



# Developmental trajectories of hierarchical visuo-spatial processing in fragile X syndrome and ASD: Within- and cross-syndrome variability



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## ABSTRACT

**Background/aims:** Despite the advances in understanding visuo-spatial processing in developmental disorders such as ASD and fragile X syndrome (FXS), less is known about the profile of those with a comorbid diagnosis, or the role of within-disorder disparities between individuals across the ASD spectrum.

**Methods and procedures:** Using a developmental trajectory approach, we tested 5 groups of children: Typically developing, FXS, FXS + ASD, ASD individuals who had low-moderate symptoms (HFA) and ASD individuals who had severe symptoms (LFA). Symptoms of ASD were assessed using the Childhood Autism Rating Scale: CARS and hierarchical visuo-spatial processing was assessed using the Navon task.

**Outcomes and results:** Crucially, results differed between HFA and LFA participants. Furthermore, the pattern of results differed between those who had a diagnosis of FXS only and FXS + ASD. Poorer performance within the FXS groups and the group who are low functioning on the ASD spectrum indicated a delayed developmental rate compared to typical controls.

**Conclusions and implications:** This study showed that diagnosis and severity of symptoms are indicative of differences in visuo-spatial processing styles. It is important that heterogeneity within FXS and ASD populations are considered in subsequent studies and look beyond diagnostic group differences.

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## What this paper adds

This paper explored the visuo-spatial hierarchical processing biases of children with fragile X syndrome (FXS) and ASD. A large sample of children with FXS, children with a comorbid diagnosis of FXS + ASD and children who had low to moderate ASD symptoms as defined by the CARS and those who had severe ASD as defined by the CARS were recruited for inclusion. Developmental trajectories were constructed with children ranging in age from 3 to 18 years on the Navon task in order to

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compare inter and intra group differences in visuo-spatial hierarchical processing. Unlike most of the literature in this field, this paper includes data from children who showed severe ASD symptoms and consequently reveals a different processing style to those who show mild-moderate ASD symptoms. Importantly, this paper reports on key differences between children who have FXS versus those who have FXS + ASD. This is significant because it highlights the impact that the presence of ASD can make in the development of cognitive abilities in single gene disorders, such as FXS. The developmental trajectories that were constructed show that FXS children and children who display severe ASD symptoms are not necessarily lacking in hierarchical visuo-spatial skills but these develop at a slower rate or slightly later in development. This highlights the importance of using cross-sectional trajectories when researching developmental disabilities.

## 1. Introduction

Effective visual perception occurs in a hierarchical manner, enabling the differentiation between global (tree) and local (leaves) percepts and thus facilitating a meaningful organisation of the visual world and an understanding of context. There is a plethora of research detailing the visuo-spatial hierarchical profiles of neurodevelopmental disorders, and, in particular, that of ASD (autism spectrum disorder) (e.g. Bölte, Holtmann, Poustka, Scheurich, & Schmidt, 2007; Lee et al., 2007; Manjaly et al., 2007; Shah & Frith, 1993; White & Saldaña, 2011). Also gaining attention is the unique profile of individuals with fragile X syndrome (FXS: Scerif, Cornish, Wilding, Driver, & Karmiloff-Smith, 2004; Scerif, Cornish, Wilding, Driver, & Karmiloff-Smith, 2007). However less attention has been given to those with a comorbid diagnosis of FXS and to the impact that ASD has on visuo-spatial processing. In this paper this examine the hierarchical visuo-spatial inter and intra group comparisons of FXS and ASD.

### 1.1. Fragile X syndrome

FXS results from a single gene mutation associated with a CGG trinucleotide repeat expansion on the 5'UTR of the fragile X syndrome mental retardation gene (*FMR-1*), located on the X chromosome. This consequently leads to a deficit in the production of the FMR1 protein (Hagerman, 1999), which causes the *FMR-1* gene to be “switched off” in affected individuals. The premutation of *FMR-1* is characterised by approximately 55–200 repeats (Hagerman et al., 2009) and the full mutation which involves more than 200 repeats, results in a diagnosis of FXS. As is the case for X linked disorders, males tend to be more severely affected than females. In addition and crucial to the current study, approximately 60% of males with FXS meet the diagnostic criteria for ASD (Clifford et al., 2007; Harris et al., 2008; McDuffie et al., 2010) which subsequently creates two separate cohorts of FXS; FXS only and FXS + ASD.

Much of the FXS research has concentrated on the cognitive phenotype but specifically there has been a focus on the domain of visual attention (Cornish, Scerif & Karmiloff-Smith, 2007; Munir, Cornish & Wilding, 2000; Scerif et al., 2004, 2007). Evidence suggests that individuals with FXS have deficits in sustained attention, inhibitory control and selective attention. Selectively attending to hierarchical stimuli can impact on higher order abilities such as executive function. This could influence other areas of development, thus possibly creating heterogeneous developmental pathways that are diagnostically significant. The current study aims to examine inter and intra group differences in the hierarchical visuo-spatial profiles amongst individuals with FXS and ASD.

### 1.2. Visual attention in FXS

In hierarchical processing, local processing refers to the perception of the individual elements of an image, whilst attending to the image as a whole figure is referred to as global processing. To date, there have been few studies investigating hierarchical visuo-spatial processing in FXS individuals, with more research focusing on the higher order deficits, such as attention that defines the whole of their visuo-spatial impairment (Cornish et al., 2007; Scerif et al., 2007). Hierarchical visuo-spatial processing is important as it allows the perceptual organisation of the visual environment, and would account for some of the results that are shown in visuo-perception and visuo- construction tasks (Cornish, Munir & Cross, 1999). Individuals with FXS display difficulties in processing sequential information, demonstrating a simultaneous processing style (Hodapp et al., 1992), but this has not been directly investigated in reference to visual processing. In part, the perceptual problems that individuals with FXS experience could be accounted for by their visual attention. Indeed Scerif et al. (2004) investigated visual selective attention in toddlers with FXS and found that they perseverated more on previously found targets than children with Williams syndrome and typically developing children. Although children with Williams syndrome and FXS made more mistakes than those with typical development, the most interesting finding was that the pattern of errors differed between groups. Although problems with perseveration and inhibition may define the FXS profile in terms of visuo-spatial processing, it is unclear whether these deficits show a typical pattern of development in relation to hierarchical processing. Studies using tasks based on a hierarchical principle such as the Block Design task have revealed impairments (Cornish et al., 1999) but it is unknown whether it is due to competing local and global stimuli or other factors.

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