

## TRACING SYNDROME-SPECIFIC TRAJECTORIES OF ATTENTION ACROSS THE LIFESPAN

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### ABSTRACT

This paper maintains that studies of atypical attention targeting one particular age group are unlikely to be informative of syndrome-specific deficits and their developmental changes. We propose a new approach to the study of attentional deficits in genetic disorders, arguing for tracing cross-syndrome developmental trajectories from infancy through childhood to adulthood. Few studies have incorporated a developmental approach to determine whether the pattern of deficits and proficiencies remains constant across developmental time. Fewer still have included a cross-syndrome perspective to address these issues. Focusing on the cognitive domain of attention and its component parts, and using a cross-syndrome developmental perspective, the present set of studies compared the trajectories of different aspects of attention in three developmental disorders: Fragile X syndrome (FXS), Down syndrome (DS) and Williams syndrome (WS). Hitherto, these syndromes have all been reported as displaying serious “attentional deficits” above those expected in the general population. We predicted that, when one considers in greater detail subcomponent processes of attention, then ostensibly common difficulties do not necessarily emerge from common developmental pathways. We addressed this question with two studies. The first focused on inhibitory control, orienting and selective attention in infants and toddlers, and the second concentrated on selective attention, sustained attention and inhibitory control in mid-late childhood. The current results and their integration with earlier findings in adults point both to commonalities and to important syndrome-specific differences in attentional component processes, questioning whether profiles remain constant across developmental time.

Key words: developmental disorders, trajectories, cross-syndrome comparisons, attentional processes

### INTRODUCTION

The past decade has witnessed unparalleled advances in the application of molecular genetic methods to the study of developmental disorders. These advances include higher resolution conventional G-banded cytogenetics, the application of molecular cytogenetics in the form of fluorescent in situ hybridisation (FISH) technology, and molecular genetic analysis for specific single gene disorders, such as Fragile X syndrome (Willemsen et al., 2004). Alongside these developments, there has been a substantial growth in the number of studies attempting to link genetic changes (deletion, reduplication or silencing of genes) to cognitive endstates and brain function, in essence to link genotype to phenotype (e.g., Karmiloff-Smith et al., 2003a; Paterson et al., 1999; Reiss and Dant, 2003; Wilding and Cornish, 2004). The rapid growth in neuroimaging techniques, notably structural and functional imaging, including magnetic resonance (MRI and fMRI), evoked related potentials (ERP), and single photon emission computed tomography (SPECT), have provided a unique opportunity to further delineate brain-behavior relationships in both typical and atypical populations (e.g., Cornish et al., 2004b; Di Martino and Castellanos, 2003; Grice et al., 2001). Together, these advances have provided neuroscientists with a unique “window”

on the cognitive phenotypic outcomes of disorders with differing genetic etiologies. Indeed, numerous studies now attest to the distinct cognitive endstates, especially in late childhood, that characterize disorders such as Fragile X syndrome (Cornish et al., 2004a), Williams syndrome (Donnai and Karmiloff-Smith, 2000), Prader-Willi syndrome (Whittington et al., 2004), Turner’s syndrome (Nijhuis-Van der Sanden et al., 2003), and others. Although these phenotypic endstates yield important information that help target syndrome-specific clinical and educational programs, few studies have incorporated a developmental approach towards understanding atypical pathways. Fewer still have included a cross-syndrome perspective that allows for dissociations in developmental disorders to be studied through development itself. Yet such an approach provides a vital framework for understanding evolving neurocognitive functions in developmental disorders (Karmiloff-Smith, 1998; Paterson et al., 1999; Scerif and Karmiloff-Smith, 2005). In beginning this journey, the present paper brings together a series of datasets (novel and previously published ones) within a developmental perspective. Previous cross-syndrome studies, including our own, have tended to focus on group differences, and not on charting developmental trajectories of performance within each group to inform cross-syndrome

comparisons (please see Ansari and Karmiloff-Smith, 2002, Karmiloff-Smith et al., 2004, and Thomas et al., 2001, for empirical and theoretical exceptions). We believe that drawing together existing studies within this framework places attention on a novel developmental focus on cross-syndrome comparisons. Admittedly, the heterogeneity of the samples presented here and the missing portions of developmental trajectories for each syndrome limit the strengths of the conclusions that can be drawn. None the less, these preliminary findings strongly motivate the need for prospective cross-syndrome longitudinal studies that chart typical and atypical developmental trajectories from infancy onwards.

Our specific focus lies within the cognitive domain of *attention* and its component parts. Research in the field of attention has undergone resurgence in recent years for a number of reasons. From a *theoretical perspective*, there has been an increasing recognition that the term “attention” does not present a unified construct but rather an array of specific sub processes that interact across many different cognitive domains (Mirsky and Duncan, 2001; Parasuraman, 1998; Posner and Petersen, 1990). Although no clear consensus has yet emerged that clearly delineates the separate components of attention, there is general agreement that the processes involved in *selective attention* can be differentiated from processes required for *vigilance* or *sustained attention* across typical and atypical development (e.g., Manly et al., 2001). Likewise, the processes that require *inhibitory control* can be differentiated from those that primarily involve *shifting of attention*. This is true of adults (Friedman and Miyake, 2004; Miyake et al., 2000) and of children (Klimkeit et al., 2004). Despite clear distinctions between components of attention, recent findings also highlight how they interact to determine performance. For example, a study by Unsworth et al. (2004) revealed contributions of both inhibitory control and orienting to variability in working memory span. Taken together, the above studies stress the need to focus on each of the multiple component processes of attention, as well as on their potential interactions in both real-time processing and over developmental time.

From a *developmental perspective*, the journey from infancy, through childhood and into adolescence and adulthood can demonstrate the importance of developmental timing in the trajectory of attention processing and its central role in development. This perspective also recognizes the interactive role across many systems: from the genetic to the neurological systems to the cognitive and the affective systems, and thence to the behavioral and environmental systems (Karmiloff-Smith, 1998). Furthermore, comparisons of attentional profiles across a range of developmental disorders can highlight the

network of atypical pathways that lead to syndrome-specific phenotypic outcomes. Focus on these comparisons has the additional benefit of facilitating the development and early timing of more effective treatment that recognizes syndrome-specific proficiencies and deficiencies in developmental disorders.

### *The Present Study*

In the present study, the relevance of cross-syndrome comparisons of attention processing and deficit is addressed in the context of three genetically-determined disorders: Fragile X syndrome (FXS), Williams syndrome (WS) and Down syndrome (DS). FXS is one of the most common hereditary causes of mental retardation in males, with a prevalence of 1 in 4000 (Turner et al., 1996). The prevalence is lower in females, who often display less cognitive impairment. FXS is caused by an expansion of the CGG repeat at the beginning of the FMR-1 gene on the X chromosome. In normal individuals, there are ~ 7-60 repeats with 30 repeats found at the FMR-1 gene site. In most clinically affected individuals, there is a significant expansion of repeats (> 200), resulting in hypermethylation and a subsequent silencing of the FMR1 gene, a lack of messenger RNA and a lack or absence of the protein product of the FMR1 gene (Verkerk et al., 1991). WS is a rarer developmental disorder occurring in approximately 1 in 7,500 to 1 in 20,000 live births, depending on the source of the estimate (Rosner and Semel, 2005). WS is caused by a microdeletion of some 28 genes on one copy of the long arm of chromosome 7 at q.11,23. The microdeletion is approximately 1.5Mb and of fairly uniform size, with the elastin gene being midway between the two breakpoints (Perez-Jurado et al., 1996). The cognitive profile of patients with smaller deletions in the WS Critical Region has been examined to assess the contributions of the LIMK1, CYCLYN2 and GTF2 genes to the WS cognitive phenotype (Tassabehji et al., 1999; Karmiloff-Smith et al., 2003a; Morris et al., 2003). Finally, DS represents the most common of known *genetic* causes of mental retardation with a prevalence of 1 in 600-800 live births. The syndrome usually (96% of cases) originates from errors during meiosis giving rise to three rather than two copies of chromosome 21 (Chapman and Hesketh, 2000). It has been estimated that only 20 to 50 genes may eventually be included in the Down syndrome Critical Region (Branchi et al., 2004).

Chronic attentional problems have been reported for all the three syndrome groups beginning in early childhood [FXS (Cornish et al., 2004a; Hatton et al., 2002; Munir et al., 2000a; Turk, 1998), DS (Clark and Wilson, 2003; Wilding and Cornish, 2004), WS (Atkinson, 2000; Brown et al., 2003; Mervis et al., 2003)], although FXS

appears to be more severely impacted in terms of fulfilling a clinical diagnosis of attention deficit hyperactivity disorder (ADHD) (Hagerman et al., 1988). We speculate, however, that even gross “commonalities” in the phenotypic outcome of these three syndromes do not necessarily indicate common developmental pathways. Instead, we predict divergent cognitive profiles that impact differently various attentional components across developmental time in the three disorders. Crucially, we present evidence that highlights the importance of investigating syndromic differences in the context of how they change over developmental time. Two studies are described, that focus on tracing within- and across-syndrome comparisons in developmental trajectories of performance for previously published and novel datasets. The original reports presented group comparisons in performance, as is most common in the literature. By contrast, here we focus on charting changes in performance with age, both within and across groups. The nature of the developmental trajectories that we present is somewhat incomplete, due to the fact that we pool across multiple studies in our laboratories to begin to draw cross-syndrome trajectories. The first study focuses on infants and toddlers from the three syndromes, as well as typically developing controls, comparing inhibitory control, orienting and selective attention. The second focuses on children with FXS and DS and typically developing controls, comparing selective attention, sustained attention and inhibitory control.

#### STUDY 1

##### DEVELOPMENTAL TRAJECTORIES OF ATTENTIONAL PROCESSES IN INFANTS AND TODDLERS WITH FXS, WS AND DS

Early precursors in infancy of the attention difficulties experienced by older children with FXS, WS and DS and their characterization in terms of component processes of attention are poorly understood. Brown et al. (2003) first described shorter and fewer periods of sustained attention in infants with DS but not WS compared to controls, suggesting that early attentional difficulties in WS do not depend on an inability to focus on their surrounding environment and must be sought amongst other components of attention, such as inhibition and orienting. However, Laing et al. (2002) and Mervis et al. (2003) reported an increased focus on people’s faces in WS during attempts at triadic interaction, suggesting atypical attention in a social context. In contrast, striking difficulties in inhibitory control have been revealed to characterize infants and toddlers with FXS (Scerif et al., 2004, 2005, in press), but it is unknown whether these extend to other components of attention.

Study 1a pits against each other the control of eye-movements and the orienting of attention to suddenly appearing stimuli in the environment. The former requires the kind of voluntary control necessary to inhibit prepotent responses and to achieve task-relevant goals, as is the case in the production of antisaccades (Hallett, 1978). Participants are required to orient away from suddenly-appearing peripheral flashes and direct eye-movements to the contralateral location in space. They must therefore deploy considerable *voluntary* eye-movement control. In contrast, orienting of attention triggered *automatically* by stimuli in the environment can be studied using the Posner (Posner, 1980; Posner and Cohen, 1984) cueing paradigm. It involves presenting participants with a cue that precedes the appearance of a target stimulus and can indicate the target’s spatial location either correctly or incorrectly (labeled respectively as valid or invalid cues). At short intervals between cues and targets, latencies to detect targets are typically faster to validly cued targets and slower to invalidly cued targets, even when cues do not predict the location of the target beyond chance. The performance by infants with FXS and mental-age matched typically developing infants on the inhibition task has been previously reported (Scerif et al., 2005). However, the direct comparison with infants with WS on this measure and performance of both groups on another attentional measure (orienting) have not been previously investigated. Furthermore, albeit limited by small sizes of infant patient samples, we provide preliminary pilot data on cross-syndrome *developmental trajectories*: indeed, inhibition and orienting may develop at differential rates and they have not been investigated concurrently in infants and toddlers with FXS and WS.

Study 1b tests selective attention in toddlers with FXS, WS and DS. As for Study 1a, while the comparison of group performance by toddlers with WS and FXS has been previously reported (Scerif et al., 2004), here we extend cross-syndrome comparisons to DS, and undertake a preliminary investigation of whether cross-syndrome differences also show up in developmental trajectories. We assessed selective attention using a visual search paradigm, as it allows for the tight manipulation of the perceptual characteristics of target and distractors. It is therefore particularly well suited to investigating group differences in the representation of task-relevant target characteristics and in the interference by irrelevant items. We specifically designed tasks to test selective attention in toddlers, adapting measures that we had previously used in older children with FXS and DS (e.g., Munir et al., 2000a). While these children with FXS displayed striking inhibitory difficulties, selective attention was an area of relative strength for them, whereas WS and DS are characterized by difficulties with selective attention

in later life. We therefore anticipated similar cross-syndrome differences in their performance as toddlers.

*Study 1a*  
*Infant and Toddler Measures of Inhibition*  
*and Orienting in FXS and WS*

*Method*

*Participants.* A total of 36 infants and toddlers constituted the final sample for analyses for the inhibition measure, whereas 37 contributed to orienting measure. Fifteen infants and toddlers (all boys) with FXS and 13 infants and toddlers with WS (9 boys) were recruited through the Fragile X Society and the Williams syndrome Foundation, United Kingdom. Cases were ascertained by local genetic services (through FISH, for WS, or analysis of the number of CGG repeats, for FXS). Of these, 5 infants with WS and either 5 (antisaccade task) or 6 (orienting measure) boys with FXS did not complete the experimental measures because of fussiness or fatigue. This left 10 boys with FXS (mean chronological age = 37 months; range = 14-55 months) and 8 infants with WS (mean chronological age = 18 months; range = 3-41 months) who completed the inhibition task. Nine boys with FXS (mean chronological age = 35 months; range = 14-55 months) and the same 8 infants with WS completed the orienting paradigm. Gender differences in our samples depended on the pattern of inheritance of the disorders of interest. FXS is heterosomal and therefore affects boys to a greater degree, so it would not be meaningful to group boys and girls within the same design. In contrast, WS is autosomal, and hence affects to similar degrees boys and girls. In order to control for potential gender differences in attentional performance in infants and toddlers, we conducted preliminary analyses of gender as a factor. We did not find statistically significant gender differences across the measures of interest [for *inhibition*,  $F(1, 31) = .325$  and  $.043$ ,  $p = .573$  and  $.837$  for cue looks and antisaccades respectively; for *orienting*,  $F(1, 32) = .286$ ,  $p = .596$ ]. We therefore collapsed data across gender.

The children's developmental level was measured using the Bayley Scales of Infant Development Mental subscale (BSID-II; Bayley, 1993), which provides an overall composite score of early verbal and non-verbal abilities and is the most commonly used standardised tool to assess infants and young children in experimental studies (Nellis and Gridley, 1994; Bradley-Johnson, 2001). For boys with FXS, mean mental age was 20 months for inhibition (range = 12-30 months) and 19 months for orienting (range = 12-30 months). For infants with WS, mean mental age was 12 months (range = 2-36 months) for both measures. These infants were compared to a larger group of

typically developing children ( $n = 18$  for the inhibition measure and  $n = 20$  for the orienting measure), henceforth referred to as "MA controls". Mental age (and chronological age) of MA controls spanned the minimum and maximum mental age equivalent for the two clinical groups. Mean mental age for MA controls was 23.5 months for inhibition and 21.6 months for orienting (range = 2-30 months for both measures). As there were trends towards a statistically significant difference in mental age equivalent between participants with FXS and WS [ $t(15) = 2.073$  and  $1.804$ ,  $p = .055$  and  $.091$  for inhibition and orienting respectively], mental age was used as a covariate in all analyses. There are inevitable practical constraints when seeking to recruit infants with genetic disorders to complete experimental tasks, over and above the fact that the average age of diagnosis generally precludes very young children from being seen during infancy. For example, in the case of FXS the lack of clear physical diagnostic markers of the condition continues to impede early diagnosis that normally does not occur until an average age of 30 months (Bailey et al., 2001), whereas both WS and DS are nowadays diagnosed at or close to birth. Nevertheless, smaller sample sizes do limit the power of statistical analyses and hence the conclusions that might be drawn from the data. We therefore addressed this concern in two ways. First, we increased overall sample size by recruiting a larger number of typically developing infants and toddlers to the studies, than the mere number that would have been sufficient to match affected children with typically developing controls using a case-control approach, increasing degrees of freedom for all statistics. Second, we conducted two-tailed compromise power analyses [G-Power (Faul and Erdfelder, 1992), with  $\alpha = .05$ ] to establish whether the sample sizes were too small to yield statistically significant results on the variables of interest. For the inhibition task (characterized by the smallest overall sample size), power was satisfactory to assess group differences (power = .79) and interactions of group with the other variables (power = .74), for a medium sized effect. Care was nonetheless taken to caution against overestimating null results. Given uneven sample sizes, caution was exercised in checking variables for normality, homogeneity of variance, sphericity with the appropriate transformations used when necessary. All statistical analyses reported here are tested as two-tailed.

*Measures.* Participants sat on their caregiver's lap, 70 cm from the centre of a large color monitor. Each trial began with the presentation of an attractive fixation display that served to ensure that the infant or toddler was looking at the centre of the screen at the start of each trial. The experimenter could see the infant by means of a video camera mounted above the display screen. In the *antisaccade task*, at the offset of the fixation

TABLE I  
Summary statistics for inhibition and orienting in infants and toddlers. Group differences and age-related changes

			MA controls (N = 18, 20)	Infants and toddlers with FXS (N = 10, 9)	Infants and toddlers with WS (N = 8)	Group differences
Inhibition (N = 36)	Percentage of cue looks	1 <sup>st</sup> half (SEM) 2 <sup>nd</sup> half (SEM)	71.4 (4.9) 54.9 (5.8)	71.6 (5.9) 73.8 (6.6)	36.6 (6.6) 34.9 (7.4)	MA, FXS > WS** FXS > MA, WS*
	Percentage of antisaccades	1 <sup>st</sup> half (SEM) 2 <sup>nd</sup> half (SEM)	13.9 (3.2) 16.1 (3.1)	12.0 (4.1) 13.3 (3.5)	6.9 (4.6) 4.9 (3.8)	n.s. n.s.
Orienting (N = 37)	Mean saccade onset to targets (msecs)	Validly cued	230.3 (25.9)	243.2 (25.9)	259.4 (27.4)	n.s.
		Invalidly cued	263.9 (26.0)	209.2 (26.0)	312.4 (27.6)	WS > FXS*

Note. Minimum p value for pairwise comparisons: \*p < .05, \*\*p < .01.

stimulus a small black circle (5°) was presented to the right or left of fixation (18°) for 100 msec and consistently predicted the appearance of an interesting animated target stimulus 700 msec after cue onset at the contralateral location in space (following Johnson, 1995). Trials were then divided into a first and a second half to compare decreases in looks towards the cue stimulus and saccades anticipating the appearance of targets at the contralateral location in the absence of orienting towards the cue. In the *orienting task*, while the fixation stimulus was present at the centre of the screen, a cue stimulus – a green diamond – was presented for 100 msec to the right or left of fixation (at the same eccentricity as in the previous task). Simultaneous presentation of the cue and fixation stimuli helped prevent overt orienting towards the cue stimulus. A target stimulus was then presented 150, 400, 700 or 1200 msec after cue onset, either in the same location as that in which the cue had appeared (validly cued targets, on 50% of cued trials) or in the opposite location (invalidly cued targets). Saccade onset (in msec) was recorded by selecting the first frame in which an eye movement to a discrete centre/left/right location was detected. For both tasks, experimental trials were preceded by control cue-only trials that tested whether infants could detect and orient towards the cues presented alone. Videotapes of children's eye movements during the task were coded off-line by a coder blind to the precise onset of the cue and target stimuli and to their location. Reliability on 20% of videotapes between two trained coders blind to the children's identity, was .9 (Cohen's K) for whether trials should be rejected or scored and 1.0 for the direction of saccades. There was a mean correlation of .85 for saccade onsets. In 98% of scorable trials coders recorded reaction times within one frame difference (40 msec).

### Results and Discussion

Summary statistics for both measures are presented in Table I. For the *inhibition measure*, a mixed 3 (group: toddlers with FXS, WS, MA controls) × 2 (Experimental half: first, second) analysis of covariance (ANCOVA) was run on the

percentage of cue looks and on the percentage of antisaccades during the first and second half of trials. Developmental level was transformed into its inverse (as this provided a better linear fit for all conditions and groups) and used as a covariate, given the trends towards group differences in mental age. Group had a statistically significant effect on the percentage of cue looks [ $F(2, 32) = 10.667$ ,  $p = .001$ ], and this interacted with experimental half [ $F(2, 32) = 3.740$ ,  $p = .035$ ]. An analysis of simple effects revealed that cue looks decreased from the first to the second half of trials for MA controls [ $t(17) = 3.389$ ,  $p = .003$ ], but not for infants with WS or FXS ( $p = .884$  and  $.619$  respectively). Infants with FXS produced more cue looks than both MA controls and WS toddlers in the second half of trials ( $p = .037$  and  $.001$  respectively, pairwise comparisons Bonferroni adjusted henceforth). Furthermore, infants with WS produced fewer cue looks than both groups during the first half of trials ( $p = .001$ ). There were no statistically significant main effects or interactions on the number of antisaccades in the first and second half of trials (lowest  $p = .152$ , for the effect of Half, with a trend towards a larger number of antisaccades in the second, on average 11.8, compared to the first half, on average 10.19 antisaccades). These findings point to some clear group differences in the ability to control cue looks. In typically developing infants, the ability to decrease looks towards the cue has been taken as a reliable measure of inhibition (Johnson, 1995). For the MA controls, looks towards informative but uninteresting peripheral cues decreased in the second half of the experiment, suggesting an ability to control them. By contrast, toddlers with FXS or WS differed from controls and from each other in a number of ways. Toddlers with FXS produced large numbers of cue looks both at the beginning and at the end of the experimental protocol, suggesting difficulties in inhibiting such reflexive saccades. By comparison, infants with WS produced fewer such looks throughout, despite the fact that they could orient towards the cue in control "cue-only" trials. The latter findings suggest that, while performance in FXS is driven by an inability to voluntarily inhibit reflexive looks, infants with WS experience difficulties in disengaging attention

from the central fixation stimulus towards briefly presented peripheral stimuli (see also Brown et al., 2003). These difficulties resemble those encountered by infants with WS in triadic social interactions, in which children are required to orient away from an adult and towards the referent of their attention (Laing et al., 2002). This is a suggestion that can be tested by focusing more directly on the orienting of attention.

For the *orienting measure*, a mixed 3 (group: toddlers with FXS, WS, MA controls)  $\times$  2 (validity: valid, invalid)  $\times$  4 (cue-target interval: 150, 400, 700, 1200) ANCOVA was run on mean reaction times to targets cropped to eliminate fast (< 100 msec) and slow outlier responses (> 1000 msec). Again, developmental level was entered as a covariate to account for differences in mental age across patient samples. There were no statistically significant effects of Validity [ $F(1, 33) = 3.530, p = .121$ ] nor of cue-target interval [ $F(3, 99) = .465, p = .693$ ]. Furthermore, the effect of Group was not statistically significant [ $F(2, 33) = .976, p = .387$ ]. However, the interaction between Group and Validity was statistically significant [ $F(2, 33) = 5.185, p = .011$ ]. None of the other interactions reached statistical significance,  $p$ -levels ranging from .353 to .792. The sources of the interaction between Group and Validity were investigated by analysing reaction time to validly *versus* invalidly cued targets separately. Groups did not significantly differ in the speed of orienting to validly cued targets [ $F(2, 33) = 1.716, p = .195$ ]. In contrast, they differed when targets were invalidly cued [ $F(2, 33) = 4.107, p = .025$ ]. Toddlers with WS were significantly slower than toddlers with FXS and MA controls in orienting towards such targets ( $p = .008$  and  $= .037$  respectively). MA controls were slower at orienting towards invalidly cued targets than towards validly cued ones [ $F(1, 19) = 7.472, p = .013$ ], as were toddlers with WS [ $F(1, 7) = 8.091, p = .025$ ], whereas toddlers with FXS did not orient to either target type faster [ $F(1, 8) = 1.910, p = .204$ ]. None of the other main effects or interactions reached statistical significance. These findings point to different effects of invalid cues: infants with WS displayed greater interference effects of invalid cues than those with FXS. This finding tends to support the suggestion of greater difficulties in disengaging from an attended location for toddlers with WS, but, given limited statistical power, inferences cannot be drawn from the absence of a validity effect for toddlers with FXS.

### Study 1b

#### Visual Selective Attention in Toddlers with FXS, WS and DS

#### Method

*Participants.* A total of 64 toddlers were included in the final sample for analysis. We

compared toddlers with FXS ( $n = 8$ , mean chronological age = 43 months, range = 34-50 months), WS ( $n = 8$ , mean chronological age = 46 months, range = 37-50 months) and DS ( $n = 8$ , mean chronological age = 63 months, range = 56-72 months) to a larger group of 40 typically developing controls whose developmental level on the BSID-II ('MA controls', mean chronological age = 35.35 months, range = 24-48 months) spanned the mental age range for the patient groups. Mean mental age was 29 months (range = 23-36 months) for toddlers with FXS, 29 months (range = 18-49 months) for toddlers with WS and 36 months (range = 28-45 months) for toddlers with DS. There was a trend in the direction of a difference across patient groups in terms of their developmental level [ $F(2, 23) = 2.517, p = .105$ ], and therefore developmental level was used as a covariate in all further analyses. In order to address concerns regarding statistical power due to small patient group sizes, we conducted compromise power analyses [G-Power (Faul and Erdfelder, 1992), with  $\alpha = .05$ ]. For the selective attention task, power was satisfactory to assess group differences (power = .86) and interactions of group with the other variables (power = .79), for a medium sized effect. As for Study 1a, power for correlations and the smallest sample sizes was not satisfactory ( $= .67$ ). We addressed this concern by using non-parametric correlations and limiting conclusions from null results.

*Procedure.* Toddlers were asked to find target large circles amongst smaller distractor circles on a 15" computer touch-screen. Before any of the experimental trials, four control acuity trials required toddlers to discriminate a single target circle from a single distractor (of both types, medium and small, see below) on a laminated card. All toddlers included in the final sample did so successfully. They then sat at a small table approximately 30 cm from the touch-screen and were instructed to find funny faces hidden under large target circles. Viewed from a 30-cm distance, each target subtended 5.7° angle. Distractors were also black circles, subtending either 2.8° (small distractors, very dissimilar from the target) or 4.2° (medium distractors, more similar to the target). All search displays contained 10 target circles and either no distractors (baseline condition), few or many (6 or 24) distractors that were either similar or dissimilar in size to the targets (experimental runs). When a large target circle was touched, a coloured square-shaped face covering approximately half the area of the target appeared and remained on display for the duration of the trial (to eliminate the requirement of remembering which targets had been previously found). The search continued until either 8 targets were found or the screen was touched twenty times. When the last of 8 targets was touched or at the location of the twentieth touch, a large face appeared for a few

TABLE II  
 Summary statistics for selective attention in toddlers ( $N = 64$ ). Group differences and age-related changes

	MA controls ( $N = 40$ )	Toddlers with FXS ( $N = 8$ )	Toddlers with WS ( $N = 8$ )	Toddlers with DS ( $N = 8$ )	Group differences
Search speed (secs, SEM)	1.81 (.9)	1.82 (.25)	2.39 (.25)	1.35 (.25)	WS > DS*
Search path (cm, SEM)	5.29 (.18)	6.18 (.41)	6.20 (.41)	5.97 (.41)	n.s.
Search errors					
Touches on distractors per run (SEM)					
Dissimilar distractors	.98 (.27)	.86 (.53)	3.0 (.49)	1.31 (.49)	WS > MA*
Similar distractors	1.10 (.23)	3.59 (.75)	6.63 (.70)	2.88 (.70)	WS > MA, DS, FXS*** FXS > MA*
Repetitions per hit (SEM)	.13 (.53)	.89 (.12)	.33 (.12)	.25 (.12)	FXS > MA, DS, WS*

Note. Minimum p value for pairwise comparisons: \* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ .

seconds and the search was terminated. Unlike most adult search tasks, this visual search task contains target present only, rather than also target absent trials, an approach that is particularly well suited for use with children.

Toddlers were presented first with a baseline run (to control for baseline non-attentional differences in motor control and speed) and then with the four experimental runs in randomised order across children. The task yielded measures of *search speed* (mean search time per hit), *search path* (mean distance between successive touches) and *errors of different types* (touches on distractors, or repetitions on previously found targets). These measures were corrected for the time and distance spent while making errors, in order to obtain measures that would be independent of accuracy and error type. To correct time, we subtracted the time spent making any type of error and divided the remaining time by the total number of hits. To correct distance, we divided the total distance between successive touches (whether they were correct or not) by the total number of touches (excluding immediate repeats on targets, which did not accrue any distance). Additional corrections were used to isolate and remove near misses due to inaccurate pointing or touches with parts of the hand other than the index finger. Variables were checked for any violations of parametric statistics, and transformations were applied when necessary.

### Results and Discussion

Table II presents summary statistics for Study 1b. Group differences have been partially reported by Scerif et al. (2004). They are presented here to introduce the new comparison to DS and to investigate anew changes in performance with development. A 2 (target-distractor similarity: dissimilar, similar distractors)  $\times$  2 (distractor number: few, many)  $\times$  4 (Group: FXS, WS or DS toddlers, MA controls) mixed factorial ANCOVA was run on measures of search speed, path, and error types. Developmental level was used as a covariate to control for differences in mental age across groups. Their correlation to average

measures of performance across conditions was also tested. There were no statistically significant differences amongst groups in terms of *search path* and *speed* (lowest  $p = .104$ ), except that toddlers with WS found targets more slowly than toddlers with DS ( $p = .037$ ). However, toddlers differed most strikingly in the *types of errors* that they produced. Groups differed in the number of touches on distractor circles [ $F(3, 58) = 16.801$ ,  $p = .001$ ], due to the fact that toddlers with WS confused targets and distractors more than any of the other groups ( $p = .003$  for all comparisons). This is despite the fact that all toddlers with WS could discriminate them in control trials. Both toddlers with FXS and WS, unlike those with DS and controls, made more of these errors when targets and distractors were similar [ $F(1, 7) = 15.557$ ,  $p = .008$  and  $F(1, 7) = 10.029$ ,  $p = .016$ ]. These differences suggest that their ability to deal with perceptual similarity between targets and distractors when under high attentional demands is lower than expected given their mental age. Repetitions on previously found targets per hit also distinguished groups [ $F(3, 28) = 15.086$ ,  $p = .001$ ], as toddlers with FXS produced more repetitions on previously found targets than any of the other groups [highest  $p = .001$  (Bonferroni adjusted)]. This pattern of performance suggests again that inhibitory difficulties characterize FXS from early in development. By contrast, children with DS did not differ from (much younger) MA control children on any of these measures, pointing to delay compared to the normal developmental trajectory. By contrast, the striking differences in error patterns for WS and FXS, on the other hand, suggests in both cases deviance from the typical developmental trajectory, in distinct ways.

#### *Preliminary Insights into the Typical and Atypical Developmental Trajectories of Attention in Infants and Toddlers*

Importantly, as we argued in the Introduction, focusing entirely on group differences in performance is not sufficient, as it ignores the possibility that *developmental trajectories* of

performance across groups may deviate from normal gradually over time. We therefore analyzed the data in Study 1a and 1b to begin to assess the relation of attentional measures to changes in developmental level and chronological age.

In Study 1a, for the *inhibition measure*, developmental level and chronological age correlated negatively with cue looks (Spearman's  $\rho = -.467$ ,  $p < .05$ ) and with the percentage of antisaccades produced in the second half of trials ( $\rho = .812$ ,  $p < .001$ ) for MA controls. Older infants produced fewer cue looks and more antisaccades than younger infants, both important measures of oculomotor control, suggesting that, in the normal child, these abilities develop over infancy and early toddlerhood. This was not the case for the two syndrome groups ( $\rho = -.255$  and  $-.299$  for cue looks, and  $\rho = .012$  and  $.031$  for antisaccades in FXS and WS infants respectively). Similar differences in correlations across the control and syndrome groups were found when a smaller ( $n = 10$ ) sample of controls matched to patients on the bases of developmental level was used for these analyses, suggesting that null correlations in the two syndrome samples could not be entirely accounted for by limited statistical power. Differences across groups in the rate of development across measures were also supported by preliminary linear regression analyses, with group, developmental level and their interactions as predictors of cue looks and antisaccades in the second half of the experiment. Both regression models were significant [ $F(3, 35) = 3.326$  and  $10.242$ ,  $p = .032$  and  $.001$  respectively], and beta coefficients for the interaction of group and developmental level reached statistical significance [stand  $\beta = .759$ ,  $t = 2.109$ ,  $p = .043$  and stand  $\beta = -.859$ ,  $t = -2.918$ ,  $p = .006$  respectively]. Despite the unavoidable limitation of small sample sizes of syndromic infants, these interaction effects begin to suggest that mental age predicted cue looks and antisaccades differently across clinical and control groups, in turn pointing to differences in developmental trajectories of inhibition across groups. Developmental level and chronological age did not correlate with *orienting measures* for all groups suggesting perhaps that inhibition and orienting may develop along different time-schedules, at least in the adequately powered MA sample. We also found a negative correlation between speed of orienting to validly cued targets and chronological age in infants with WS ( $\rho = -.755$ ,  $p < .05$ , and a trend in this direction for correlations between developmental and speed of orienting in valid trials), a finding that would be predicted if, as they got older, orienting in infants with WS was increasingly affected by a sudden peripheral onset. Coefficients for these correlations in the other groups were not as steep, as also suggested by the marginally significant interaction

of group and developmental level as predictors of speed in valid trials (stand  $\beta = -1.196$ ,  $t = -2.049$ ,  $p = .048$ ). Importantly, null findings for the other groups need to be treated as preliminary, due to the relatively small sample sizes assessed here, which we are currently testing with greater samples of infants.

In Study 1b, developmental level and chronological age correlated significantly with search measures for MA controls only ( $p$  ranging from  $p < .05$  to  $< .001$ ), suggesting a gradual development for measures of search efficiency in this group. However, null results in the syndrome groups may have been driven by the small sample sizes. Also suggesting similar trajectories across groups, group membership and developmental level or age did not interact significantly as linear predictors of search performance. Again, the strength of the conclusions that we can draw from these data is, of course, limited to some extent by the sample sizes of the syndrome groups. We therefore try to trace more reliably developmental trajectories in these domains, with a much larger sample of older children with DS and FXS, to which we now turn.

## STUDY 2 DEVELOPMENTAL TRAJECTORIES IN CHILDREN WITH FXS AND DS

There are now numerous studies to attest that by late childhood, the cognitive profile of children with FXS and DS is not characterized by global mental retardation. Instead, the syndrome-specific profiles are characterised by uneven abilities within and across cognitive domains. In FXS, for example, difficulties in speech fluency characterised by repetitive and impulsive speech (Belsler and Sudhalter, 2001) are often accompanied by difficulties in grammar and pragmatics (Bennetto and Pennington, 2002), with many children with FXS only reaching the level of MA-matched control children. In contrast, individuals with DS do not show the specific pragmatic problems suffered by individuals with FXS, but instead have difficulties in syntax and morphology (Chapman et al., 1991; Fowler, 1990; Naigles et al., 1993). With regard to working memory deficits, children with DS have worse verbal working memory than visual-spatial memory (Jarrold et al., 1999, 2002), a pattern that is reversed in FXS where there is a tendency to have a relative strength in verbal memory especially for recalling meaningful information with long or short delays (Freund and Reiss, 1991; Munir et al., 2000b). One of the most striking aspects of the FXS profile in particular are the observed attention impairments, which have been widely documented at the behavioural level (e.g., Baumgardner et al., 1995; Wilding and Cornish, 2004), and more recently at

the cognitive level. These studies highlight the need to differentiate performance across attention sub-domains (selective, sustained, inhibition) rather than assume a domain-general vulnerability. Most notably when performance is compared to typically developing children, children with FXS have a profound impairment in inhibitory control, particularly apparent for skills that require attentional switching and the inhibition of task-irrelevant responses. Other aspects of attention performance appear to be less profoundly impaired (Cornish et al., 2001b; Wilding et al., 2002). This phenotypic profile, at least in FXS seems to continue into adulthood, with adult males showing greatest difficulty in the ability to switch attention set and inhibit irrelevant responses (Cornish et al., 2001a; Loesch et al., 2003a). However, to date no published study has yet addressed the extent to which the pattern and severity of the FXS profile can be distinguished from other developmental disorders, not only at the group level, but also in the extent to which different syndrome profiles represent convergent or divergent developmental pathways across childhood. In order to answer this question, we need to investigate changes in performance over developmental time on tasks that tap different attention sub-domains, and with larger sample sizes. To this end, study 2 will examine developmental trajectories in performance of individuals with FXS and DS from mid to late childhood.

### Method

#### Participants

A total of 100 children constituted the final sample for analyses. Twenty-five boys with FXS and 25 boys with DS were recruited through the Fragile X Society and Down syndrome Support Groups, United Kingdom. Fifty typically developing boys also participated in the study. For the males with FXS, the mean chronological age was 10.88 years (range = 8.06-15.09) and the mean verbal mental age, as measured by the British Picture Vocabulary Scales (BPVS; Dunn et al., 1997), was 6.77 years (range = 4.0-10.9). For the boys with DS, the mean chronological age was 11.17 years (range = 7.0-15.09) and the mean verbal mental age, as measured by the BPVS, was 6.09 years (range = 3.06-9.1). Performance was compared to that of typically developing children, who were matched as closely as possible to the FXS and DS children on mental age (mean verbal mental age was 7.37 years and range = 4.05-10.03) and were therefore chronologically younger than the two syndrome groups (mean chronological age of 7.78 years and range = 5.02-10.09). Although there were no significant differences in mental age between the FXS group and the control group, the DS group did demonstrate a significantly lower

mental age than the control group ( $p = .005$ , *post-hoc* Scheffe). Accordingly MA was used as a covariate in the subsequent group analyses.

#### Measures

The battery of tasks consisted of recently published standardized attention tests: the Test of Everyday Attention for Children (TEA-Ch; Manly et al., 1999) and the computerized Wilding Attention Test for Children (WATT; Wilding et al., 2001). In the *selective attention task* (Map Search Task- TEA-Ch), children are required to visually search a map (Philadelphia area, USA) during a total of one minute for symbols of knives and forks paired together and to circle them with a pen. There was a maximum of 80 knife-and-fork symbols to locate and the score was the total number of correctly circled symbols. In the *sustained attention task* (Vigilan-WATT), a computer display consisting of a river, trees and a variety of different colored "holes" on a green background was presented to each child. A target stimulus (a 'monster') then appeared randomly on the screen and children were told to quickly click on the monster each time it popped up from a "hole" before it disappeared. A total of 20 targets was presented one at a time, at irregular intervals. There was one run only, with a pre-demonstration. The number of targets detected (maximum 20) and the mean time (seconds) taken to click onto a target were recorded. In the *Inhibition task* (Walk task-TEA-Ch), the ability to withhold a response and to delay a response is assessed by asking children to mark (using a pen) each successive square on a paper "path" as they hear successive identical tones played on an audiotape. Children are told that one of the tones in each item will end differently from the rest (in the cartoon like exclamation 'D'oh!') meaning that the next step should not be taken. There were four practice trials followed by 20 actual trials (20 columns) with a maximum possible score of 20 correct responses.

#### Procedure

All children were tested individually in a quiet room at school, in two 35-minute sessions with a 15-minute interval.

#### Results and Discussion

A multivariate analysis of variance (MANOVA) was used to assess group differences across the attention measures. This revealed a significant main effect of group [ $F(2, 96) = 12.43$ ,  $p = .001$ ], and a significant group by task interaction [ $F(2, 96) = 22.87$ ,  $p = .001$ ] indicating that the pattern of performance across the groups was different for different scores. Separate ANOVAs across the different attention scores followed by *post-hoc*

TABLE III  
 Summary statistics for selective attention, sustained attention and inhibition in childhood (boys). Group differences and mental and chronological age-related changes

		MA controls (N = 50)	Children with FXS (N = 25)	Children with DS (N = 25)	Group differences
<i>Selective</i>	Mean targets detected	21.3 (11.3)	20.6 (11.1)	11.2 (5.6)	FXS, MA > DS***
	MA – related changes	.574***	.549***	.311	
	CA – related changes	.661***	.427**	.656***	
<i>Sustained</i>	Mean targets detected	18.9 (.98)	18.3 (1.5)	18.1 (1.2)	n.s.
	Mean time taken	3.3 (.92)	4.1 (1.9)	3.9 (.79)	n.s.
	MA – related changes	.429**	.454*	.201	
		– .624***	– .126	– .518**	
	CA – related changes	.403**	.410**	.304	
	– .518***	– .055	– .462*		
<i>Inhibition</i>	Mean trials correctly completed	14.2 (3.7)	8.6 (5.2)	13.5 (4.9)	FXS < DS, MA***
	MA – related changes	.566***	.386	.380	
	CA – related changes	.417**	.254	.616***	

Note. Minimum p value for pairwise comparisons: \*p < .05, \*\*p < .01, \*\*\*p < .001.

Scheffe tests were used to analyze the main and interaction effects in detail. However, to reduce the likelihood of Type I errors, the Bonferroni correction test was used where only those results meeting an alpha level of  $.05/4 = .01$  were considered statistically significant. See Table III for a summary of findings across groups.

For the *selective attention measure*, performance differed significantly between groups [F (2, 96) = 16.805, p = .001], with the DS group performing significantly worse than the FXS group (p = .002, Scheffe) and the controls (p = .001, Scheffe). On the *sustained measure*, there was no significant main effect of group on number of targets detected [F (2, 96) = 2.175, n.s.] or on mean time taken to locate targets [F (2, 96) = 3.117, p = .049, n.s.]. On the *inhibition measure*, performance again differed significantly between groups [F (2, 96) = 16.010, p = .001], with the FXS group producing more errors than both the DS group (p = .001, Scheffe) and the controls (p = .001, Scheffe). These findings point to some clear group differences in the ability to process attention across its component levels. Impairments in inhibition characterize children with FXS, while impairments in selective attention are characteristic of children with DS.

#### Analyses of Changes Related to Developmental Level and Chronological Age

In order to evaluate developmental trajectories of performance within each group, Pearson Product moment correlations between performance, chronological age and mental age (all transformed to z scores) were calculated. These statistics are reported in Table III. On the *selective attention measure*, there was a significant correlation between CA and targets detected across all groups, indicating an increase in performance commensurate with increasing chronological age. However, and in contrast to the FXS and control children, there was no correlation between selective attention

performance and increasing MA in children with DS. On the *sustained attention measure*, there was a significant correlation between CA and MA and the number of targets detected in the FXS group and the controls, but not in the DS group. However, in terms of speed, both controls and DS children became quicker with increasing CA and MA, whereas there was no such correlation in FXS. On the *inhibition measure*, there was a significant correlation between CA and performance in DS and controls, but not in FXS. In contrast, only the controls demonstrated a significant correlation between increasing MA and performance.

Differences in how performance changed with developmental level and chronological age across groups was also assessed using linear regression models. When group membership, chronological age and their interaction were entered as predictors of *selective attention* abilities, the interaction between age and group was the only statistically significant predictor [stand  $\beta = .345$ , t = 3.633, p = .001]. This was also true for both *sustained attention* measures [stand  $\beta = .289$ , t = 2.991, p = .004 and stand  $\beta = -.370$ , t = -3.942, p = .001 for targets detected and for mean time taken, respectively]. In the case of *inhibition*, groups also differed in how performance changes over chronological age [stand  $\beta$  for the interaction = .604, t = 7.284, p < .001]. The interaction of developmental level and group membership was also a significant predictor of *inhibition* [stand  $\beta = .510$ , t = 5.873, p < .001], and of *sustained attention* (mean time taken) [stand  $\beta = -.408$ , t = 14.421, p < .001]. These statistics all suggest that performance changed differently with chronological age and developmental level across groups. Furthermore, two different (albeit related) techniques, ANCOVA and linear regression, both suggest that age and mental age can predict performance differently across typical and atypical groups.

These data provide the first evidence of the *complexity* of atypical trajectories in attention performance in childhood. Clearly, the relationship

is not one of a simple general “delay” reflective of mental retardation per se, but instead syndrome profiles reflect a unique blending of strengths and difficulties that interact differently with both chronological age and mental age across attention sub-domains and across developmental time. For example, children with DS performed better than children with FXS on the task that tapped inhibition. Likewise children with FXS performed better than those with DS on the task of selective attention. In both cases, performance was comparable to that of control children. However, unlike controls who displayed co-linearity between task performance, CA and MA, there was a differential impact of CA and MA on performance by the clinical groups that appears to be syndrome specific and likely to reflect the divergence between performance in the syndrome groups and what is expected given developmental level and chronological age. Of note, this divergence cannot be simply characterized as mental retardation, as it differs across syndromes and across different attentional processes. In addition, on a task that required sustained attention, although all three groups show comparable performance at the cognitive level, performance in DS is not associated with increased CA or MA, unlike the children with FXS and controls who demonstrate a significant correlation between CA/MA and the sustained attention task performance.

#### GENERAL DISCUSSION

The two studies described above provide a series of novel and converging, syndrome-specific findings across developmental trajectories. Both similarities and differences in component processes of attention characterize the atypical groups, highlighting the importance of cross-syndrome comparisons in dissecting what seem at first blush to be syndrome-general “attentional difficulties”. For example, by mid-late childhood, *sustained attention* is a relative strength in both DS and FXS where performance reaches a comparable level to that of typically developing control children. This finding suggests that at least one attention sub-domain is relatively proficient (although, we would argue, not ‘intact’) in these syndrome groups. In contrast, with respect to *inhibition*, children with FXS display greater difficulties than children with DS. Conversely, *selective attention* is weaker in DS than in FXS who perform at a comparable level to control children. Closer inspection of any age-related findings during mid to late childhood suggests a differential impact of chronological and developmental level to task performance that diverges across syndromes. Together, these findings indicate differing developmental trajectories that are syndrome specific and not merely characterizable as general mental retardation.

When we consider performance earlier in life, our findings with infants and toddlers remain preliminary because of the small samples that could be recruited at these younger ages. Nevertheless, they are important, because they aid our understanding of timing differences in the development of cross-syndrome attentional profiles. Beginning with *selective attention*, while older children with DS displayed poorer performance than control children and children with FXS, their earlier performance falls within what is expected given their developmental level. In contrast, search performance by toddlers with FXS (unlike that of any of the other groups) displays striking perseverative errors, a marker of the *inhibition* difficulties that characterize the syndrome later in childhood. Toddlers with DS did not display this type of error, as might have been predicted from their later performance on an *inhibition* measure. Therefore, early performance by the two syndrome groups illustrates both differences and continuities with the attentional profiles that characterize them later in childhood.

We were also able to compare performance by these two groups with that of infants and toddlers with WS: slower search differentiated these toddlers from toddlers with DS even when group differences in chronological age and developmental level were taken into account. Striking difficulties in differentiating targets from distractors, especially when these were very similar, affected WS ability to select targets more than any other group. This was not due to visual problems since they could easily distinguish distractors from targets in the baseline condition. In terms of *orienting*, infants and toddlers with WS also differed from infants and toddlers with FXS in their ability to disengage from central fixation and from a previously attended location, a difficulty that may well account for their later search difficulties. In future studies, selective attention difficulties will certainly need to be charted in later childhood in WS, as we have done for children with DS and FXS. Intriguingly, these early difficulties in shifting attention overtly from a central stimulus are documented in infants with WS engaged in attempts at triadic interactions (Laing et al., 2002; Mervis et al., 2003), pinpointing potential implications of cognitive attentional difficulties for their social cognition. Despite limited overt orienting towards the periphery, infants with WS were affected greatly by attended cues and this trend increased with age. Interactions across social and non-social aspects of attention do indeed deserve further investigation across all syndromes, both cross-sectionally and longitudinally.

In order to complete our understanding of atypical developmental trajectories, it is crucial that studies begin to define the trajectory of attention performance across the lifespan. Although we have already made reference to the relative dearth of

studies defining the infant cognitive phenotype, fewer still have defined the adult phenotype (Cornish et al., 2001a; Loesch et al., 2003a). Of these, important syndrome-specific profiles of proficiencies and deficiencies within the domain of attention have emerged. As in infancy and childhood, the greatest difficulty for adult males with FXS relates to *inhibition*, with performance significantly poorer than DS adult males and mental-aged matched typically developing males (Cornish et al., 2001a; Loesch et al., 2003a). Further evidence that inhibition follows an atypical developmental pathway in FXS comes from the recent findings that inhibitory impairments represent a core deficit in fragile X pre-mutation ('carriers') adult males compared to performance across other cognitive domains (Cornish et al., 2005; Loesch et al., 2003a, 2003b). In contrast to FXS, inhibitory performance in DS, although pointing to developmental delay, appears to remain relatively proficient at a functional level (Welsh and Elliott, 2004). In terms of *selective attention*, adults with FXS display more proficient performance than adults with DS (Cornish et al., 2001a). This pattern is similar to that reported in childhood for both syndromes, but not in earlier in life. The limited sample of toddlers with DS tested here will need to be increased in order to draw strong inferences, but this finding of early relative unimpaired performance by toddlers with DS is consistent with a similar finding for infants with DS and sustained attention (Brown et al., 2003).

Novel information on syndrome-specific trajectories of attention came from considering how performance changed in line with chronological age and developmental level across groups. Syndrome groups, control infants, toddlers and children differed in this respect in a way that we could not have anticipated from simply comparing group performance. Similar critical findings come from closer examination of age-related changes in adults with DS and FXS whose attentional deficits we had previously reported (Cornish et al., 2001a). Charting changes with age reveal that selective attention performance remains stable with age across both syndromes. In contrast, individuals with DS continue to improve with age on inhibition and sustained measures, whereas individuals with FXS demonstrate no improvement with age on these measures.

Many pieces of the puzzle obviously remain to be explored. For example, although attention in infants and toddlers with WS has been tested, children and older adults with the syndrome have not yet been assessed with similar measures. None the less, preliminary findings obtained using a visual search paradigm with adolescents and adults with WS (Grice and O'Riordan, unpublished) suggest that their performance is only at the level expected for their overall developmental level. This in turn points, at a minimum, to gross delay in

selective attention for this group. Future studies will ascertain whether this is due to visuo-perceptual difficulties in discriminating targets from distractors under greater attentional demands (as is the case for toddlers with WS) and/or to difficulties in disengagement from searched locations.

Our aim in this paper was to begin to fill gaps in our knowledge of syndrome-specific developmental trajectories of attention across three genetic disorders: FXS, WS, and DS. We pinpointed differences across ages in each syndrome in the extent to which performance remains static or improves. In the main, despite large overall delay and greater adult difficulties with selective attention, individuals with DS showed improvements by adulthood, whereas those with FXS did not, especially for measures tapping inhibitory control. This divergence in syndrome-specific trajectories of performance also occurs in the field of number where DS but not WS shows improvement with age (Paterson et al., 2006). As with all studies of relatively rare genetic disorders, and particularly the recruitment of infants, issues of statistical power place some limits on the inferences that can be made for the youngest groups, but even so they attest to the fact that the development of certain attentional measures proceeds more slowly in some of the groups studied here. This suggestion is supported by the data obtained on older children and adults.

Taken together, these studies underscore the significance of three combined aspects of our approach to developmental disorders of attention. First, we believe that a cross-syndrome perspective is vital in investigating atypical cognitive functioning. Second, our work has shown that all cognitive domains must be broken down into their component parts if we are to fully capture the subtleties of cross-syndrome similarities and differences. We have demonstrated here how three syndromes previously all characterized as having "attentional problems" differ radically from one another once attention is studied in any depth. Third, it is crucial to study full developmental trajectories from infancy through adulthood, rather than targeting a single age group, as dissociations in group performance may emerge from diverging developmental trajectories (Karmiloff-Smith et al., 2003b). Our findings point to differences across syndromes in the extent to which deficits remain constant or change with age. It is our view that only once scientists embrace this three-pronged level of detail in cross-syndrome, developmental studies of genetic disorders will be able to examine properly the relationship between genotype and phenotype.

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