Gender Ratios in Autism, Asperger Syndrome and Autism Spectrum Disorder

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Dr Whiteley, Ms Todd & Mr Carr were employed by the University of Sunderland over the course of data collection.

Abstract: Skewed sex ratios indicative of a greater preponderance of males over females (approximating 4:1) has perhaps been the most constant collective finding in autism spectrum conditions. More recent investigations have indicated a potential change to traditional estimates of gender ratios. We undertook analysis to calculate contemporaneous gender ratios based on collective and individual sub-diagnoses. A sample of 1963 children diagnosed with autism (n = 460), Asperger syndrome (n = 366) or autism spectrum disorder (ASD) (n = 1137) were included for study. The overall gender ratio based on a year of birth between 1986–2007 was 7.38:1. Differences were found amongst the sub-diagnoses for the same period (autism = 6.54:1, Asperger syndrome = 12.07:1; ASD = 6.84:1). Analysis of annual trends indicated an irregular upwards tendency to gender ratios indicative of increasing over-representation of males with an autism spectrum condition despite no indication of greater disparity in population sex ratios at birth. Further independent studies are required to corroborate our findings.

Keywords: Pervasive Developmental Disorder (PDD), autism, Asperger syndrome, autism spectrum disorder (ASD), gender ratio, genetics, environment
Introduction
Investigations continue into the multiple aetiologies and pathologies of the numerous conditions expressed under the label Pervasive Developmental Disorders (PDDs). In over 60 years of research and clinical description of autism, Asperger syndrome (AS) and autism spectrum disorder (ASD), comparatively little progress has been made in ascertaining universal constants in relation to these conditions. Outside of minor revisions to diagnostic procedures combined with an increasing realisation that each is a complex spectral state in terms of heterogeneity, fluidity and relationships with other co-morbidities, unanimous findings remain elusive.

Perhaps the major constant in most autism diagnoses is the finding of skewed gender ratios. A greater preponderance of PDD diagnoses, excluding Rett syndrome, in males approximating 4:1 has been consistently reported in the scientific literature stretching back to the earliest descriptions of autism. More recent investigations have reported greater gender disparity. Skewed gender ratios towards increased numbers of males have given rise to a number of gender-specific notions implicating potential genetic/chromosomal effects and onward functional consequences to sex hormones such as testosterone as being involved in autism spectrum conditions.

The aim of the current study was to ascertain an overall male:female gender ratio for PDD sub-groups individually and collectively based on our cohort of participants. We also undertook to establish trends based on sub-groups across specific time periods in comparison to general population trends.

Methods
Information on participants diagnosed with PDD was collected via a parent-report questionnaire previously detailed. Cross sectional analysis of responses held on an electronic database were included for records received between October 2001 and July 2009 (N = 4544). Completed responses for participants born in the UK or Republic of Ireland and also resident in these countries at the time of questioning, aged between 2–16 chronological years, and in receipt of a formal diagnosis of autism (n = 460), Asperger syndrome (n = 366) or autism spectrum disorder (ASD) (n = 1137) [ICD (international statistical classification of diseases) codes F84.0, F84.5, F84.8] with a specific date of diagnosis (month/year) were included for study. Criteria for formal diagnosis have been previously described and included: parental indication of a child’s receipt of a formal PDD diagnosis, indication of a specific categorical PDD diagnosis (autism, Asperger syndrome, ASD), recorded date of diagnosis (month/year), details of diagnosing clinician and place where diagnosis was given. Parents were also encouraged where possible to provide copies of the feedback provided during diagnostic assessment detailing the type of instrument used during assessment and any observations made by the diagnosing clinician/s.

Statistical analyses were performed using Analyse-itTM for Microsoft Excel (v2.20) (Analyse-it Software Ltd, 2009). Time trends for gender ratios were examined by linear regression. All data were held in accordance with the 1998 Data Protection Act.

Results
Analyses were conducted on several combinations of participant groups according to total and categorical PDD sub-diagnoses also covering various time periods based on participants’ year of birth. Missing gender ratios in data for sub-diagnoses are reflective of no cases in one or both of gender categories.

All Participants
Data for total participants (n = 1963) were analysed (males = 1729; females = 234). There was a significant difference in the total numbers of males and females included for study (t = 4.68, df = 21; P = 0.0001). Figure 1 plots graphically the number of male and female participants used in the current dataset as a function of year of birth (1986–2006). Peak participant numbers were observed in those born in 1999. Figure 2(a–c) shows numbers of participants by gender per diagnostic sub-grouping. The majority of participants were resident in the UK over the Republic of Ireland (90.9% vs. 9.1%). The majority of parents were described as White British or White Irish (mothers = 89.7%; fathers = 89.5%). Mean chronological age at time of study was 5.42 years (SD = 2.9). Mean age at receipt of diagnosis was 51.91 months (SD = 27.3). The overall gender ratio (male:female) covering all time periods (1986–2007)
included for study was 7.38:1. Figure 3 shows the gender ratio (male:female) per year of birth for all participants irrespective of PDD sub-diagnosis alongside UK population gender ratios at birth for the same periods.\(^4\) No correlation was observed between the datasets (correlation coefficient \(R = 0.0138\)). Following a ratio on or below 4:1 (1986–1988), an irregular upward trend in the sex ratio was observed in subsequent years. A scatter plot showing gender ratio against year of birth including the linear fit line and confidence intervals (CI) is shown in Figure 4. For the whole study period, the regression co-efficient (\(\beta\)) was 0.2668 (\(R^2 = 0.23\)). An analysis of variance (ANOVA) showed a statistically significant relationship between increasing skewedness in gender ratios in PDD and year of birth (\(F = 5.81; P = 0.0262\)).

**Autism Diagnosis**

Data for participants diagnosed with autism (\(n = 460\)) were analysed (males = 399; females = 61). Mean chronological age at study was 5.38 years (SD = 3.0) with a formal diagnosis received at a mean age of 44.56 months (SD = 20.7). The gender ratio (male:female) for all time periods was 6.54:1. Figure 5 shows male:female gender ratios by year of birth for participants diagnosed with autism.

**AS Diagnosis**

Data for participants with AS (\(n = 366\)) were analysed (males = 338; females = 28). Mean chronological age at study was 7.63 years (SD = 2.9) with a formal diagnosis received at a mean age of 79.74 months (SD = 31.3). The gender ratio (male:female) for all time periods was 12.07:1. Figure 6 shows male:female gender ratios by year of birth for participants diagnosed with AS. Gender ratios peaked in 1995 and 1996.

**ASD Diagnosis**

Data for participants with ASD (\(n = 1137\)) were analysed (males = 992; females = 145). Mean chronological age at study was 4.72 years (SD = 2.4) with a formal diagnosis received at a mean age of 45.92 months (SD = 22.3). The gender ratio (male:female) for all time periods was 6.84:1. Figure 7 shows male:female gender ratios by year of birth for participants diagnosed with ASD.

**Discussion**

Our finding of an overall gender ratio of 7.38:1 (male:female) in collective cases of PDD is higher than the traditional estimate of approximately 4:1. Our figure

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Figure 2. Participants by year of birth and gender grouping (1986–2006) per diagnostic sub-grouping used in current dataset.
is however consistent with estimates ranging from 6.8–8:1 reported by more contemporaneous investigations of PDD where participants are born and/or residing in the UK.\(^2,^3\) This is contrasted with studies of gender ratios in other parts of the world which seem to indicate a lower ratio particularly in Asia where male:female ratios of between 2.5–3:1 have been reported.\(^8,^9\) Isolated reports from Asian countries have also suggested equality in gender ratios for autism although this has yet to be substantiated.\(^10\)

Disparity in the gender ratio according to PDD sub-diagnosis suggestive of a higher male ratio in participants diagnosed with Asperger syndrome compared with other PDD sub-diagnoses concurs with

Figure 3. Gender ratio for all participants (1986–2006) per year of birth. Population gender ratios are also shown according to birth year for the same period.

Figure 4. Scatter plot showing linear fit of gender ratios per year of birth.
other research specifically allowing for differentiation on the basis of ability across the sub-groups.\(^2\) Gender ratios for AS participants in 1995 and 1996 are particularly note-worthy given the high male preponderance in these years.

The associated finding indicative of a widening of the gender gap following analysis of annual trends provides scope for further inquiry. Corresponding analysis of population gender ratios by birth in the UK has not shown any demonstrable differences during the period included in our analysis\(^{11,12}\) remaining constant around 105 males per 100 females. Our reliance on participants both born and currently resident in the UK or Ireland discounts any bias based on immigration or emigration. The majority of our participants were categorised as White British or White Irish on the basis of parental ethnicity, hence excluding any significant cultural or racial preference for boys over girls.\(^{13}\) Comparison of our dataset in relation to ethnicity was also consistent with UK population trends derived from the most recent UK census data (2001) showing an approximate 8% ethnic minority population.\(^{14}\) As per our previous studies\(^5,6\) data for this investigation were drawn from specific studies on the biochemical nature of PDD. Despite the large sample group used we are unable to rule out any bias on

![Figure 5. Gender ratio for participants diagnosed with autism (1986–2006) per year of birth. Missing data indicate periods where no ratio could be calculated due to zero values in male or female participant numbers. Data for these periods are: 1988: 1 male, 0 females; 1989: 3 males, 0 females; 2005: 6 males, 0 females; 2006: 1 male, 0 females. Data for 2007 are not shown but were: 0 males, 0 females.](image)

![Figure 6. Gender ratio for participants diagnosed with AS (1986–2006) per year of birth. Missing data indicate periods where no ratio could be calculated due to zero values in male or female participant numbers. Data for these periods are: 1986: 0 males, 0 females; 1987: 3 males, 0 females; 1989: 5 males, 0 females; 2000: 20 males, 0 females; 2004: 3 males, 0 females; 2005: 0 males, 0 females; 2006: 0 males, 1 female. Data for 2007 are not shown but were: 0 males, 0 females.](image)
Gender ratios in autism spectrum conditions

the basis of the participants being included given the biochemical focus of the research. That being said, we would not expect any sex-specific bias for those becoming involved given that these studies are not gender-related.

By means of the data showing the average age at diagnosis and distribution of participants over the time periods, the drop in subject numbers included in our dataset after 2003 may possibly be reflective of delays of between 4–6 years before children are in receipt of a formal diagnosis and hence eligible for study inclusion. In this way, data presented for 2006 in particular cannot be taken as reflective of any true drop in the ratio from the previous years high. Likewise small participant numbers for the early years (1986–1990) may have affected the reporting of gender ratios during this period.

The precise reasons for our results are complex and perhaps multiple. Our results for autism spectrum conditions contrast with that derived from other developmental conditions; many of which can be co-morbid. Studies on sex ratios for attention-deficit hyperactivity-disorder (ADHD) for example, show estimates ranging from 1.9–5:1 (male:female)\(^{15,16}\) although with a suspicion of under-diagnosis in girls.\(^{17}\) Similar estimates of sex ratios in dyslexia and reading disability, whilst skewed towards males (1.3–2.7:1) have not indicated such a massive disparity between the genders.\(^{18}\)

On balance it is therefore unlikely that the over-representation of males can be purely ascribed to any notion that males are somehow more inclined towards autism solely because of some wholly inherited genetic “weakness” or potential as described by some authors.\(^{19}\) The added fact that sex ratios appear to have so dramatically widened over a period of 20 years casts further doubt on any entirely genetic explanation.

Whilst one cannot discount any potential gender bias in the screening, detection and diagnosis of autism spectrum conditions, suspicion must rest with some role for the environment at least partially accounting for our results. Outside of cultural or racial explanations, many environmental candidates have been put forward to explain sex ratio changes in the general population. Climate, lifestyle and pollutants represent the most consistent factors; some variables such as pesticide exposure overlapping with investigations in autism.\(^{20}\) Specific organophosphate pesticides for example, are known to interfere with testosterone metabolism\(^{21}\) following previous implication of sex hormones in relation to autism spectrum conditions.\(^{4}\)

The varying effects of hormones such as testosterone and oestrogen on the metabolism of other environmental stressors such as heavy metals have also been put forward as explanations for the gender disparity in autism. Results from in-vitro studies of mercury and in particular the mercury containing preservative thiomersal, suggest differences in the action of sex hormones on exposed neuronal cells which may place males at some disadvantage.\(^{22}\) Further discussion on

Figure 7. Gender ratio for participants diagnosed with ASD (1986–2006) per year of birth.
Missing data indicate periods where no ratio could be calculated due to zero values in male or female participant numbers. Data for these periods are: 1986: 1 male, 0 females. Data for 2007 are not shown but were: 1 male, 0 females.
the potential role of any such factors in light of our data is not possible given the lack of accompanying biological measures.

In summary, we found evidence of a dynamic, increasing gulf in gender ratios for autism spectrum conditions, in conjunction with sub-diagnosis disparity. Further large-scale studies are required to corroborate our findings based on suitable population and other condition comparators.

Acknowledgments
This research was supported by funds from the Autism Research Unit at the University of Sunderland, the Robert Luff Foundation and ESPA Research. The authors wish to acknowledge the University of Sunderland where all authors were affiliated over the course of data collection.

Disclosures
This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors report no conflicts of interest.

References

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