Sex differences in the phenotype of children with autism of known genetic aetiology

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BACKGROUND

Autism is less commonly diagnosed in girls than boys (1:3). But there have been consistent reports over many years that the sex ratio tends toward equality in children with moderate to severe intellectual disability (ID). This observation may be linked to the finding that pathogenic genetic anomalies are relatively more common among girls with autism than boys.

Research question: Are the phenotypes of non-autistic symptomatology (e.g., adaptive function, emotional difficulties, hyperactivity) similar or different in girls with ID-associated autism compared with boys of equivalent ID?

OBJECTIVES

1. Identify the range and severity of autism symptomatology and co-occurring psychopathology in boys and girls with autism of genetic aetiology.
2. For comparison purposes, we undertook an equivalent analysis of sex differences in terms of common co-occurring symptom clusters (e.g., ADHD, anxiety) in a sample of children with ID of genetic aetiology that was not associated with autism traits.

METHODS

Participants were identified from the IMAGINE-ID study, a national investigation of children with ID of genetic aetiology (pathogenic CNV or SNV) identified by the UK National Health Service.

Autism diagnoses were assigned by clinicians (validation study Wolstencroft et al., 2023)

The **Strengths and Difficulties Questionnaire (SDQ)** measured behavioural and emotional adjustment.

The **Adaptive Behaviour Assessment** (*ABAS)* assessed functional skills necessary for daily living

RESULTS

• Data were obtained on 776 participants with ID and autism (4 to 19 years; M=9.1, SD=3.9), (36.1% female) and 1,410 participants with ID that was not associated with autism traits (48.2% female).

• Among those with autism, there were no significant sex differences on the ABAS general adaptive composite score (p=.8) or on parental estimates of mental age (p=.8).

• Girls with autism were significantly more likely to have emotional difficulties (p<.001) and better prosocial abilities (p=.03) than boys.

• There were no sex differences on conduct or hyperactivity problems by sex.

• Among those with ID who lacked autistic traits, there were significant sex differences in emotional difficulties and prosocial abilities, as well as significant differences in hyperactivity and conduct problems.

	No Autism			Autism		
	Boys n= 730	Girls n= 680	p-value	Boys n= 496	Girls n= 280	p-value
Participant characteristics, M (SD)						
Age	9 (3.7)	9.2 (4)	**.8**	9 (3.8)	9.7 (4)	**.012**
Mental age	4.9 (3.1)	4.9 (3)	**.9**	5 (2.9)	5 (2.8)	**.8**
ABAS	64.1 (14.3)	67.7 (15.2)	**.001**	60.6 (12.3)	60.1 (11)	**.8**
Strengths and Difficulties Questionnaire, M (SD)						
Emotional difficulties	3.9 (2.7)	4.3 (2.8)	**<.01**	5.2 (2.7)	5.9 (2.9)	**<.0001**
Conduct problems	3.3 (2.4)	2.9 (2.3)	**<.0001**	3.9 (2.4)	3.9 (2.3)	**.9**
Hyperactivity problems	7.7 (2.2)	7.2 (2.3)	**<.0001**	8.3 (1.9)	8 (2.1)	**.14**
Prosocial ability	5.5 (2.8)	6.2 (2.7)	**<.0001**	4 (2.6)	4.4 (2.5)	**0.031**

Table1. Sex differences in IMAGINE children with and without autism

• Sex differences in emotional difficulties and prosocial ability in children with autism remained unchanged when tested by multiple linear regression models using chronological and developmental age as co-variates.

INTERPRETATION

• There are sex differences in those with autism of genetic aetiology in terms of emotional dysregulation and prosocial behaviour, both of which are significantly greater in girls.

• These sex differences are not exclusively found in those with autism. They can also be observed among children with equivalent degrees of ID without autism.

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