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REVIEW

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The prevalence of autism spectrum disorders

Recent evidence and future challenges

Abstract *Background*: Until recently best estimate prevalence rates for autism spectrum disorders (ASD) were 0.5/1,000 for autism and 2.0/1,000 for the broader spectrum. Three recent studies have suggested a significantly higher prevalence rate for ASD of 6.0/1,000 (mean 95 % CI = 4.8–8.0). *Method* Possible determinants of the apparent increase in the prevalence of ASD are outlined. Methodological aspects of the three recent studies are examined. *Findings* Increased recognition, the broadening of the diagnostic concept over time and methodological differences across studies may account for most or all of the apparent increase in prevalence, although this cannot be quantified. *Conclusions* Findings from ongoing studies should help confirm or disconfirm the putative rate of 6.0/1,000 for all ASD. The possibility that autism has been over-diagnosed in recent studies needs to be ruled out. Notwithstanding these outstanding questions, it appears likely that the current true prevalence of ASD is considerably greater than previously recognised. This has significant implications for our scientific understanding of ASD and for families and services. Future directions for epidemiological research are outlined.

Key words autism spectrum disorders – Asperger syndrome – PDD – prevalence – epidemiology

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Introduction

Autism spectrum disorders (ASD) are characterised by impairments in social and communicative development, and by the presence of repetitive and routinised behaviours, in preference to imaginative and flexible patterns of behaviour and interests. These characteristics can vary in combination and severity, both within individuals over time and between individuals. Both the DSM-IV [1] and the ICD-10 [49] classification systems include similar but not identical (and differently named) diagnostic categories for individuals who show some but not the full compliment of impairments necessary to meet criteria for 'childhood autism' (ICD-10) or 'autistic disorder' (DSM-IV). Asperger syndrome, atypical autism and pervasive developmental disorder-unspecified (in ICD-10) or pervasive developmental disorder-not otherwise specified (PDD-NOS) (in DSM-IV) are assumed to be disorders related to autism, and together they constitute the group of disorders referred to as the pervasive developmental disorders (PDD), sometimes called 'autism spectrum disorders' (ASD) [32]. This group may be a mix of those with greater severity in one area than others, mild impairments in several areas or late onset. The classification systems also include two other disorders under the same PDD heading (Rett syndrome, childhood onset disintegrative disorder), although these are separated from the core ASD in terms of course and aetiology [27, 44].

Best estimate prevalence estimates up until 1999

Since the first epidemiological study of autism was published by Lotter in 1966 [33] over 30 epidemiological surveys have been published [16, 47]. The majority of studies published up until the end of the 1990s found

prevalence rates for childhood autism close to the figure of 0.4/1,000 obtained by Lotter [13, 20]. Prevalence rates for the broader autism spectrum of up to 2.0/1,000 were found in several studies [17, 48].

Two meta-analyses that adopted slightly different inclusion and exclusion criteria were published in 1999 and reached broadly similar conclusions. Fombonne [17] found the median rate of autism in 22 studies was 0.52/1,000 (mean 95 % CI ± 0.52). Fombonne concluded that the minimum prevalence estimate (relying on more recent studies and excluding a number of studies with methodological limitations) for all ASDs was 1.87/1,000. Gillberg and Wing [20] presented data from studies broken down by year of publication and found prevalence rates for autism of 0.44/1,000 (95 % CI = 0.33–0.58) for the earliest studies conducted between 1966–1973 but a higher rate of 0.96/1,000 (95 % CI = 0.84–1.08) for studies conducted between 1990–1997. Fombonne [17] also conducted a time-trend analysis and found a rate of 0.72/1,000 for autism for studies conducted since 1989 (mean 95 % CI = ± 0.97). The 'best-estimate' prevalence of autism on the basis of these reviews could be considered about 1.0/1,000 and that for the broader ASD about 2.0/1,000. Note, however, that such best-estimate figures involve the aggregation from a diverse range of studies, employing different diagnostic criteria, methodologies and surveyed populations, and thus should not necessarily be considered the likely 'true' figure.

More recent prevalence findings and focus of attention on the prevalence of ASD

However, three studies published in the past two years found prevalence rates for autism between 1.7/1,000 (95 % CI = 1.1–2.5) and 4.0/1,000 (95 % CI = 2.8–5.6) and rates for all ASD between 5.8/1,000 (95 % CI = 4.3–7.7) and 6.7/1,000 (95 % CI = 5.1–8.7) [2, 5, 7]. These rates were significantly higher than the current 'best estimate' derived from the meta-analyses described above. This apparent increase in prevalence rates coincided with an increased focus on the prevalence of autism in both the scientific and lay communities. First, there was an increase in the number of children being registered on service databases with a confirmed diagnosis of autism [6]. Second, a suggestion was made that regressive autism was increasing and was associated with bowel symptoms, and further that that this increase in cases was associated with the MMR (measles, mumps and rubella) vaccination [45, 46]. Subsequent research has demonstrated no temporal association between the introduction of the MMR vaccination and increases in the number of registered cases of autism on health and education service databases [11, 14, 26, 41]. Furthermore, research evidence provided no plausible causal association between MMR, bowel symptoms and autism [22, 40], nor evidence for an increase in autism in association with a regressive course or bowel symptoms [18, 42]. Reviews by the US Institute of Medicine, the American Academy of Pediatrics and the UK Medical Research Council have concluded that no association existed between the MMR vaccination and prevalence rate of autism [22, 35, 40].

Increases in the number of children registered with a diagnosis of ASD on health and education service databases most probably reflected changes in diagnostic and administrative practices. Children who would formerly have been entered as developmentally disabled were now registered as having autism, indeed in one study the size of the increase in children registered as having autism was closely matched by a decrease in children registered as having mental retardation [10]. In addition, these administrative figures were still significantly below current clinical prevalence estimates [10, 11, 14, 26]. Database registration or recording figures will always provide a less reliable estimate of true prevalence than epidemiological studies.

Possible reasons for an apparent increase in prevalence

Possible explanations for higher prevalence figures for ASD in recent studies include artefacts that have produced a false increase in prevalence estimates, factors that indicate that the current rate is correct but that do not indicate a true increase, and factors that indicate that the current rate is correct and indicate a real increase.

Artefacts that might have produced a false increase include an over-expansion of the diagnostic category of ASD such that children receive a 'false positive' diagnosis and a particular sampling bias in the studies that have found higher prevalence estimates. The first point is difficult to prove either way as no 'litmus test' such as a specific biological or genetic marker is currently available to determine true caseness. Thus, case definition is reliant on the behavioural and developmental picture alone. Furthermore, it is likely that the behavioural phenotype of autism and the broader ASDs includes individuals with different ultimate aetiologies, so even when a marker is found it would not be present in all individuals with the phenotype. These considerations go beyond mere niceties of nosology and classification. They are critical to an understanding of whether the increase in prevalence is real or apparent.

Factors that may have led to an apparent but not a true increase in prevalence relate to diagnostic and methodological considerations. Kanner's [25] initial criteria for autism were narrower than the current classification of childhood autism [49]. Wing and Potter [47] estimated that only one third to one half of children meeting ICD-10 criteria for childhood autism would

meet Kanner's criteria. Thus, the diagnostic boundary of even the core presentation of autism has broadened over the decades. Another significant factor is the increasing recognition of a broader spectrum of autistic disorders [48]. With sub-threshold severity or combination of symptoms, or atypical onset, an individual can meet diagnostic criteria for atypical autism, PDD or Asperger syndrome. These individuals are considered to share some but not the full phenotypic presentation of individuals with the classic presentation. These phenotypic variants were not included in earlier diagnostic classification systems, nor in many of the earliest epidemiological studies. Thus, the broadening of the definition of core autism and the increasing recognition that presentation of autistic symptoms falls along a spectrum is likely to account for some of the apparent increase in prevalence.

Another way in which the diagnostic concept of ASD has been broadened (both in application and conceptualisation) is the increasing recognition that an ASD can co-exist with comorbid disorders. These include Down syndrome, cerebral palsy, Tourette syndrome, Turner syndrome, tuberous sclerosis and in individuals with hearing and visual impairment [21]. Another factor is the increasing recognition that individuals with average IQ may have an ASD. The proportion of cases with IQ > 70 in the three most recent epidemiological studies has varied from 29 % to 60 % for childhood autism and from 51 % to 94 % for individuals with atypical autism, PDD and Asperger syndrome.

The prevalence of Asperger syndrome is particularly difficult to estimate. Two small-scale studies reported prevalence estimates of 2.85/1,000 (95 % CI = 0.06–5.65) [12] and 4.8/1,000 *(*95 % CI = 1.3–12.4*)* [24]. However, neither employed strict application of ICD-10 criteria and the very small target populations (1,519 and 826, respectively) led to very wide confidence intervals for the prevalence estimates derived. Fombonne [15] has summarised the relative prevalence rate of Asperger syndrome in six studies that also identified cases of autism and found that autism was five times more prevalent that Asperger syndrome, suggesting that the two Swedish studies might be over-estimates of the true prevalence. One difficulty for future research is that the diagnosis of atypical autism, PDD and Asperger syndrome has been found to be less reliable than that of childhood autism [34, 43]. Establishing a reliable lower threshold for the boarder spectrum of autistic disorders will be a significant challenge for future epidemiological studies.

Another critical methodological consideration is the effectiveness of case-finding methods. The majority of studies have relied on a two-stage procedure where an initial screening phase is followed by a more intensive case ascertainment and diagnostic phase. Some recent studies have used serial ascertainment methods over time to identify cases [2, 23]. Although estimates of the specificity of initial screens can be calculated (see Fombonne, 1999, Table 3), estimates of the sensitivity have rarely been ascertained (see 2; for an exception). Another important factor is the population initially surveyed. Some prevalence studies have only included individuals within the special educational system, by definition excluding cases of ASD within mainstream education. Cases are also missed when studies only ascertain cases already identified and diagnosed by clinical services as their sample. The size of the population sampled has been shown to systematically relate to the prevalence rates found, with higher rates being found in smaller samples, presumably due to more intensive and comprehensive coverage, although at a cost to the width of the confidence intervals [13]. In summary, multiphase detection mechanisms that target a whole population of medium size are likely to provide the most accurate prevalence estimates.

Put another way, historical prevalence estimates for autism and the broader autism spectrum might well have been underestimates of the true prevalence. In addition to the use of narrower diagnostic criteria (e. g. Lotter's criteria) and surveying of restricted subpopulations only (e. g. clinic or special school attendees only), methodological factors such as the use of a single means of ascertainment at one timepoint may have resulted in only a proportion of true cases being identified.

In the absence of a clear demonstration that the increase in prevalence found in recent studies has been real and not apparent, speculation on putative reasons for a real increase are premature. However, confidently answering whether the increase is real or apparent is difficult (if not impossible), as we are unable to estimate quantitatively the impact of the changing diagnostic and methodological factors summarised above. Only two studies have used repeat survey methods on the same population over time. One found evidence for an increase between 1980 (0.40/1,000) and 1988 (0.95/1,000) but concluded that this could be accounted for by improved detection and changes in diagnostic criteria [19]. The second found no evidence for an increase between 1985–1990 and 1992–1993 [17]. Attempts to compare across different surveys conducted by different research teams, on different populations, using different methodologies and screening and diagnostic practices are inevitably limited. Factors such as the increased public and professional awareness of ASDs and an increasing focus on registering clinical diagnosis within education and health registers will also impact on studies conducted at different points in time. This does not mean that attempts to answer the question of a true vs. an apparent increase should not be made. Rather, our ability to do so retrospectively on the extant empirical base is extremely limited. Notwithstanding these limitations, establishing the *current* prevalence of ASD is im-

portant for clinical and educational planning, and for the families and individuals with ASD themselves [8].

Three recent prevalence studies

Baird et al. [2] reported on a 6-year follow-up of the CHAT screen [4]. In order to determine its sensitivity an attempt was made at age 7 years to identify all cases of ASD within the 16,235 screen sample drawn from 10 health districts in South East England. Some cases were prospectively identified by the screen and assessed at 20 and 42 months of age [9], others were identified by subsequent attempts at screening as well as inward referral to the diagnostic centre. At age 7 a case note check was conducted in collaboration with local clinicians in order to identify as yet undetected cases. Only 24 from 50 cases (47 boys, 3 girls) of childhood autism (inclusive of 5 cases of Asperger syndrome) and 27 from 44 cases (36 boys, 8 girls) of other PDDs were directly assessed by the research team (including administration of the ADI-R; Lord et al. 1994). The diagnostic check on cases diagnosed by local services included a case note check against ICD-10 criteria and discussion with clinicians who made the diagnosis. From these methods Baird et al. [2] estimated the *provisional* prevalence to be 3.08/1,000 (95 % CI = 2.29–4.06) for childhood autism (including Asperger syndrome) and an additional 2.71/1,000 (95 % CI = 1.97–3.64) for atypical autism and pervasive developmental disorder-unspecified. A study is currently underway to confirm diagnosis on these cases at age 10 years as well to estimate any additional undiagnosed cases missed at age 7.

One notable feature of this study is the use of multiple ascertainment methods, targeting the same population at five timepoints. Ten cases (from 50) of autism were identified prospectively by the screen at 18 months, a further 6 from a second screen at 42 months, 2 from a third screen at 60 months, 8 from clinical referral between 18 and 84 months, and 24 from the casenote review described above. Sixty percent of the Baird et al. [2] childhood autism sample were estimated to have IQs > 70. One limitation is the lack of direct diagnostic and IQ measurements on all identified cases. However, for the proportion of cases of ASD seen by the research team (51/94), the diagnostic assessment included the current "gold standard" instrument the ADI-R and many cases had their diagnosis confirmed on more than one occasion. Note, however, that the ADI-R was developed to identify cases of ICD-10 childhood autism and DSM-IV autistic disorder. Its reliability at identifying atypical and less severe PDD presentations has not been firmly established (Catherine Lord, personal communication, September 2002). Notwithstanding this point, even the prevalence estimates derived from this proportion of the cases (1.47/1,000 childhood autism, 1.66/1,000 other PDDs) were higher than the current 'best estimate' figures discussed above.

Chakrabarti and Fombonne [7] screened 15,500 children aged 2.5 to 6.5 years in Staffordshire, UK. Health professionals including health visitors, speech and language therapists, general practitioners and paediatricians received training in early identification of developmental problems. All children (mostly aged 2 to 2.5 years) with identified developmental problems in social, speech and language, motor, play, attention and behaviour were referred for consultation to a specialist paediatrician (the first author) or a child development team. Children thought to have moderate or severe problems were seen for a multidisciplinary assessment. Of 576 cases, 103 were thought to have a possible ASD, the others to have other developmental problems. Of these 103 cases, 98 agreed to have a further assessment that included the ADI-R [29] and psychometric assessment. ASD diagnoses were confirmed in 92 from 98 cases assessed. An ASD diagnosis was confirmed in 5 additional cases by an independent clinician (no ADI-R was conducted in these cases). 77 cases were boys and 20 were girls. The prevalence estimate for all ASD was 6.26/1,000 (95 % CI = 5.08–7.63). This included 26 children with DSM-IV autistic disorder (1.68/1,000) (95 % CI = 1.10–2.46), 13 children with Asperger syndrome (0.84/1,000) (95 % CI = 0.45–1.43), 56 children with PDD-NOS (3.61/1,000) (95 % CI = 2.73–4.69), 1 child with Rett syndrome and 1 with childhood disintegrative disorder. IQ was > 70 in 31 % of cases with autism, 92 % of cases with PDD-NOS and by definition all cases of Asperger syndrome.

The third recent study was conducted in Brick Township, New Jersey, USA [5]. The sample was 3 to 10 year children in a population of 8,896 (calculated from 1990 census records using a school-role derived inflation factor, see Bertrand et al. (2001), p. 1157). Potential ASD cases were ascertained via school records, paediatric records, local parent organisations and self-referrals to the project following publicity. Diagnoses were confirmed or ruled out following a multidisciplinary assessment including standard psychometric tests of IQ and language ability and administration of the ADI-R [29] and ADOS-G [31]. From 75 possible cases 53 participated in the multidisciplinary diagnostic assessment described above and the school and/or clinician records of the remaining 22 were evaluated. Thirty-six children met DSM-IV criteria for autistic disorder (4.0/1,000) (95 % CI = 2.8–5.6) and an additional 24 children met criteria for PDD-NOS or Asperger syndrome (2.7/1,000) (95 % CI = 1.7–4.0), giving an overall rate for all ASDs of 6.7/1,000 (95 % CI = 5.1–8.7) (44 boys, 16 girls). For the 39 children on whom IQ data were available 51 % had an IQ > 70.

The patterns of main findings from these three recent studies are summarised in Table 1: base population, age,

proportion of direct and indirect assessments, prevalence of autism and other PDDs, sex ratio, IQ distribution. There is considerable overlap between the studies in terms of base population size and age, and all shared the methodological feature of multiple ascertainment methods. The prevalence figures for all ASDs are also similar. The clearest difference is in the relative proportion of cases given autism vs. other PDD diagnosis. In the Chakrabarti and Fombonne study this proportion is 26:71 (0.37:1.0), compared to 50:44 (1.14:1.0) in the Baird et al. study and 36:24 (1.5:1.0) in the Bertrand et al. study. This suggests that the application of criteria for classic vs. atypical forms of autism was applied differently across the three studies. The inclusion of 5 from 50 cases of Asperger syndrome in the childhood autism classification in the Baird et al. study does not significantly change this picture. This decision was made on the basis that all cases had sufficient symptoms to meet ICD-10 childhood autism criteria and under the hierarchical rule the latter diagnosis applies. The nosological validity of Asperger syndrome remains uncertain [28, 36]. The inclusion of one case of Rett syndrome and one case of childhood disintegrative disorder in the Chakrabarti and Fombonne study (not identified in the two other studies) also does not change this pattern. The sex ratio and IQ ratio also show some variation across the studies, although in relation to IQ the use of different psychometric instruments and the proportion of cases on which direct psychometric measures of IQ was achieved might contribute to this difference.

Taken together these three recent studies strongly suggest that the prevalence of ASDs is many times the recent 'best estimate' [13, 20]. If the prevalence figure for ASD of approximately 6.0/1,000 is confirmed in repeat assessments that are currently underway in these three samples, and replicated in other samples, then ASD should no longer be considered a rare disorder.

Table 1 Comparison of Baird et al. (2000), Chakrabarti & Fombonne (2001) and Bertrand et al. (2001) studies

	Baird et al.	Chakrabarti & Fombonne	Bertrand et al.
Base population size	16,235[a]	15,500	8,896[b]
Age	7 years	2.5–6.5 years	3–10 years
Proportion of direct assessments	46 %	95 %	71 %
Prevalence autism[c]	3.08/1,000	1.68/1,000	4.0/1,000
Prevalence other PDDs[d]	2.71/1,000	4.58/1,000	2.7/1,000
Prevalence all ASDs	5.79/1,000	6.26/1,000	6.7/1,000
Boys: Girls all ASDs	83: 11	77: 20	44: 16
	88%: 12 %	79 %: 21 %	73 %: 27 %
IQ > 70/< 70 all ASDs	78 %: 22 %[e]	74 %: 26 %[f]	51 %: 49 %[g]

[a] 16,235 children from 40,818 screened with the CHAT
[b] Estimated from 7,117 1990 census by school-role factor
[c] ICD-10 childhood autism in Baird et al., DSM-IV Autistic disorder in Chakrabarti & Fombonne and Bertrand et al.
[d] Asperger syndrome categorised as autism in Baird et al.; as other PDD in Chakrabarti & Fombonne and Bertrand et al.
[e] IQ data available on N = 36 cases
[f] IQ data available on N = 91 cases
[g] IQ data available on N = 42 cases

Outstanding questions and research strategies for future epidemiological studies

Perhaps the most urgent (and probably most straightforward) research task is to confirm the apparent prevalence of ASDs of 6.0/1,000 indicated by the three recent studies [2, 5, 7]. Studies should adopt multiple case finding ascertainment methods, and employ rigorous and standardised approaches to assessment and diagnosis in large, well-defined and representative populations. The use of comparable ascertainment and diagnostic procedures across studies will allow investigation of whether differences between studies in diagnostic classification, sex ratio and IQ are due to systematic differences in methodology or whether they are indicative of real differences in prevalence (though it is unclear at present why these might occur). Although the early and later life course of individuals with ASD is of interest for reasons of health surveillance and identification of levels of service need, an appropriate age of study is between 8 and 12 years. This is when autistic symptoms are well established and recognisable in most individuals across the IQ spectrum [16]. Furthermore, this is an age at which we know most about how the systematic assessment of symptoms relevant to making a diagnosis work (ADI-R; 30; ADOS, 31), although currently available instruments are more reliable at identifying autism than the related PDDs. For a developmental disorder such as autism whose onset is difficult to ascertain (and may vary from individual to individual) point incidence estimates are less informative than total lifetime prevalence estimates [47].

A more challenging research question to answer is that of whether the prevalence of ASDs has increased. Methodological differences in studies over time and increased recognition of ASD in individuals with low and high IQ, and with other medical conditions, is likely to account for a substantial proportion of the increase [16, 47]. However, post hoc quantitative estimation of the size of these effects (and extrapolation of previous prevalence figures on the basis of this estimation) is not possible. An alternative long-term strategy that might provide different data (at some point in the future) would be to conduct prevalence studies using two cohorts of adults born some time apart. This would assume that methodological and diagnostic factors that would differ between comparing an adult and a child population would be minimised. The difficulties of such a study include cost, the time required and the uncertainty of a conclusive outcome. Previous studies have

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shown that it is possible to identify cases of ASD from special hospital (learning disabled) and adult psychiatric clinic samples [38, 39]. However, an attempt to fully ascertain a total population prevalence of ASD in adulthood across the ability range and across service users and non-users has not been attempted. It would be extremely expensive and the risks include our reduced knowledge and confidence in diagnostic procedures and instruments in adult samples. If such a study were possible (for example comparing a 25 year old cohort to a 40 year old cohort) and difference prevalence rates were found then any systematic difference found between the sample characteristics in IQ or medical characteristics might signify that a systematic factor has influenced prevalence. Another obstacle would be the reduced amount and quality of developmental and historical information available on such cohorts. In tandem with the expense, these methodological challenges and risks make it unlikely that such a study would be considered worthwhile to fund. Wing and Potter [47] suggested an alternative approach of applying previous diagnostic criteria (e. g. Lotter's criteria) to current prevalence samples. This has some merit but does not avoid the methodological differences in ascertainment and sampling between previous and current studies.

A more fruitful line would be to expand and improve methodological approaches in future prevalence studies to provide more data on as yet unanswered scientific questions regarding the nature, course and aetiology of ASD. Fombonne [16] suggests that a symptom as well as a syndromic approach needs to be adopted. This is critical as there is an increasing consensus that autism is not a unitary disease entity or disorder but an end phenotype of a number of complex, distinct and overlapping aetiologies at several levels of causation including genetic and brain development. The nosology of the current classification systems may well change as new scientific evidence about the nature of ASDs emerges [32]. Another strategy would be in depth prospective study of a population cohort from birth in order to marry prevalence data with onset and disease course data. The relative rarity of ASDs would make this prohibitively expensive to do on a population wide basis (e. g. 5,000 children might only yield 30 cases of ASD and perhaps only 15 or less of autism). One suggestion is that younger siblings of already diagnosed children make a suitable high risk sample to prospectively study [47]. This is attractive from the point of view of tracking early development of autism [3]. However, the disease course of such families may differ from those in which the genetic loading for autism is lower and where other factors have a greater determination on the development of ASD.

Another question for future research is whether to concentrate on the core presentation of autism or on the broader spectrum. Although no clear evidence has emerged that an evidence-based line can be drawn between autism and the related PDDs, the reliability of diagnosis, in particular the setting of a lower threshold, is lower for PDD than for autism. For epidemiological research this is a critical obstacle and although in time biomedical or genetic markers may emerge they may only identify a subset of cases. On the other hand, recognition of the broader phenotype has had important scientific and clinical implications for our understanding of autism.

Future epidemiological research should be conducted hand-in-hand with other relevant branches of science so that as answers emerge about ASD this new knowledge can be applied post hoc to epidemiological datasets. The nesting of biological and genetics research designs within future epidemiological studies will provide information to better answer questions about heterogeneity of presentation and aetiology. Because the behavioural phenotype of autism and the broader autism spectrum disorders includes individuals with different ultimate aetiologies, even when biological or genetic markers are found they will not be present in all individuals with the phenotype. The fact that autism is not a unitary 'disorder' presents significant challenges but also opportunities for future epidemiological research.

One hope for the future is that once clear aetiological causes are identified for at least a subgroup of individuals who have ASD, it may be possible to determine more precise prevalence figures for 'regressive autism', 'serotonin autism' or 'tuberous sclerosis autism'. Other relevant areas for such nested epidemiological designs include familial medical and behavioural information and neuropsychology. However, the field needs to be open for unexpected and as yet unexplained findings, such as the recent discovery of elevated neuropeptides and neurotrophins in neonatal blood of children subsequently diagnosed with autism [37]. Such research may provide data that in the future will enable us to answer questions regarding the prevalence of ASD that have not yet been framed.

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