Autism – 25 years on: a lot has changed!

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According to current international classification systems (DSM-5, ICD-11) Autism Spectrum Disorders (ASD) are defined as a combination of social communication and social interaction deficits, alongside a set of other conceptually unrelated symptoms. These comprise restrictive, repetitive and inflexible patterns of behaviour such as routines, rituals and over-focussed interests, sensory sensitivities, together with stereotyped motor actions (such as hand flapping). The so-called triad of impairments, which had persisted in our conceptualization of autism since 1980 (DSM-III) has been superseded as new evidence has emerged, supporting a dyadic view of symptom constellations (Skuse et al, 2020). Twenty-five years ago, autism was considered to be excessively rare, and a distinction was made between subtypes (such as Asperger syndrome and other so-called pervasive developmental disorders). The apparent prevalence was confidently reported to be no more than about 0.6% when all subtypes were combined (Chakrabarti and Fombonne, 2001). There has been an exponential increase in recorded prevalence since then, but this apparent rise is due to changes in definition and in awareness of the diversity of the autism spectrum in otherwise typically developing individuals. The prevalence of recognised ASD varies world-wide but it is higher in countries with greater experience of diagnosing the condition (Fombonne, 2020). Within Europe and North America, the proportion of children with a diagnosis is at least 1.5%, of whom 70-90% do not have generalised learning disabilities (Lord et al, 2018).

We now know that social communication and social interaction competencies are continuously distributed in the general population (Skuse et al, 2009). Levels of social skill vary without a clear division between abnormal and typical behaviour. This reconceptualization has presented a dilemma to those attempting to define prevalence reliably. Extreme incompetence in social communication skills may imply ASD, but it is important to be aware that generalized Intellectual Disability is also associated with degrees of social communicative impairment. The most recent redefinitions of autism (DSM-5, ICD-11) have abolished diagnostic subtyping, but the delineation of boundaries between autism and intellectual disability remains a conceptually important area of research (Satterstrom et al, 2020). Whether genetic specificity exists for autism, independent of such generalized disability, is hotly debated (Myers et al, 2020).

Until just a few years ago, the stereotypical autism phenotype was ‘male and intellectually disabled.’ This view has evolved as the characteristic features of ‘milder’ (less prominent) autistic traits have been recognised. Unfortunately, most standardised methods of establishing a diagnosis (interviews/observations) have yet to adapt, to prevent potential ascertainment bias in the assessment process against more intellectually able individuals, especially females (Mandy et al, 2012). Until very recently, there was a widely held supposition that if females had autism, there were likely to be intellectually disabled as well (Werling and Geschwind, 2013). The sex ratio used to be regarded as a firm figure, because it was found to be 4:1 almost everywhere standardized measures of assessment were employed. Until recently, the bias in ascertainment inherent in such measures went unappreciated. For instance, they sought evidence for restricted interests that were stereotypically male (e.g. properties of numbers, collections of arcane objects), but failed to emphasise the importance of a lack of interest in cooperative social play. The former emphasis on ‘poverty of imagination’ has been removed from current diagnostic criteria, as it proved impossible to define unambiguously. Identifying the relatively subtle symptoms that indicate restricted interests, resistance to change and sensory sensitivities in children with ASD whose IQ is within the normal range, requires considerable clinical experience. Unlike social communication deficits, they cannot reliably be assessed by observation alone. When assessing girls or women with suspected ASD, clinicians should be sensitive to

differences in their focused interests which are likely to be socially unexceptional (e.g. animals, celebrities, clothes, makeup) and hence differ from those of many autistic boys, although they are equivalently restricted and of similar intensity. Unfortunately, this clinical observation has yet to permeate the scientific literature, which continues to perpetuate the erroneous assertion that "females (with ASD) demonstrate fewer stereotyped and repetitive behaviours than males throughout development' (McFayden et al, 2019).

A minority of people with ASD are non-verbal, the proportion of such individuals being higher in cultures where clinical diagnoses are made largely among those with severe or profound learning disabilities. Children with ASD who do not speak by the age of 6 years are unlikely ever to acquire verbal language, but they may not be disabled in all other aspects of development, a point of clinical significance. However, the proportion of individuals with autism who are non-verbal is much lower than the 30-50% quoted in some earlier studies (Pickett et al, 2009). This is due largely to the recent recognition that most newly diagnosed cases of ASD are not associated with intellectual disability (Lord et al, 2018). Another erroneous assumption from 25 years ago concerns the frequency with which people with autism develop epilepsy. That figure that was sometimes claimed to be as high as 23% (Rossi et al, 1995), in contrast to about 0.5% of typical children and adolescents. A recent literature review (Lukmanji et al, 2019) suggests an incidence of 9% is more accurate, but even this may be an overestimate because of ascertainment bias. Young people whose autism is due to rare syndromes associated with mutations in single genes or pathogenic copy number variations, are at much higher risk (>30%) (Keller et al, 2017; Coe et al, 2019).

No single symptom or symptom cluster is characteristic of ASD and no specific feature of the phenotype either confirms or rules out the diagnosis. Many subtle traits consistent with this disorder are observed in typical children, but do not amount to overtly autistic behaviour nor warrant a diagnosis. Each of the individual symptoms of ASD can be observed in children who are not clinically on the autism spectrum. No behavioural feature (e.g. sustained eye contact) rules out a diagnosis of ASD either, a point that is often overlooked by inexperienced clinicians. The core characteristics of an ASD are *a failure to recognise another person's social cues and to respond appropriately*. 25 years ago, many clinicians believed people with ASD are generally uninterested in having close friendships (Hauck et al, 1995), but this is wrong. Many want social relationships with their peers but are unable to build such relationships successfully. People with ASD lack social competence, due to abnormal social cognition. Unlike individuals with severe intellectual disability, in ASD that difficulty cannot better be explained by generalised developmental delay. The widely held view that people with autism lack empathy (Ramachandran and Oberman, 2006) led to the blind alley of the 'deficient mirror neurons' theory (Iacoboni, 2009), and in any event it is an oversimplification. Our understanding of this so-called 'core deficit' that typifies people with autism has undergone radical revision in recent years (Fletcher-Watson and Bird, 2020). To my mind, it reflects so many other myths about autism. They exemplify the gulf between the many influential researchers (and publishers) in this field whose personal experience of interviewing and observing people with ASD is in the limited to non-existent range, and the complex realities of the autism experience that busy clinicians recognise but do not have the skills or time to describe in academic journals.

We have begun to recognise that children without intellectual disabilities often try to disguise or compensate for their autistic traits. For instance, they may suppress motor stereotypies such as hand flapping and learn to avoid situations that are associated with subjectively unpleasant sensory experiences. The impact of ASD traits on educational progress depends on the environmental response to the idiosyncrasies of the child, and the tolerance of unusual or disruptive behaviours. Some children respond well to the rules that apply in schools but behave much less well in unstructured situations (such as when they are with their families!). This drive to disguise autistic behaviours is especially characteristic of girls with the condition and has recently been termed 'camouflaging behaviour' (Hull et al, 2017). The idea that children with autism can become self-aware and deliberately disguise their autistic symptoms would have been regarded as heretical 25 years ago.

Many individuals with ASD have both strengths and weaknesses in their verbal or nonverbal skills. It is of great clinical importance that their cognitive profile is therefore usually exceptionally uneven. Unless this is quantified by psychometric testing, progress through education can be compromised, and without remedial action the areas of weakness can have a major impact on their everyday life. That said, the pattern of verbal and nonverbal skills, working memory and executive functions, is unpredictable and highly variable. 25 years ago, influential research was published suggesting that most people with autism could be distinguished by their special skills in certain non-verbal tasks such as the block design subtest of the Wechsler Intelligence

Scales (Shah and Frith, 1993), or by their ability to detect embedded figures (Jarrold et al, 2005). These assertions have not been supported by more recent research (Mandy et al, 2015; Constable et al, 2019). However, once they have taken root, they are remarkably difficult to shift.

Twenty-five years ago, the 'Theory of Mind' theory of autism dominated the research landscape (Happe and Frith, 1995). How has it withstood the test of time? As it happens, the answer is remarkably well. The heuristic remains a useful way of conceptualising the difficulties experienced by many people with an autism diagnosis, although challenges in measuring this elusive ability continue to this day (Livingston et al, 2019).

In summary, we have moved a long way in our conceptualisation of autism over the past 25 years. Have we come much further in our understanding of what the 'basic deficits' are in this complex condition? Have we found a 'smoking gun' in terms of genetic predisposition or a biomarker? We have not. Perhaps an appropriate place to end this brief review is with one of my favourite pieces of research on the fraught issue of genetic risk. A recent general population study measured social communication difficulties in children and linked these to polygenic variation (Robinson et al, 2016). The authors concluded that 'multiple types of genetic risk for ASDs influence a continuum of behavioral and developmental traits, the severe tail of which can result in diagnosis with an ASD or other neuropsychiatric disorder'. Does autism really exist as a distinctive condition, or is it a construct carved out of a continuum of neurodevelopmental risk? Perhaps we will know the answer 25 years from now.

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