male participants and in 54% of female participants, indicating that shielding the face is a major component of social escape behavior of fraX (cf., Cohen et al., 1988). Forty-six percent of males and 30% of females also engaged in eye-rubbing, a behavior that has not previously been reported in the literature in fraX. Correlation analyses indicated that eye-rubbing was significantly associated to face-hiding, suggesting that these behaviors formed a response class. Anecdotally, it appeared that many individuals engaged in eye-rubbing while shielding their eyes with their hands.

It is interesting to note that hand-biting, a behavior considered to be highly prevalent in this population, occurred in only 26% of males and 15% of females. It is possible that hand-biting may have been observed if the session duration had been longer and/or if we had sampled a larger variety of environmental events. To date, prevalence estimates of hand-biting in fraX have relied almost exclusively on questionnaire and checklist methodology. In a postal survey of 55 boys with fraX aged 2–12 years, for example, Symons, Clark, Hatton, Skinner, and Bailey (2003) found that hand-biting occurred in 72% of participants. We hope that further observational studies of individuals with fraX

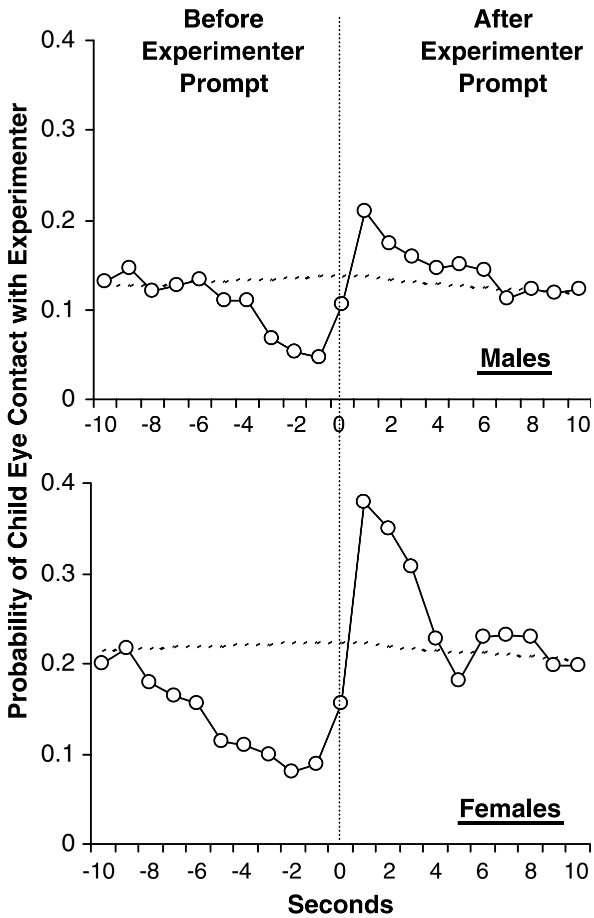

Fig. 3 Probability of child eye contact prior to and following prompts for eye contact delivered by the experimenter

that sample a broader range of antecedent events will be conducted in the future in order to provide better estimates of the true prevalence of these behaviors and to determine under what conditions they are most likely to occur.

Analysis of the behaviors observed in the different conditions indicated that in both groups, behavior problems were more likely to occur in the interview and singing components of the session than in the silent reading and oral reading components of the session. These data suggested that behavior problems in fraX were highly sensitive to changes in social-environmental events, namely specific social and performance demands. In their postal survey, Symons et al. (2003) found that behavior problems were reported to occur in response to changes in routine in 87% of participants, and in response to task demands in 65% of participants. In only 3% of participants were behavior problems reported to occur in order to obtain adult attention. These data need to be confirmed in observational studies that directly manipulate these social-environmental events.

In male participants, problem behaviors appeared to be differentially affected by social and performance demands. For example, hand-biting was significantly more likely to occur in the interview component of the session while refusals, face-hiding and leaving the chair were more likely to occur in the singing component of the session. These data suggested that the performance aspect of the singing task evoked particular escape behaviors that in the past were more likely to terminate the task (i.e. refusing to do the task, leaving the room and face-hiding). In the interview condition, experimenter social demands (i.e. repeated questioning) and prompts for eye contact appeared to evoke hand biting in male participants and again, it seems likely that in the past, this behavior may have been likely to lessen or terminate social demands and eye contact prompts. For females with fraX, problem behaviors predominantly occurred in the singing task, suggesting that the performance aspect of the singing task was more aversive than the social component of the interview. To our knowledge, this is the first study to demonstrate differential effects of social and performance demands on escape behaviors in a school age population of children with a specific syndrome.

It is important to point out that in the present study we manipulated only specific antecedent environmental events (task and social demands). Future studies should manipulate other antecedent conditions (e.g. low levels of stimulation and/or low levels of attention) to determine whether these or other events may also increase the probability of problem behaviors appearing in the child's repertoire. In addition, manipulation of consequent social-environmental events (e.g. the contingent removal of social demands or contingent presentation of attention) would allow researchers to determine whether consequent social-environmental events could shape and maintain behavior problems in children with fraX via the processes of positive and negative reinforcement. It should, however, be pointed out that in this study the conditions were administered in the same order, thus there was the potential for order effects. We administered the Interview condition first because our aim was to determine whether social escape behaviors would be evoked immediately during a brief social exchange. Future studies could investigate whether the same effect would be produced when the order of conditions was randomized across participants. Similarly, it should be pointed out that the duration of the tasks varied across participants and that this may have affected the results. For example, individuals who were asked to read a passage usually took longer to read it than those who were asked to read single letters. To overcome this problem, future studies could employ fixed task durations.

These data also have implications for interventions. Oliver, Oxener, Hearn, and Hall (2001) for example conducted an antecedent analysis of multiple topographies of aggressive behavior shown by a young woman with severe mental retardation. By repeatedly exposing the subject to close proximity social interaction without the opportunity to escape, these authors found that a hierarchy of aggressive behaviors were evoked and then extinguished over time. Given that the function of the behaviors observed in the present study appeared primarily to escape the social and performance demands delivered by the experimenter, prolonged exposure to these environmental events without the opportunity to escape (i.e. escape extinction) might be a successful intervention for children with fraX. Surprisingly, we know of no studies that have implemented this intervention strategy for children with fraX. One potential obstacle for the implementation of an extinction procedure is the possibility that other, more problematic, behaviors may appear in the person's repertoire as a result of the process itself. We found no increases in the probability of other problem behaviors given repeated experimenter prompts for eye contact in our sequential analyses, however.

Eye contact aversion is a prominent feature not only in fraX but also in children diagnosed with autism. Nine male participants failed to establish eye contact with the experimenter throughout the videotaped session, the remainder establishing eye contact during the interview for only 20% of the time on average while female participants established eye contact with the experimenter for 40% of the time on average. These percentages indicate that eye contact maintenance for individuals with fraX is extremely problematic, particularly given that the experimenter provided prompts for eye contact throughout the interview. In males with fraX, we found that higher levels of salivary cortisol were predictive of lower levels of eye contact and higher levels of fidgeting behavior. These data suggest that biological factors (e.g. HPA dysfunction) may interact with environmental factors to evoke social escape behaviors in males with fraX. Interestingly, Curin et al. (2003) suggested that the HPA axis may also be dysfunctional in children with autism. However, in their study they found that individuals with autism typically had lower levels of cortisol whereas in the Hessl et al. (2002) study, individuals with fraX were found to have higher levels of cortisol than their typically developing siblings. In this study, no associations were found between FMRP levels and social escape behaviors in either group. It is possible that low levels of FMRP may act only indirectly on behavior in fraX, or that blood levels of FMRP may not accurately reflect levels of FMRP in the brain.

Lag sequential analysis of the association between experimenter prompts for eye contact and subsequent child eye contact indicated that despite the low levels of eye contact observed, both groups of participants were responsive to prompts for eye contact, i.e. in both groups, prompts for eye contact were followed by a significant elevation in the probability of child eye contact, particularly for females with fraX. Given a prompt for eye contact, however, eye contact was maintained for only 1 or 2 s. These data indicate that social skills training, in which particular attention is paid to the importance of maintaining eye contact while speaking and listening, may be beneficial to individuals with fraX.

One issue concerning the decision to implement an intervention for social escape behavior in fraX is to consider whether or not these behaviors are ''adaptive'' responses to social anxiety or can be labeled ''problem behaviors''. It is likely that levels of eye contact aversion and face-hiding play a significant role in the ability of individuals with fraX to initiate and sustain friendships with significant others. For example, it is instructive to note that only 35% of male participants established eye contact during the initial greeting with the experimenter. We therefore believe that interventions focused on increasing levels of eye contact, and reducing levels of face-hiding, eye-rubbing and hand-biting behaviors, could also be beneficial for individuals with fraX.

One weakness of the present study is that we did not include a comparison group of children diagnosed with autism and/or a developmental age-matched group of children with which to compare these data. Data from a study conducted by Cohen et al. (1991) for example indicated that the manner in which children established eye contact with their parents differed between children with fraX and those diagnosed with autism. Specifically, children with fraX appeared to establish eye contact with the parent only when the parent was looking elsewhere. In our study, in order to keep the level of social demands continuously high, the experimenter very rarely looked away from the participant. Thus we were therefore unable to determine whether this interaction style occurred in our study participants. Future studies should investigate the nature of this apparent approach-avoidance conflict.

There are several other caveats of the present study that should be taken into account when interpreting these data. Firstly, the participant had been subjected to a lengthy test battery prior to the observational session being conducted. This testing schedule may have increased the probability of observing problem behaviors in the observation session simply due to participant fatigue. These data need to be set in this context. Secondly, we designed the schedule in this study so that one of the researchers, the experimenter, had experienced minimal social contact with the participant prior to the session. This was done so that we could examine levels of eye contact and problem behaviors occurring during social interaction with an unfamiliar person. However, it would be of interest to compare these data to those obtained with familiar adults or siblings under similar conditions. In the Lesniak-Karpiak et al. study, for example, conditions were also set up during which participants were asked to read silently and aloud to a familiar person as well as presenting a speech to two familiar adults. Unfortunately, in that study, data concerning any escape behaviors that might have occurred during those conditions were not presented.

Taken together, these results add to the literature on the effect of social–environmental events on problem behaviors in children with genetic syndromes. We have shown that both biological and environmental factors may contribute to the maintenance of problem behaviors in children with fraX. In particular, we suggest that there may be an interaction between biological and environmental factors in that specific escape responses may be evoked both by high levels of cortisol and maintained by environmental contingencies. We hope that future studies will investigate the determinants of these behaviors in young children with fraX (Hall et al., 2001) and that behaviorally based interventions will be implemented to reduce behavior problems and eye contact aversion in these children.

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