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Are autism spectrum conditions more prevalent in an information-technology region? A school-based study of three regions in the Netherlands.

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Running head: Prevalence of ASC in three Dutch regions

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Summary

We tested for differences in the prevalence of autism spectrum conditions (ASC) in school-aged children in three geographical regions in the Netherlands. Schools were asked to provide the number of children enrolled, the number having a clinical diagnosis of ASC and/or two control neurodevelopmental conditions. Prevalence was evaluated by negative binomial regression and adjustments were made for non-response and size of the schools. The prevalence estimates of ASC in Eindhoven was 229 per 10,000, significantly higher than in Haarlem (84 per 10,000) and Utrecht (57 per 10,000), whilst the prevalence for the control conditions were similar in all regions. Phase two is planned to validate school-reported cases using standardized diagnostic methods and to explore the possible causes for these differences.

Keywords: Autism Spectrum Conditions, prevalence, regional differences, hyper-systemizing theory.

Autism spectrum conditions (ASC), which includes autistic disorder (also known as ‘classic autism’ and ‘childhood autism’), Asperger syndrome (AS), pervasive developmental disorder-not otherwise specified (PDD-NOS) and atypical autism, are characterised by impairments in social interaction and communication, alongside unusually narrow activity and interests (DSM-IV-TR; APA 2000; ICD-10; WHO 1993). Classic autism is one of the most severe neurodevelopmental conditions (Volkmar et al. 2004); the cause of both classic autism and ASC as a whole is strongly genetic (Rutter 2005; Ronald and Hoekstra 2011). The ratio of boys to girls affected by ASC is 4:1 for classic autism, and 9:1 for Asperger syndrome (Scott et al. 2002).

The prevalence of ASC is much higher than was previously thought. The first survey of autism in 1979 estimated a prevalence of 4 per 10,000 (Lotter 1966). By 1999, Fombonne (1999) estimated the prevalence of classic autism to be 10 per 10,000, and of all ASC to be 30 to 60 cases per 10,000. These estimates were based on studies from Europe, US, Canada and Japan. Recent research in the UK estimated the population prevalence of ASC to be about 1% (116 per 10,000 and 94 per 10,000) (Baird et al. 2006; Baron-Cohen et al. 2009). Several explanations have been proposed for the apparent increase in ASC prevalence, including improved recognition and detection, changes in study methodology, an increase in available diagnostic services, increased awareness among professionals and parents, and a widening of the diagnostic criteria (Wing and Potter 2002). There has been little opportunity to examine variation in prevalence in autism, although the Center for Disease Control (CDC) surveillance system collected data from 11 Autism and Developmental Disabilities Monitoring (ADDM) Network sites in the US. Besides an average prevalence of approximately 1%, differences in prevalence were found between the sites ranging from 4.2 per 1,000 in Florida to 12.1 per 1,000 in Arizona and Missouri, likely due to differences in ascertainment source (Rice 2009).

There are reasons for expecting that ASC may be more common in populations enriched for systemizing. 'Systemizing' is the drive to analyse how systems work, and to predict, control and build systems (Baron-Cohen et al. 2003). These skills are required in disciplines such as engineering, physics, computing and mathematics. Evidence for a familial association between a talent for systemizing and autism includes the following: Fathers and grandfathers of children with ASC are over-represented in the field of engineering (Baron-Cohen et al. 1997). A recent study suggested that mothers of children with autism may be more likely than those of controls to work in highly technical occupations (Windham et al. 2009). ASC is more common in the siblings of mathematics students (Baron-Cohen et al. 2007). Parents of children with ASC are also faster and more accurate on the Embedded Figures Test (EFT), a measure of excellent attention to detail, and a prerequisite for strong systemizing (Baron-Cohen and Hammer 1997; Bölte and Poustka 2006; Happé et al. 2001). Finally, parents of children with ASC show atypical neural activation during fMRI whilst performing the EFT (Baron-Cohen et al. 2006). These family studies suggest first degree relatives have the broader autism phenotype (BAP) (Piven et al. 1997), that is, a cognitive profile that is milder but qualitatively similar to the defining features of autism, and that this profile includes a talent for systemizing.

Evidence for an association between 'systemizing' and diagnosed ASC includes the following: People with ASC score higher on the Systemizing Quotient (Baron-Cohen et al. 2003; Wheelwright et al. 2006) and are faster on the EFT (Shah and Frith 1983; Jolliffe and Baron-Cohen 1997). Mathematicians have higher rates of diagnosed ASC (Baron-Cohen et al. 2007), and students in the natural and technological sciences, including mathematics, show increased rates of autistic traits (Baron-Cohen et al. 2001). These findings have been replicated in a

range of cultures (UK, Netherlands, Japan), suggesting they are independent of culture (Wakabayashi et al. 2006; Hoekstra et al. 2008).

According to the hyper-systemizing theory (Baron-Cohen 2006, 2008) people with ASC have an unusually strong drive to systemize. We hypothesized that an area that included a high proportion of systemizers might lead to a higher prevalence of autism in offspring. To investigate this theory we tested if ASC was more prevalent in the information technology (IT) region of Eindhoven. This region contains the Eindhoven University of Technology, as well as the High Tech Campus Eindhoven, where IT and technology companies such as Philips, ASML, IBM and ATOS Origin are based. The Philips factory has been in Eindhoven since 1891. Since then, the region has attracted businesses in IT and technology. The growth of the High Tech Campus Eindhoven has led to Eindhoven becoming a major technology and industrial hub: 30% of jobs in Eindhoven are now in technology or ICT, in Haarlem and Utrecht this is respectively 16 and 17% (Statistics Netherlands Website 2008; LISA Website 2010). Media reports have raised concerns about an apparently higher prevalence of ASC in Eindhoven (Wiercx 2009), but this has never been scientifically tested.

The study reported here therefore aimed to ascertain whether there are significantly higher rates of school-aged children with a formal diagnosis of ASC in a defined population in and around Eindhoven, compared to two control populations in the Netherlands. This constitutes the first prevalence study of diagnosed ASC in the Netherlands, and the first study to examine whether regional variations in the prevalence of ASC may be related to systemizing. The prevalence as recorded from routine school records using administrative information was established using school-report, a method that has been used previously (Scott et al. 2002).

Method

Participants

This project received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge, UK. Schools in three regions in the Netherlands were invited to take part in this study: (a) The *Eindhoven* region, comprising the municipalities of Eindhoven, Veldhoven and Waalre; (b) the *Haarlem* region, comprising the municipalities of Haarlem and Haarlemmermeer; and (c) the *Utrecht* region, comprising Utrecht-city. The two control regions (Haarlem and Utrecht) were selected because of demographic similarities to the Eindhoven region. The populations of Eindhoven, Haarlem and Utrecht regions respectively are 269,504, 285,215 and 288,401. The three regions have a similar average income per household, a similar percentage of children with special needs, and similar rates of individuals with mental health problems (Statistics Netherlands Website 2008). There are some differences between the regions, including a higher population density in Haarlem, a slightly higher proportion of young (aged <20 years) residents in Haarlem and a higher percentage of non-Western foreigners living in Utrecht-city (Statistics Netherlands Website 2008).

In all three regions, we focused on children aged 4-16 years who were enrolled in primary or secondary education, in either special or mainstream schools. All mainstream schools within the boundaries of the selected regions were invited to take part. Children with special needs could be living in one of the three designated areas, but attend a special school that is located outside the target municipality. To ensure that these children would not be missed in the count, all special schools within a radius of 50 km of the three regions were invited to participate. Children attending a special school were only included in the count if they were *living* in one of the target municipalities. A total of $n = 659$ schools were included in the study.

In the Netherlands, children with special needs are either enrolled at special schools, or receive financial support to obtain extra care within mainstream schools. The Dutch *Commissie voor Indicatiestelling* (CvI) is an independent committee that decides whether children should be considered for receiving special education or financial support based on *national* criteria. Because a majority of the children diagnosed with ASC are likely to receive financial support (or are enrolled at a special school), their diagnoses will be ascertained and registered by the CvI and will be known to the schools as registered clinical diagnoses. Children with milder forms of ASC who receive mainstream education and are not in need of extra support may not have disclosed their diagnosis to the school, so their diagnosis may be unknown to the schools. Therefore the estimated prevalence based on a school count is likely to be lower than the true prevalence of ASC.

Procedure

Before inviting the schools to participate in this research, the school boards governing the schools were sent a letter informing them of the study and requesting them to encourage the schools to take part. Schools were provided with an invitation letter, consent form, information sheet, freepost envelope and questionnaire, and were asked to return the questionnaire to the research team by post or email. Two months after the initial invitation, non-responding schools received an email reminder to encourage them to take part. Shortly after, schools were contacted by telephone and encouraged to participate either by providing the data over the phone or by filling in the survey. Five months after the initial invitation, non-responding schools who had initially expressed interest in the study but who had not yet responded were contacted again to enquire about the total number of pupils registered at the school. Based on these numbers, a reliable estimate of non-response could be included in the analyses.

Questionnaire

The questionnaire enquired about the total number of children registered at the school, specified by age and gender, and about the number of children with a diagnosis of an ASC, including autistic disorder, Asperger syndrome, PDD-NOS and other autism spectrum conditions. The latter category was included to cover rare ASC diagnoses (Rett's disorder, childhood disintegrative disorder) and ICD-10 (WHO 1993) terminology (including atypical autism). Since both attention-deficit hyperactivity disorder (ADHD) and dyspraxia are also developmental conditions and have a similar diagnostic process to ASC, the number of cases with a formal diagnosis of ADHD and dyspraxia were also examined as control conditions. The schools were asked to provide a count of the total number of children in the school with any of these developmental conditions, specified per diagnostic subtype and by age and gender. The schools were instructed to only include *formal* diagnoses in their count (i.e. diagnoses made by a clinical professional, e.g. a clinical psychologist or psychiatrist). The questionnaire survey represents phase one of this study and is reported here, whilst phase two is planned and will involve diagnostic assessments on all reported cases for validation purposes.

Data analysis

Data were analysed using STATA (version 10.0, Texas, USA). Inverse probability weighting by strata was used to adjust the prevalence estimates for non-response bias associated with special schools, primary or secondary schools and region. Information on the total number of pupils within each type of schools has been used to adjust the estimates for the relative difference in the size of the schools. Prevalence was calculated separately for all ASC, autistic

disorder only, ADHD and dyspraxia. Negative binomial regression was used to investigate the multivariable effects of region and school type, with an additional model to investigate the differences between boys and girls.

Results

Of the 659 schools invited, 369 schools (56.0%) took part, providing diagnostic information on 62,505 children. Response in the Eindhoven region was higher (75.5%) than in the Haarlem (49.8%) and Utrecht regions (45.7%). Special schools were twice as likely to respond as mainstream schools. No difference was found in response between primary and secondary schools after adjustment for region and type of school (special or mainstream) ($p=0.9$). There was some evidence that responding schools were larger than non-responding schools (secondary schools $p=0.15$, primary schools $p=0.03$) and the weighting takes this into account. Table 1 and Figure 1 show administrative prevalence by region. As predicted, administrative prevalence of ASC was significantly higher in the Eindhoven region (229 per 10,000) compared to the Haarlem (84 per 10,000) and Utrecht (57 per 10,000) regions. Autistic disorder alone was also more common in the Eindhoven region compared to the other two regions. ADHD and dyspraxia prevalence were not significantly associated with region. Table 2 shows the prevalence of ASC by type of school and by gender. As expected, ASC in boys was more than four times higher than in girls, and this ratio did not vary by region ($p>0.2$). The prevalence of ASC in secondary schools was higher than in primary schools, which was expected because children with a late diagnosis were included in the secondary school count.

[Insert Tables 1 and 2 and Figure 1 here]

Discussion

The aim of this study was to test a prediction from the hyper-systemizing theory (Baron-Cohen 2006, 2008) that ASC are more common among children in areas where individuals who are talented systemizers are attracted to work and raise a family. Eindhoven is a candidate region of this kind, being the hub for IT and technology in the Netherlands. We examined the prevalence of ASC in the formal administrative records of school-aged children in the Eindhoven region, compared to two ‘control’ regions: the Haarlem and Utrecht regions. As predicted, this estimate of the prevalence of school-aged children with a formal ASC diagnosis was significantly higher in the Eindhoven region, compared to the Haarlem and Utrecht region. This is consistent with the idea that strong systemizing in parents could be a risk factor for having a child with ASC, although there are other factors that could relate to the increased prevalence in the Eindhoven region.

An alternative interpretation of these data is that the higher administrative prevalence in the Eindhoven region may be due to *over-diagnosis* of ASC in this region. DSM-IV and ICD-10 leave room for subjective judgment. It is therefore possible that broader criteria have been used in the Eindhoven region, to diagnose milder forms of ASC. Evidence against this explanation comes from the finding that the prevalence of autistic disorder, the most severe form of ASC, was also significantly higher in Eindhoven. This suggests that the higher ASC prevalence in the Eindhoven region is not due to over-diagnosis of borderline cases, although further research is required to verify diagnoses of reported cases.

A second alternative interpretation of these data is that the higher prevalence in the Eindhoven region may have arisen because of *increased awareness* about autism among parents and

professionals in Eindhoven, either as a result of well-coordinated clinical facilities, a good social structure in which information about autism is easily available (Liu et al. 2010) and/or media coverage about autism. Against this interpretation, ASC has received a significant amount of coverage in the national and international press, not just the regional press. Because we cannot completely exclude these mechanisms at this point, we will address them in future research.

A third possibility is that ASC may be *under*-diagnosed in the Utrecht and Haarlem regions. The prevalence estimates of ASC in these regions were slightly lower than the expected 1% reported in recent British studies (Baird et al. 2006; Baron-Cohen et al. 2009). The relatively low prevalence in the Utrecht region may be partly explained by a higher percentage of non-Western migrants living in this region (21%), in comparison with the regions Eindhoven (13%) and Haarlem (12%) (Statistics Netherlands Website 2008), since results from a previous Dutch study showed that ASC is often under-diagnosed in children from ethnic minorities (Begeer et al. 2009). However, if there is an under-diagnosis of ASC in the two control regions, this cannot explain why elevated levels of ASC are found in Eindhoven (compared to the most recent prevalence estimates elsewhere) unless families are moving to Eindhoven from the other two regions because services are better. Testing if services are equivalent in all three regions will constitute a difficult challenge for future research, since an alternative reason why families would have moved to Eindhoven would be for jobs in the IT sector.

Finally, the response to the survey in the Haarlem and Utrecht regions was lower compared to the Eindhoven region. However, the results were weighted for non-response and therefore adjusted for the differences in response between the three regions. If the responding schools

are representative of the comparable schools in the region, the difference in response should not have confounded our findings.

In conclusion, this is the first study to examine the prediction that ASC is more common in 'high systemizing' regions. Regions known for their high tech (IT-rich) employment rates can be used as a proxy for higher rates of strong systemizers in the population. Our study suggests a two- to four-fold higher ASC rate in the Eindhoven region, whilst the prevalence of ADHD and dyspraxia were similar in the three regions. This striking difference in the prevalence of ASC is in line with the hyper-systemizing theory and will require the phase two study using diagnostic assessments and screening methods, to determine the exact nature of regional differences in population prevalence. Future research should test if this higher prevalence in a high tech region is found in other cultures (e.g., in Silicon Valley, California), and should confirm cases identified via school report using standardized interview/observation-based diagnostic methods. Other factors that could contribute to regional differences in prevalence (including socioeconomic status, ethnicity, social factors, availability of services, and over- and under-diagnosis) will be formally tested in our planned follow-up study.

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Figure Caption

Figure 1. Prevalence and 95% Confidence Intervals by Region and Diagnosis.

Figure 1 Top

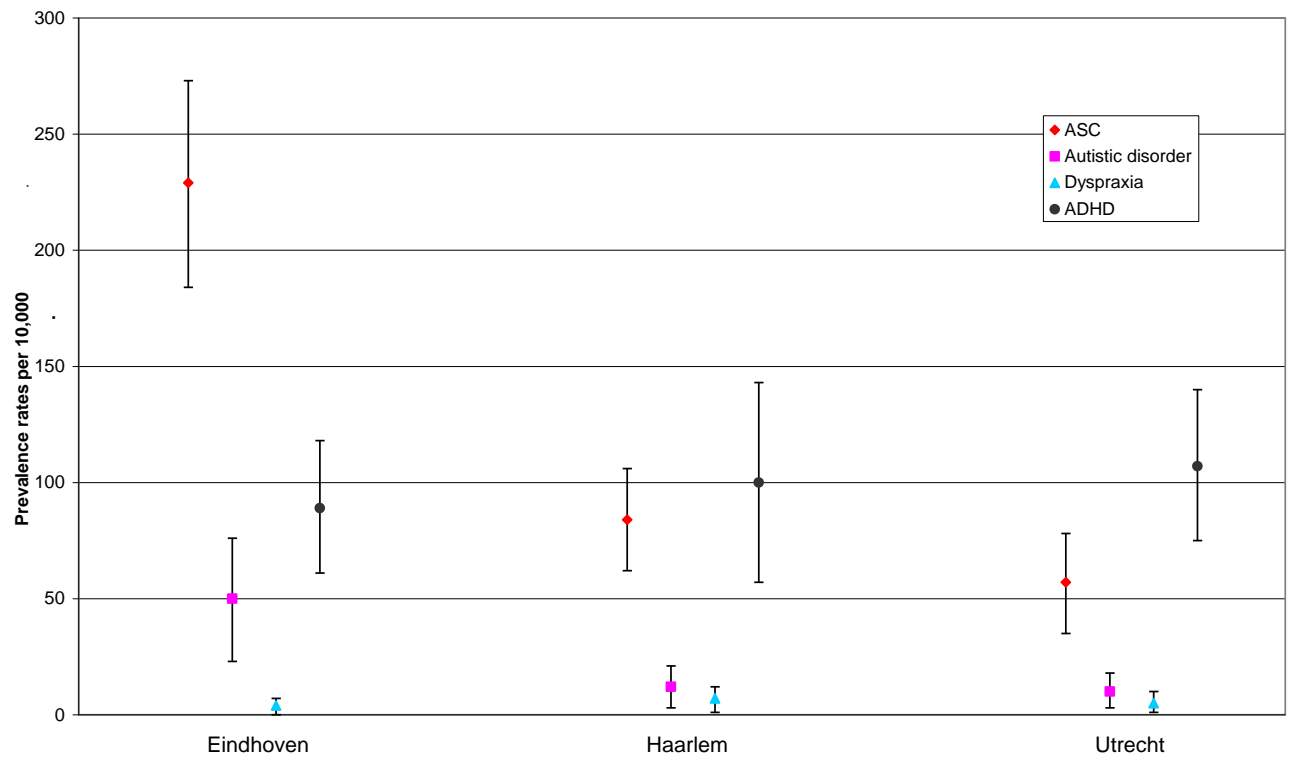


Table 1. Prevalence by region (expressed per 10,000 children), with a 95% confidence interval and rate ratios relative to Eindhoven (adjusted for school type).

		Eindhoven	Haarlem	Utrecht
ASC	Prevalence	229 (184-273)	84 (62-106)	57 (35-78)
	RR	1.0	0.6 (0.4-0.8)	0.2 (0.2-0.4)
	autistic disorder only -	50 (23-76)	12 (3-21)	10 (3-18)
	RR	1.0	0.6 (0.3-1.4)	0.3 (0.1-0.7)
dyspraxia	Prevalence	4 (0-7)	7 (1-12)	5 (1-10)
	RR	1.0	2.1 (0.4-9.9)	1.2 (0.2-6.0)
ADHD	Prevalence	89 (61-118)	100 (57-143)	107 (75-140)
	RR	1.0	1.4 (0.9-2.2)	1.3 (0.9-1.9)

ASC, autism spectrum conditions; ADHD, attention-deficit hyperactivity disorder; RR, rate ratio

Table 2. Prevalence of ASC by type of school and by sex (expressed per 10,000 children), with a 95% confidence interval.

	Eindhoven	Haarlem	Utrecht
ASC – Primary schools	176 (145-207)	79 (56-103)	45 (21-69)
ASC–Secondary schools	343 (255-431)	98 (43-153)	111 (74-147)
ASC – Boys	369 (301-438)	178 (120-236)	110 (68-152)
ASC – Girls	94 (65-123)	27 (14-40)	30(13-48)
Ratio Boys:Girls [†]	4.3 (3.1-6.0)	8.2 (4.4-15.2)	4.0 (1.9-8.4)

ASC, autism spectrum conditions; ADHD, attention-deficit hyperactivity disorder

[†] Adjusted for type of schools