

ETEVA

A Research Review on Autism

DEDUKTIA

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Executive summary

■ Research has significant potential to bring beneficial change to autistic people and their families. Nevertheless, despite a growth in our understanding, there are still many unanswered questions and research has led to very few changes in actual practice. The topics of research and their funding have traditionally been focussed on identifying deficits, and some have been concerned with preventing autism occurring or finding a cure. This has led to understandable scepticism and concern, but recent years have seen improved engagement with autistic people and families around setting the research agenda, as well as better funding for studies that will ultimately bring about beneficial changes.

There are a number of reasons as to why autism research has not progressed in the way many expected it would twenty or thirty years ago. Significant challenges include both the heterogeneity and increasing breadth of the autism spectrum. In addition, there has been a reluctance to include autistic people with an intellectual disability in research. This has hindered our efforts to identify the biological basis (e.g. genetics and neurobiological) of autism, but there is emerging evidence that there may be different causes for the intellectually disabled compared to those with a normal intelligence level.

The characteristics of autism that are observable (e.g. the social and communication difficulties) are well documented and have helped our understanding of autism in the early years and what should be included in diagnostic assessments. However, an emerging trend has been the focus on those difficulties that often co-occur with autism (e.g. anxiety, sleep problems, gastrointestinal issues), which can impair an individual's daily functioning and impact on home life. A growing number of therapeutic options for these difficulties have been warmly received by autistic people and their families.

Research has advanced our understanding of what the earliest behavioural and biological signs of autism are, but these findings have not led to a lowering of the average age of diagnosis. In some countries, however, this knowledge has been used to improve the training and knowledge of child and family health professionals. Diagnostic practice has benefited from the use of standardised assessment tools that, in many cases, were developed as part of research programmes. These will continue to be the bedrock of diagnostic practice and guide the development of management plans.

Early intervention research in autism has grown in the number and quality of studies over the last fifteen years. Research has provided a stronger evidence base for what works, but we still don't know what works for which children. Despite the growing evidence there are few studies of the effectiveness of these interventions in the environments where they will be delivered. A range of technologies have shown significant potential as an intervention tool, but there will be a need in the future to assess their long-term usefulness and cost effectiveness.

Despite the strong focus on intervention, most children and young people on the autism spectrum spend the majority of their time in schools. Much is known about what educational practitioners find useful when teaching autistic children, and this has been disseminated to great effect as part of training programmes. More needs to be done to increase the amount of research conducted in educational and adult intellectual disability settings. In advancing this research it will be important to form meaningful partnerships between researchers, autistic people, their families and practitioners.

The future of autism research will likely have a stronger focus on investigating the effectiveness of what is delivered in educational, health and social care services. This will be more relevant to governments and organisations who are looking to alleviate some of the economic costs associated with the lost opportunities (e.g. to employment) autistic people face. There needs to be greater coordination of future efforts so that there is a consensus over research objectives, a plan of how to reach these objectives and the resources to achieve success in place. The voice of autistic people and their families must be central, including those from culturally and linguistically diverse communities. This feels to many as an important junction for autism research and the future looks brightest if we are ambitious and have meaningful change in our sights.

Introduction



What is autism?

Autism is a condition that affects the way a person responds to the world around them and how society responds to them. The terminology used in the most recent revisions of diagnostic manuals^{1,2} is Autism Spectrum Disorder (ASD). To meet criteria for a diagnosis an individual must have social and communication difficulties, as well as demonstrating repetitive and rigid behaviours and hyper- or hypo-sensitivity to certain stimuli. In respect to some people's dislike of the word disorder (see the section below on terminology), we will use autism in this review.

Autism is described as a spectrum condition as it affects different people in different ways. Autistic people can reach adulthood with limited speech, have measured IQs in the severely disabled range and have few, if any close relationships. By contrast, some autistic people can study at the best universities, have meaningful relationships, including marrying and having children, but can struggle to learn the rules of social engagement and may feel socially isolated.

Beyond the core social and communication difficulties, people on the autism spectrum can have a number of other challenges. These include suffering from high rates of mental health problems, behaviours that challenge (e.g. self-harm), sleep difficulties and sometimes dietary and gastrointestinal issues. These co-occurring difficulties can be life-limiting and/or increase the chances of early mortality and they are frequently highlighted by autistic people and families as important targets for intervention.

Autism means different things to each affected person. Some autistic people embrace their autism and it provides them with a sense of identity and an explanation as to why they feel different. Others dislike having autism and shy away from speaking about it because of associated stigma and stereotypes about what autism is. Others were diagnosed in childhood, went through schooling and as adults rarely think about being autistic. A consistent message from autistic people and families, however, is that the way society fails to include autistic people is damaging to their mental health and prospects³.

Theoretical considerations

Terminology and models of disability

Terminology has become a widely debated issue in the autism field^{4,5}. Some authors have challenged the notion of autism as a disorder as they argue that this has negative connotations⁶, because it implies autistic people are faulty^{7,8}. This suggestion has led to discussion about describing autism as a condition rather than a disorder⁹. There has also been debate about whether to use the terms ‘autistic person’ or ‘person with autism’. Kenny et al.¹⁰ elicited the views of UK community members in the field of autism and found that a large percentage of autistic adults and their families preferred the term ‘autistic’, whilst the term ‘on the autism spectrum’ was endorsed by the majority of professionals. Many autistic rights campaigners have argued that autism is a core part of their identity, and that they therefore see themselves as ‘autistic’ rather than ‘with autism’¹¹. Within the context of these debates, the disability rights lobby have argued for engendering positive acceptance of autism. Rather than looking for cures and treatments, it has been argued that the focus should be on the rights of disabled individuals, and on access, participation and inclusion⁶.

Debates around terminology illustrate a growing challenge to the medical model of disability^{11,12}. Criticisms focus on the fact that the medical model is based on a classification of autism as a disease and an abnormality⁴, with a strong focus on the impairments of autistic people⁶. Those who advocate for the social model of disability, on the other hand, see disability arising from an interaction between a physical impairment or neurological difference and the environment. They argue that the focus then changes from ‘fixing’ the person to giving consideration to removing barriers and adapting the environment⁵.

Shakespeare and Watson¹³ acknowledge that much discomfort with the medical model is based on an opposition to being defined solely on the basis of impairment, and that there is a need to challenge both the reduction to a medical condition, as well as stigma and negative cultural meanings around autism. Furthermore, they highlight that different impairments can have different social and individual implications as there is a complex dialectic of biological, psychological, cultural and socio-political factors, which cannot be extricated, except with imprecision.

This has led to proposals for an integrated bio-psycho-social model¹⁰. The bio-psycho-social model assumes that multiple domains of human

experience influence autistic people¹⁴. In this model, the person's health, care and service-related needs are considered as well as the effect of the physical and social environment on the person, so it takes into account the medical, the psychological, and the social and how these interact in a person's life¹⁵. This holistic way of approaching autism and how autism might impact on individuals at different points in their life, accepts that the biological and social are not necessarily opposites or even distinct, but that the biological, social and environmental interplay with one another. The authors of this report therefore take into account that the biological (e.g. the medical, neurological, genetic or psychiatric), psychological (e.g. emotional, cognitive, developmental) and social (family, culture, interpersonal, school) interact in complex ways, and that they all need to be taken into account in order to fully understand autism.

Challenges for the autism research field

There are different ways of measuring success in a field of research. One may be the discovery of something new, another may be the development of a better intervention. A broader measure could be how much research is conducted now compared to some years ago. The summary of the state of autism research by Prof Michael Rutter in the late 1960s¹⁶ revealed a field in its infancy, where researchers were still unsure as to whether autism was genetic or not, what the underlying biological mechanisms were and what interventions may help. Jump forward 45 years and we have greater confidence in describing the range of behaviours shown, the role certain genes play and how to provide support. Nevertheless, as Prof Rutter states:

*...some of the findings provide a 'wake-up' call to alert us to the need for reconceptualization and for an avoidance of claims that go beyond the evidence. It is very much to be hoped that research over the coming decades will allow a much more positive evaluation than that provided here, but for that to be possible, changes in approach will be needed.*¹⁷ (p. 1754)

Despite the increase in research funding and output, particularly over the last fifteen years¹⁸, there still remain more things we don't know than we do and, as the scale of autism research increases, so does the list of unknowns. Of course, there may be a lag between when this research investment was made and the generation of novel advances but to date there have been significant barriers to progress.

One barrier is the heterogeneity of the autism phenotype (i.e. the observable characteristics that result from underlying genetic and environmental factors) and the broadening of the autism spectrum over time to include many more individuals. Even the diagnostic terms used by clinicians have changed repeatedly over the last thirty years, making it hard to be certain that there is full agreement as to what precisely each term means. Indeed, as researchers have been looking to understand autism better, they have been dealing with shifting targets, making it much harder to find definitive answers. Additionally, the autism phenotype has significant crossover with the phenotype of other neurodevelopmental (e.g. Attention Deficit Hyperactivity Disorder) and psychiatric conditions (e.g. social anxiety), increasing the chances of misdiagnosis and creating “noise” in the data. As a way of overcoming some of these challenges, researchers have looked to increase sample sizes by creating large consortia of research teams (e.g. The Autism Genome Project¹⁹), but the additional statistical power has not been enough to weed-out answers from a complex and often hard to categorise group of individuals.

Despite phenotypic heterogeneity, researchers have tended to study autistic people as a homogeneous group (i.e. comparing the performance of groups of individuals either with or without autism). This approach means we have often ignored the differences between individuals with autism. Moreover, as the autism spectrum has broadened, we have also conducted relatively less research on intellectually disabled autistic individuals, particularly when it comes to neuroimaging and psychological research. Research with intellectually disabled individuals with autism presents practical and ethical challenges (e.g. understanding the nature of the study, providing consent to participate or the use of a surrogate to provide consent on their behalf) and their relative exclusion means that research outputs are often not relevant to them. Some concerns around inclusion may also have been born out of historical cases of exploitation in research of the intellectually disabled (e.g. a hepatitis study at Willowbrook School, New York). Autistic adults and females are two other underrepresented groups in autism research. These shortcomings in terms of the representativeness of research samples have made it difficult to generalise findings to advance our understanding of the whole autism spectrum. For practical reasons research has also tended to focus on providing a snapshot at a specific stage in life (e.g. early years) and, although it can be time-consuming and costly, very little data has been published on how and why autistic people change over time.

For many years, intervention research was a neglected area, often small sample sizes and weak methodologies. Thankfully the last 10–15 years have seen an increase in funding for intervention research and the publication of many more randomised control trials (RCTs) - the gold standard methodology – but there remains uncertainty about what intervention approaches really work and for which individuals. RCTs have often been conducted in controlled environments (e.g. lab settings) by expert researchers. We still know very little about what works in the community (e.g. schools, hospitals) and what degree of impact we can expect to observe. Generally speaking, research has generated few practical benefits for autistic people and their families. One reason for this failing is that there have been few examples where health, education and social care practitioners have been included as partners in research design, implementation and dissemination (see²⁰ for a working model in education).

Research funding increased 15 years ago in part due to parents raising funds, increasing public awareness and lobbying governments. With increased funds there has been greater collaboration, organisation (e.g. setting up the International Society for Autism Research in 2001) and dissemination of autism research, but the research community can still be disjointed, lacking consensus and unduly competitive. Autistic people and parents have traditionally not had their opinions shape research priorities. This has led to many families distrusting what the goals of research are and whether they should be taking part.

Research priorities of autistic people and their families

The majority of autism research funded has focussed on basic or discovery science, formed around a model that research should aim to identify differences that will lead to future interventions or even a cure^{21,22}.

In the past, research funders in the US and UK had objectives within their science strategies to cure or prevent autism, which did not align with what many autistic people and family members were looking for²³. Nevertheless, some autistic people and parents are interested in knowing where “the gene” came from or what are their chances are of having their own or a second autistic child^{3, 24}.

Only recently have efforts been made to look at the priorities of autistic people, parents and non-research practitioners^{3,22,24}. There are between country differences in priorities (e.g. vaccination research is a higher parental priority in the US), but broadly speaking there is a call from non-research

communities to increase the amount of research into services, to make research deliver practical change, to include the opinions of autistic people and to target co-occurring difficulties. An exercise that recently developed a list of the research priorities of autistic people, family members and non-research practitioners in the UK found the top five to be: 1. improved mental health support; 2. communication interventions; 3. improved social care; 4. reducing anxiety; 5. research into education support (<http://www.jla.nihr.ac.uk/priority-setting-partnerships/autism/top-10-priorities/>). There is some evidence that the research community and funders are responding to these calls with an increasing amount of research funded that will have an immediate impact on people's daily lives^{21,25}.

Prevalence and economic models

Prevalence

Human Epidemiology is the scientific discipline concerned with counting the number of individuals with a condition within a population and identifying at a population level associated factors such as age, sex, race/ethnicity, geographical distribution, environmental exposures etc.²⁶.

Prevalence is the technical term used to describe the number of individuals with a condition or trait within a defined population at a particular point in time²⁷ and has been the preferred epidemiological measure for the study of autism²⁸. The earliest of these epidemiological studies, which were conducted in the 1960s, suggested that autism was a rare condition affecting only 2–4/10,000 children²⁹. Over the last 20 or so years there has been a significant increase in detected prevalence with current estimates from different countries suggesting that autism may affect between 1 (e.g. UK³⁰) and in excess of 2.5 % of children (e.g. South Korea³¹); even the lowest of these estimates represents a 50-fold increase in detected prevalence since data have been collected. The few epidemiological studies of autism in adulthood have found very similar rates to those reported in children of approximately 1 %³².

Despite the wide variation in prevalence estimates, it is possible to draw some reasonably robust conclusions from the research findings. First, different approaches to counting the number of autistic individuals tend to produce different prevalence estimates, even within a country. For instance, in the USA the most recent CDC estimate of prevalence is that one in 59 children (1.69 %) aged eight years are autistic³³; a figure based on data from 11 sites within the USA. By contrast data from the 2016 US

National Survey of Children's Health³⁴ suggested that 2.5 % of children aged 3 to 17 years were autistic. Secondly, even within studies there is considerable geographic variation in detected prevalence; the CDC found that prevalence varied between 1.31 and 2.93 % at different US sites³³ whereas in the National Survey of Children's Health the rates at different sites varied from 1.54 to 4.88 %³⁴. These significant geographical variations most likely relate to differences in the types and availability of diagnostic and intervention services, as parents will sometimes move to access better services. Thirdly, although all studies find a significantly higher proportion of autistic boys than girls, there are also variations in the sex ratio across sites within studies. For instance, the male:female sex ratio in the CDC data varied from 3.2:1 to 4.9:1 and possibly such variation reflects challenges in identifying autistic girls. Fourthly, there are notable differences in detected prevalence between different ethnic/racial groups within the US studies^{33,34,35}, with the highest detected prevalence rates recorded in white non-hispanic children, suggesting that cultural and socio-economic factors may influence access to diagnostic services. Fifthly, researchers who have both counted children with an existing diagnosis and also actively identified new cases find significant numbers of previously unidentified autistic children^{31,36}. Sixthly, in studies where annual prevalence estimates are available, the detected prevalence of autism is rising³⁷. Finally, the increase in detected prevalence does not appear to relate to changes in the diagnostic terms used in DSM IV to DSM V (DSM is the Diagnostic and Statistical Manual used to guide clinicians)^{33,38}.

Given the substantial differences in prevalence rates identified across the USA, it seems likely that the current reported prevalence rate of approximately 1 % in Europe^{30,39,36} does not represent a meaningful difference from the US data. Finnish incidence rates (the number of new diagnosed cases in a population) increased and then plateaued during the 1990s⁴⁰ but to date there is no methodologically sound study of autism prevalence in Finland.

These relatively consistent recent prevalence data beg the question of why there has been such a large increase in detected prevalence. There is a general consensus that a considerable proportion of the detected increase relates to the broadening in the diagnostic criteria since the first epidemiological studies. Indeed, Baxter et al⁴¹ argue that there was no meaningful change in prevalence between 1990 and 2010 once variations in methodology are taken into account. Early prevalence research reported that the majority of

individuals on the autism spectrum had Intellectual Disabilities (ID) and would never acquire speech. Although the current rates of identified ID in autistic children vary between studies, there is a general consensus that they are now in the region of 20–30 %^{42,33} supporting the view that more recent prevalence studies identify individuals with less intellectual difficulties. Finally, young autistic children can have comorbid ADHD (Attention Deficit Hyperactivity Disorder) and it is possible that clinicians are now better at recognising autism, even when overactivity and inattentiveness are the presenting complaints⁴³. Nevertheless, there is still the possibility that we are seeing an increase in ‘true’ as opposed to detected prevalence. Currently there is no agreement on an approach that would definitively answer that question.

Economic models

Economic models for health conditions are typically generated as part of government planning around service delivery and to explore the financial benefits of certain interventions⁴⁴. Such models have been generated in autism, primarily in the UK and the US. The economic estimates are usually calculated by making a number of educated assumptions about the autism population within country (prevalence, proportion with intellectual disability, the services that are typically accessed etc.), accessing cost data for certain items (services, restrictions on employment etc.) and then working out the total costs for an individual across their lifetime. The lifetime economic cost for someone with autism and intellectual disability in the UK is estimated to be £1.5 million and for someone with intellectual abilities in the typical range it is £0.92 million; in the US the equivalent figures are \$2.4 million and \$1.4 million respectively⁴⁵. The total annual costs for all autistic children in the UK are estimated at £3.1 billion and for all autistic adults at £29 billion (overall total £32.1 billion)⁴⁵. When these costs have been broken down, the main expenditures in childhood are for special education/intervention services and loss of parental productivity (work); for adults the main costs are for accommodation (including staff costs) and loss of individual productivity (limited employment).

Another area of inquiry has been whether certain interventions and supports alleviate some of these costs. The research evidence in this area is scarce but there is emerging evidence that early intervention^{46,47} and supported employment programmes⁴⁸ may reduce total economic costs. This area of research is particularly important in terms of providing evidence

for local and national governments as to where funds are best directed. There are recent recommendations in the UK for cost-benefit analysis to be a future focus of autism intervention and education studies⁴⁹. A project for the Scottish Government used a “microsegmentation” approach to look at the factors that increase economic costs. They argue that an autistic person’s intellectual level, co-occurring conditions (e.g. mental health) and symptom profile are all factors impacting on outcome profiles (e.g. whether someone is employed or living independently) and therefore the level of economic cost⁵⁰. Depending on the effectiveness of the intervention used, the authors argue that savings upward of £223 million could be made by the Scottish Government per year.

It is worth noting that the terminology used in this field of research (e.g. economic burden) has negative connotations for some autistic people and their families as it implies that autism is a drain on resources and a cost to society, whereas with the right opportunities autistic people do and can contribute to the economy and society.

PART 1:

Discovery research

■ Research, particularly within medicine, is often described as working through a pipeline: uncovering new facts and then testing them to be confident that they will be effective in the community. The US National Institute for Health (NIH) defines the research pipeline as starting with discovery or basic science (gaining knowledge and understanding difference) before evaluating efficacy (whether something identified can be altered – e.g. by a drug)⁵¹. This model has been expanded somewhat to now include implementing research findings in practice (akin to effectiveness research) and the subsequent impact on the population⁵². As has been noted by Pellicano et al²², most autism research investment has been made in basic or discovery science to further our understanding of what genetic, biological, cognitive and behavioural differences occur in autistic people compared to non-autistic people.

Causes of autism

Genetics

Since the 1960s we have known that families who have one autistic child are at increased likelihood of having a second. Twin studies (for a meta-analysis see Tick et al⁵³) have shown that this familial effect arises largely because of genetic influences; in other words, the majority of individuals who develop autism do so because they carry genes that increase the likelihood of this neurodevelopmental outcome. Also, other family members can sometimes have difficulties similar to autism but of milder degree; a phenomenon usually referred to as the broader autism phenotype (BAP).

Current estimates of the “recurrence” of autism if parents already have one autistic child vary considerably according to the samples being examined (the estimates tend to be greatest in intensive studies of high-risk infants who have an older autistic sibling). In a large Danish total population cohort, the estimated average recurrence was 6.9 %⁵⁴ but the rate was nearly doubled in a large Swedish cohort⁵⁵; in both cases this recurrence risk is several times higher than the population prevalence. The patterns

of recurrence in different types of family strongly suggests that autism usually arises on the basis of the action of multiple genes. Once automated genotyping became available in the mid-1990s, significant resources were devoted to trying to identify genetic variants that can predispose to autism. The findings from these studies have been quite different from what was anticipated.

Although two single gene disorders (Fragile X and Tuberous Sclerosis) show a strong association with autism, together they account for less than 5 % of the autism population. Genetic differences that are probably causal for autism have been identified in over 100 genes (for reviews see^{56,57,58}), but for the majority of these genes each individual change has only been identified in a very small percentage of individuals studied. Therefore, these changes are often referred to as rare variants and in total they account for only a very small proportion of the genetic causes of autism.

The vast majority of genetic changes detected in individuals with autism were not inherited from their parents but have arisen spontaneously during the generation of either eggs or sperm. Quite contrary to expectations, autistic and intellectually disabled individuals can sometimes carry multiple different rare variants, which can even differ between individuals within multiplex families (where there are at least two autistic people)⁵⁹. The nature of the changes is quite variable, but none of the identified mechanism underlying change are unique to autism. Overall these de novo changes in DNA sequence have been identified much more frequently in individuals where autism is accompanied by intellectual disability. Additionally, there have been replicated findings of an association between increased parental age and the chances of having an autistic child (see for instance Durkin et al⁶⁰). This association could arise either because there is greater opportunity for genetic change in the germ cells of older parents or because parents with the BAP [or other psychiatric disorders associated with autism] delay reproduction or because both factors are operating. There is some variation between studies with regard to whether the parental age effect occurs in just one or both parents, and the analysis of this data is becoming increasingly sophisticated (see for instance Sandin et al⁶¹). Nevertheless, as is the case with the association between Trisomy 21 (the commonest genetic cause of ID) and increased maternal age, because most parents have children when they are younger, the overall impact of any parental age effect is relatively small.

Genetic change that is de novo cannot account for the tendency for autism to recur in families; there must be other genetic factors at play that are present in the population and which can be passed from parent to child, usually referred to as common variants⁶². The usual approach to detecting this type of change is to look for common gene variants that are associated with an increased likelihood of a specific condition. The first attempts at such studies had only very limited success. It was believed this indicated that large numbers (in the hundreds or thousands) of different genetic variants were associated with autism and that very large number of families would be required to detect these variants. Indeed, the recent successful attempt to identify common variants by pooling data from different samples has a sample size of over 18000 individuals and the analytical approach took advantage of genetic findings from other conditions⁶³. Of course, given the size of the samples required to detect these common risk variants, replicating findings in independent samples will not be straightforward. Interestingly Grove et al⁶³ found that there may be some meaningful genetic differences between individuals defined according to the older diagnostic categories. Thus, genetic liability conferred by common variants seemed to be higher for individuals diagnosed with Asperger Syndrome than those with a more classical form of autism.

Taken together the genetic findings suggest that autism may represent two overlapping groups of individuals: one with lower intellectual abilities in which rare and de novo variants have a causal role and a higher functioning group of individuals in which the above-mentioned inherited variants have a much more significant role.

It is noteworthy that when scientists studying different psychiatric conditions embarked on large scale genomic studies, it was generally assumed that genetic susceptibility would probably be disorder specific. In fact, autism shows a very strong association with other psychiatric disorders, particularly in individuals without ID⁶⁴, and genetic analysis suggests that there is some degree of overlap in genetic factors between diverse neurodevelopmental and psychiatric disorders⁶⁵, which is perhaps not surprising given the very large number of genes that are involved.

Environmental factors

Although genes clearly play a significant role in the development of autism⁵³, environmental factors could sometimes be sufficient or contributory factors to the development of the condition. Indeed, the dramatic increase in

the detected prevalence of autism has often led to the assumption that this increase must be a consequence of an environmental change, as genetic causes are likely to have remained stable over a relatively short time period. Very many environmental factors have been proposed to be involved in the genesis of autism (see Bolte et al⁶⁶ for an overview of putative factors) and we can only focus on a few key issues here.

The claim that the measles component of the MMR vaccine is a causative factor for autism has led to long-lasting drops in vaccination rates and a re-emergence of measles outbreaks, particularly in populations where vaccination rates are very low. Significant resources have been devoted to investigating this claim and, despite an exhaustive search, no evidence for a causal role for the MMR vaccine in the development of autism has been identified (see DeSteffano et al⁶⁷ for a review of this and other claims related to vaccine safety). More recently it has been suggested that specific serotonin reuptake inhibitors (SSRIs) taken during pregnancy, usually for the treatment of depression and/or anxiety, increase the chances of having a child on the autism spectrum³⁶. Again, many groups have investigated this claim as untreated depression during pregnancy is known to be detrimental to maternal and child health. The findings from many high-quality studies illustrate the difficulty in identifying true environmental factors in a condition in which the same genes can influence the development of several disorders (e.g. autism and depression). The association between maternal SSRI use during pregnancy and autism in offspring appears to be due to a phenomenon known as confounding by indication⁶⁸. Put simply, the inherited genes that confer an increased likelihood for development of autism also predispose to the development of depression, and therefore pregnant women seeking treatment for their depression are more likely to receive an SSRI than other pregnant women. That these mothers are at increased risk of having an autistic child, independent of medication use, is clearly demonstrated by those families in which the mother had two pregnancies in which the child was subsequently diagnosed with autism, but only took SSRIs during one of these pregnancies.

Overall most environmental researchers have focused on factors which are known to be harmful, for instance air pollution or exposure to other chemical hazards, such as pesticides. With regard to air pollution, a meta-analysis found limited evidence for toxicity⁶⁹. A recent large epidemiological study⁷⁰ of potential exposure to pesticides in the perinatal period found a small (10 %) increase in the chances of having an autistic child. As it is

generally recognised that exposure to these chemicals should be avoided, the authors recommendation that this advice also applies during pregnancy seems uncontentious. Nevertheless, this study did not document actual exposure to pesticides. In studies where exposure has been directly assessed by measuring the metabolites of pesticides in the urine of pregnant women, the findings are by no means clear cut, for instance, a finding of no increased risk to male foetuses but an apparent small increase in risk in female foetuses⁷¹. Clearly further studies with much larger samples are going to be required to determine whether measured exposure during pregnancy conveys a specific risk for the development of autism.

Some environmental factors potentially hazardous to the foetus are independent of external factors. Historically there was very little evidence that autism had an association with premature birth or being small for dates, which are both statistically associated with developmental difficulties. But as the survival rates for children born very prematurely have increased significantly over the last 20 or so years (and intensive follow-up of these children has become routine), it has become apparent that premature birth is associated with an increased likelihood of a later autism diagnosis⁷². A challenge for future studies is to determine whether prematurity represents a major environmental risk factor that acts in isolation, or whether there is evidence that autistic children born prematurely also carry genetic risk factors for autism. Somewhat similar issues arise with respect to the claimed association between a maternal immune reaction to the foetus and the subsequent development of autism in the child. Some large-scale epidemiological studies suggest that this is likely to be an infrequent cause of autism⁷³, but also point out that even when such a reaction does occur that the foetus might have a shared genetic risk both for autism and for generating an abnormal immune response.

Neuroscience

Because autism is such a distinctive condition it was initially assumed that the changes in brain structure and/or function leading to autism must also be unique. So, for instance, over the years it has been suggested that autism could be a consequence of abnormalities in many different neurotransmitter systems (e.g. GABAergic, Serotonergic, Glutamatergic) but the data suggest that these putative abnormalities are usually only found in a subgroup of individuals.

It is possible to investigate neurobiology at many different analytical levels, ranging from genes to the functioning of large networks of neurons. We will briefly outline the scope of the approaches. Nevertheless, the overarching conceptual challenge is immediately apparent at the genetic level of analyses. Not only have an extraordinarily large number of genes been implicated as risk factors for autism, contrary to expectations they do not appear to act through a common mechanism. So, for instance, changes have been identified in genes that influence: chromatin structure, and hence the action of many other genes; synaptic structure and function; cell migration and eventual position in the developing brain; the outgrowth of nerve cells that eventually form fiber tracts; and in many, many other functions. To date most of the identified genetic variants have been found in individuals who also have ID. Consequently, there is considerable interest in knowing whether there will be greater convergence at some level of analyses as we begin to identify more of the common variants that seem to underlie autism without ID⁶³.

Although some rare genetic variants are known to effect synaptic structure and function, to date there has been relatively little investigation of synaptic structure in brains from individuals with autism who have died, in part because of the limited availability of brain tissues. The published postmortem studies have tended to focus on cell position and shape and have found differences in cell position (see Ecker et al⁷³ for a summary) in several regions of the cortex, which usually have been interpreted as evidence of broader underlying differences in cortical organization. Indeed, one influential observation has been that the ways cells are grouped within cortex show subtle differences from non-autistic people⁷⁵, which potentially could be associated with changes in the way neurons are locally connected to one another. Currently we have no techniques for directly investigating local circuitry organization in human brains, either in post mortem tissue or living people.

The strong association between autism and patterns of EEG (electroencephalogram) activity is indicative of functional differences in the organization of large circuits of neurons that underlie the production of brain waves. Nevertheless, it is difficult to tease apart whether the changes are due to differences in connectivity within local areas of the cortex or between more distant regions (see O'Reilly et al⁷⁶ for a discussion). Brain imaging studies of autism have produced extremely heterogenous findings, both in terms of the size of different brain regions and the connections

between them. As pointed out by Ecker et al⁷⁴, currently it is not possible to determine whether differences in either the grey or white matter of the brain are truly primary, but overall there is a consensus that the cerebral cortex is probably organized in a somewhat unusual way in individuals with autism.

In an effort to minimize heterogeneity, some research groups have focused on particular subsets of autistic individuals, for instance those with increased head circumference or a history of regression or delayed language development. Another potentially fruitful approach could be to focus on groups of children with autism defined by the rate at which they gain skills early in development, which seems to be very variable⁷⁷.

Areas of difference

Social and communication

Difficulties in the social and communication domains have defined autism from the original descriptions by Kanner and Asperger in the early 1940s onwards. Kanner⁷⁸ described the autistic children he saw in his clinic as having difficulties relating to others from the beginning of life and that some failed to develop speech, or were delayed in their language development. Asperger^{79,80} described children who on occasion were more interested in their own preoccupations than being with their family and whose speech was lacking a social quality. These early clinical descriptions are still relevant today in delineating social and communication difficulties across the autism spectrum.

Interest in social stimuli is typically present from birth and many believe this preference is “hard wired”⁸¹. Analysis of first-birthday videotapes (i.e. before the child has a diagnosis) have noted differences in pointing, showing of objects, looking at others and responding to own name⁸². Retrospective reports from parents report reduced eye contact and reduced interactive play in early development⁸³. Social differences have also been documented in young childhood, around the time of diagnosis (3–5 yrs of age), including: not enjoying physical contact with parents; failing to respond to own name; poor understanding of other people’s feelings and facial expressions; difficulty forming friendships; unusual greeting or responding to social approaches⁸⁴. In the teenage years, autistic children are often bullied and victimised and can suffer from social isolation⁸⁵. These challenges continue into adulthood with lower rates of friendship, romantic relationships and social independence⁸⁶.

Arguably, the most important social cues available to humans are the face and eyes⁸⁷. Some autistic people are known to not show the typical expertise in discriminating pictures of faces compared to pictures of objects (e.g. cars)⁸⁸. They may also be averse to eyes looking at them⁸⁹ and have difficulties recognising facial emotion⁹⁰.

Theories as to why social difficulties occur in autism have suggested that the key problem is in understanding the thoughts and feelings of other people (Impaired Theory of Mind)⁹¹. It has also been suggested that the innate social drive to interact with others is absent or reduced in autism⁹² and that consequently people on the autism spectrum pay less attention to social information in their environment⁹³. Either way, the “social brain”, or the neurobiological regions that work in synchrony underpinning our social expertise, are likely to function differently in autistic people^{94,95,96}.

In the most recent revisions of the manuals clinicians use to diagnose health and psychiatric conditions^{1,2} the social and communication domains of impairment are not treated separately. This makes sense as the key purpose of communication is its social aspect⁹⁷. Communication has many different components. There is expressive communication such as spoken language (e.g. words and syntax), receptive communication (e.g. our understanding of what others are saying), the pragmatic component of language (social elements like the conversational back and forth) and non-verbal communication (gestures, pointing, facial expressions). Autistic people have been shown to have difficulties in most areas of language and communication, but these vary depending on the nature of a person’s autism⁹⁸.

In the first year of life autistic infants have communication difficulties in imitation, positive affect, play skills, joint attention and social games such as peek-a-boo^{99,100,101}. In the second year of life autistic children are slower developing early spoken language skills¹⁰² and they can experience regression in their speech, such as losing any single words they have developed¹⁰³. There are also emerging differences in pragmatic (social communication) skills as autistic children tend to use language to meet their own needs rather than for social interaction¹⁰⁴. Autistic children may make an overly literal interpretation of what is being said to them¹⁰⁵, have more formal or pedantic speech and difficulties in modulating eye gaze correctly during conversational exchanges¹⁰⁶.

There is a great deal of variability in the trajectory of spoken language development across autistic individuals, with some not developing much

or any spoken language and others developing an extensive vocabulary¹⁰⁷. The factors that affect these developmental trajectories include IQ¹⁰⁷, level of early expressive language skills¹⁰⁸, having access to early intervention services¹⁰⁹ and engaging in joint attention (using communication to draw someone's attention to an object)¹¹⁰. Some autistic children have a superior vocabulary compared to non-autistic children¹¹¹, while others have a longer developmental arc and continue developing their spoken language skills into adulthood¹¹². It happens rarely, but some autistic people are able to speak but choose not to, otherwise known as selective mutism¹¹³.

Restricted and Repetitive behaviours

The term restricted and repetitive behaviour (RRB) in autism is an umbrella term to capture behaviours that may be repeated over time, are unusual in appearance, regarded as inappropriate to the context or follow rigid patterns. In the current version of the Diagnostic and Statistical Manual (DSM-V) used to guide clinicians on what should be present for an autism diagnosis¹ the section on RRB includes: repeated actions of movement (e.g. hand movements), speech (e.g. repeating the same phrase over and over) or using objects (e.g. lining up toy cars); being very routinised, having to stick to certain patterns of behaviour and insistence on sameness; strong interests that are unusual in nature or intensity.

RRBs are not exclusive to autism and are observed in non-autistic children¹¹⁴ and people with mental health conditions¹¹⁵. Despite there being overlap in terms of the type of RRB displayed between autistic children and non-autistic children, autistic children show these behaviours at a higher frequency^{116,117}.

RRBs are observed in very young autistic children¹¹⁸ but may diminish as autistic individuals reach adulthood¹¹⁹. Research is unclear as to how RRBs change over time and what predicts these developmental patterns, but there is some evidence that behaviours classed as repetitive and sensorimotor remain high, whereas insistence on sameness starts low and increases with age¹²⁰. The relationship with IQ is also a little unclear. One large study found that as non-verbal IQ (NVIQ) increased so did the likelihood of some RRBs being present (e.g. limited interests), although most RRBs became more frequent as NVIQ fell (e.g. hand and finger mannerisms)¹²¹.

Sensory sensitivities

The two manuals for clinical diagnostic guidance (The Diagnostic and Statistical Manual and The International Classification of Disease) now include sensory sensitivity as an item under the RRB domain for autism^{1,2}. Three categories of sensory responses have been identified: 1. hypersensitivity (a behavioural overreaction to or avoidance of a sensory stimulus); 2. hyposensitivity (a behavioural underreaction to a sensory stimulus); 3. sensory seeking (strong interest in a particular sensory stimulus)¹²². Levels of sensory hypersensitivity correlate with levels of RRBs¹²³, explaining its inclusion in that domain within the diagnostic manuals¹²².

Sensory sensitivity occurs at a very high rate (upward of 90 %) in autism^{124,125} and include differences in responses to the taste, feel, sound, sight or smell of things or people. Beyond the traditional external senses, autism researchers have also identified differences in systems that integrate internal sensory inputs¹²⁶, i.e. proprioception (awareness of one's body in space)¹²⁷ and vestibular (balance)¹²⁸. Sensory differences in autism seem to be global in nature, so that sensitivities related to one sense increase the likelihood of differences occurring in another sensory modality¹²⁹.

Sensory sensitivity is observed in autistic toddlers¹³⁰ through to adults¹³¹. Some autistic people describe it as being a central (positive and/or negative) component of their lives¹³². Sensory hypersensitivity has been shown to be related to the feelings of stress and anxiety reported by some autistic people¹³³, which underlies the importance of adjusting school and work environments so that they are optimised for autistic people's participation¹³⁴.

Measures of IQ

IQ, or intelligence quotient, is an ordinal measure of a person's ability to complete a set of discrete tests of intelligence. IQ tests are normalised such that the average score in a population is around 100. There are a number of different tests that can be used but the most common are the Weschler tests for children and adults that provide scores of verbal IQ (VIQ), non-verbal IQ (NVIQ) and full IQ (FIQ).

The Weschler tests of IQ include a number of verbal (e.g. saying how two words are alike - *Similarities*) and non-verbal (e.g. arranging blocks so they match an exemplar pattern - *Block Design*) subtests. There have been consistent reports of an uneven or "spikey" profile across IQ tests/subtests and early reports suggested that autistic people had a higher NVIQ than

VIQ¹³⁵. As an increasing number of individuals with Asperger syndrome were diagnosed, the opposite pattern was observed with superior VIQ skills. Researchers have reported finding superior performance on those tasks that involve segmenting visual puzzles (e.g. Block Design; Ravens Progressive Matrices – RPM)^{135,136,137} and simultaneous difficulties with comprehension (a measure of verbal reasoning and conceptualisation)^{136,138}.

The uneven profile and the social and verbal demands of IQ tests have led some to suggest that traditional measures of IQ are not adapted to autistic people's strengths and are underestimating their level of intelligence^{137,139}. In addition, the role of motivation is an under-researched area of cognitive testing in autism, but in the general population it has been reported as an important influence on IQ scores¹⁴⁰. Lastly, the IQ testing environment typically involves social and communicative interactions between the examiner and examinee (e.g. responses to questions), meaning that autistic individuals may be at a disadvantage even before testing starts.

Areas of strength

The cognitive profile of autistic people has shown strengths in some areas and difficulties in others¹⁴¹, but broadly speaking there has been a tendency within autism research to focus on “deficits”¹⁴². It has been proposed that “strengths-based assessments”, which include autistic individuals' special interests and reframing their behaviour to look at the positives, can improve the dynamic between parents and practitioners, as well as lead to more ambitious targets of what is achievable for the individual¹⁴³.

Superior or “savant” skills can be defined in two different ways:

1. compared to non-autistic individuals/groups; 2. relative to the individual's general ability¹⁴⁴. Early savant research focussed on identifying those individuals falling under definition 1, associated with an exceptional skill in a specific area (e.g. calendrical calculation), but where the individual in question may also have an ID¹⁴⁵. As the definition of savant abilities has broadened to include definition 2¹⁴⁴, it is now estimated that almost a third of the autistic population qualify as savants¹⁴⁶. It is often assumed that many of these savant abilities are achieved by being able to focus on details and having superior attentional skills for their topic of interest^{147,148}.

In addition to the IQ research showing strengths on certain sub-tests, researchers have also reported superior performance on a number of cognitive tasks. This has included identifying a subset of autistic individuals (with a diagnosis of Asperger Syndrome) who score well on standardised

vocabulary tests¹⁴⁹. The ability to form and manipulate mental images has also been put forward as a superior cognitive skill in autism¹⁵⁰ and may explain some of the abilities in completing puzzles¹⁵¹. The skills autistic people have in terms of concentration, understanding rules and patterns, memory etc. mean that they are in a position to potentially exceed the performance of non-autistic individuals within education and the workplace¹⁵².

Co-occurring difficulties

For many years research focussed on the social and communication difficulties in autism but the last ten years have seen an increasing trend for researchers to study the intellectual, psychiatric and physical challenges that frequently exist alongside autism¹⁵³. These are called co-occurring difficulties.

There are numerous co-occurring difficulties that have been identified. Some of the common biological difficulties studied include: epilepsy; sleep; gastrointestinal; co-ordination¹⁵⁴. The common co-occurring psychiatric disorders studied include: attention deficit hyperactivity disorder (ADHD); anxiety; depression; schizophrenia; obsessive compulsive disorder (OCD); Tourette's¹⁵⁴. A large survey of British parents found that the highest rates of emotional and behavioural difficulties were: aggression; sleep; dietary issues; overactivity; anxiety¹⁵⁵. From this research, 53 % of parents reported that their children frequently had four or more types of emotional or behaviour difficulties.

Despite the frequency of these difficulties, there is some reluctance by clinicians to make additional diagnoses, particularly for autistic individuals who are intellectually disabled¹⁵⁶. Even within the diagnostic manuals there has previously been a resistance to allow two common neurodevelopmental disorders (autism and ADHD) to co-exist¹⁵⁷. It remains unclear as to what biological and environmental causes underly these difficulties; whether they are a manifestation of a shared causal mechanism or from multiple factors¹⁵⁸.

Intellectual disability (ID)

The World Health Organisation² classifies disorders of intellectual development as being caused by various factors (e.g. genetic or acquired through brain injury), usually evident early in development and

characterised by intellectual functioning that is at least two standard deviations below the average level of intelligence. There are different levels of Intellectual Disability (ID): mild, moderate, severe and profound. A meta-analysis of previous research estimated the prevalence of ID in the general population to be 10.37/1000¹⁵⁹, with the majority of individuals with ID (approximately 85 %) being classified as having a moderate ID¹⁶⁰.

As the detected prevalence of autism has increased over time, and we have become more sensitive to the breadth of the spectrum, there has been a downward shift in the proportion of individuals on the autism spectrum who have intellectual disability¹⁶¹. In a 1974 publication, DeMeyer and colleagues reported that out of 115 autistic children tested, 94 % had an IQ lower than 68¹⁶²; a study of children from south London in the early 2000s found that 55 % had an IQ < 70¹³⁸; recent American surveillance data reported that 31 % of children had an IQ <70⁴². When Brugha et al., (2012) looked at adult ID populations they found that prevalence of autism increased with the level of ID. Amongst adults with ID living in social care establishments the prevalence of autism was estimated at 31 %¹⁶³.

Mental health

A large UK questionnaire in 2015 asked for the research priorities of autistic people, parents and practitioners (health, education and social care). Nearly 1300 people responded, and the number 1 research question was:

“Which interventions improve mental health or reduce mental health problems in people with autism?”

And the fourth one was:

“Which interventions reduce anxiety in autistic people?”

(Page 4 <http://www.jla.nihr.ac.uk/priority-setting-partnerships/autism/downloads/Autism-PSP-final-report.pdf>)

Mental health issues negatively impact on all members of the family¹⁶⁴ and poor mental health is a risk factor for early death in autism through suicide^{165,166}. A survey of autistic children in the UK aged 10–14 years of age found that 70 % met criteria for a psychiatric disorder using the Child and Adolescent Psychiatric Assessment (CAPA) and 40 % met criteria for at least two psychiatric disorders¹⁶⁷. The most common psychiatric

disorders identified in this study were anxiety (41 %), in particular social anxiety disorder (29 %), as well as attention deficit hyperactivity disorder (ADHD, 28 %) and Oppositional Defiant Disorder (ODD, 28 %). In this study the rates of depressive disorder were low (1.4 %), and as in the general population, depression becomes increasingly common after puberty¹⁶⁸. Despite the high rates of mental health and psychiatric conditions in young people and adults with autism, there is evidence to suggest that the prevalence of these conditions may decline in older adult life, particularly with regard to social anxiety¹⁶⁹.

There is significant cross-over in the symptoms of autism and other common mental health or psychiatric conditions. For example, both autism and ADHD affect areas of social, communication and attention¹⁷⁰ and there are similar difficulties observed in autism and social anxiety disordered individuals¹⁷¹. The presence of a co-morbid mental health condition can have an additive effect in terms of the autism symptoms¹⁷² and require adjustments to the type and intensity of interventions.

High levels of psychiatric comorbidity mean that autistic individuals are more likely than the general population to access services for therapy¹⁷³. It is common to use medication to manage co-occurring mental health difficulties in autism^{174,175} but these often come with adverse effects and have not been approval-tested for use with autistic people¹⁷⁶. The last ten years has seen a significant increase in research demonstrating the efficacy of behavioural treatments such as Cognitive Behavioural Therapy (reviews^{177,178}) and mindfulness (review¹⁷⁹) to improve the mental health of autistic people. Nevertheless, there remains a lack of these therapies delivered in community settings. Moreover, they have rarely been adapted to the social, communicative and environmental needs of autistic people¹⁸⁰. In many countries individuals with ASD have difficulties accessing mental health resources.

Poor mental health affects the whole family. Parents of autistic people, particularly mothers, are at increased risk of significant mental health problems^{181,182}. As with autistic children, there is growing evidence to suggest that behavioural-based therapies can significantly improve the resilience and mental health of parents¹⁸³.

Behaviour that challenges

The term behaviour that challenges has most recently been adopted as an alternative to the term challenging behaviour¹⁸⁴. The previous term saw

“the problem” existing in the individual with ID and did not take into account the reason why the individual exhibits that behaviour. The 2015 National Institute for Health and Care Excellence (NICE <https://www.nice.org.uk/guidance/ng11>) Guidance for health practitioners states:

“Behaviour that challenges’ is not a diagnosis and is used in this guideline to indicate that although such behaviour is a challenge to services, family members or carers, it may serve a purpose for the person with a learning disability”

The focus has now shifted to understanding what the behaviour may mean and the role that practitioners, society and the environment play in interpreting, eliciting and intervening with these behaviours:

“an individual with challenging behaviour is not the only one requiring treatment and to therefore ensure that other elements such as the environment, skills, attitudes of carers/staff and service capabilities are simultaneously assessed and are also the focus of intervention”
(p. 24 Tanwar et al¹⁸⁴).

Matson and Rivet¹⁸⁵ identified four key categories of behaviour that challenges: 1. Aggression/destruction (e.g. banging on objects); 2. Stereotypy (e.g. unusual vocalisations); 3. Self-injury (e.g. biting, swallowing objects); 4. Disruptive (e.g. removal of clothing). In each of these categories autistic adults, whether intellectually disabled or not, exhibit behaviours significantly more often than IQ-matched individuals with ID and no autism¹⁸⁵.

Based on expert opinion and research, Pilling et al¹⁸⁶ identified a number of “triggers” that can lead to behaviour that challenges, including: the sensory environment; physical disorders and discomfort; the social environment (e.g. unfamiliar people); changes to routines; communication issues; co-occurring mental health or psychiatric problems. Matson et al¹⁸⁷ reviewed the research literature and found that gaining attention and escaping the environment were noted as the two most common functions of behaviour that challenges, but self-stimulation and seeking items (e.g. food) were also important.

An emerging area of autism research relevant to what can cause behaviour that challenges to escalate is poor emotional regulation^{188,189,190}, or the ability to use behaviours, skills or strategies to modify or balance one’s emotional

state¹⁹¹. Research suggests that autistic people tend not to use social contact as a way to regulate their emotions and instead rely on removing themselves from the stressful environment¹⁹². There is also evidence that autistic individuals may have more difficulties in appraising the way they think or feel about a situation and find it a challenge to suppress their emotional reactions¹⁹³. Nevertheless, certain intervention strategies, such as Cognitive Behavioural Therapy, may help in this regard¹⁹⁴.

In the recent NICE Guidance on Challenging Behaviour (NICE 2015), experts in the field reviewed the evidence behind Positive Behaviour Support (PBS) and reported there was a lack of research that could demonstrate beneficial effects on behaviours that challenge. However, proponents of PBS suggest that there is evidence to support its use with individuals who have the most behaviours that challenge but they concede that there is a small number of studies to review from¹⁹⁵. UK NICE Guidance on intervening with challenging behaviour in autistic adults recommends that a psychosocial intervention should be tried before any consideration of medication. If drugs are prescribed that adverse effects and quality of life should be carefully monitored and reviewed regularly¹⁸⁶. Evidence has supported the use of risperidone and aripiprazole for reducing challenging and repetitive behaviours in autism but with the caveat that these medications come with a number of side effects¹⁹⁶, particularly weight gain.

Sleep

One of the factors that increases the frequency of behaviours that challenge in autistic people is poor sleep^{197,198}. Sleep disturbance is extremely common in autism and prevalence rates upward of 80 % have been reported, although these figures vary depending on the ages of individuals studied and the presence of ID¹⁹⁹. In young autistic people with ID, poor sleep was used to predict increased rates of aggression, self-injury, tantrums and property destruction²⁰⁰, with the frequency of night awakenings having the greatest impact on behaviours that challenge²⁰¹.

The benefits of a good night's sleep in terms of mood, emotion regulation, cognition and behaviour are well known²⁰². Autistic people tend to have less sleep than non-autistic individuals, including those with other developmental disabilities²⁰³. The nature of sleep difficulties in autism have been identified as: settling difficulties; frequent waking; long sleep latency; early waking; disturbed sleep routines; daytime sleepiness; restless sleep; abnormal objective measures of sleep patterns (actigraphy)²⁰⁴. Although

the causes of sleep disturbance remain unclear, a recent paper outlining expert opinion in the field suggested that insomnia-related behaviours are the consequence of cognitive hyper-arousal (becoming fixated on certain topics) and/or heightened physiological arousal (e.g. body temperature, increased heart rate)²⁰⁵. Measures of EEG (electroencephalography) and REM (rapid eye movement) in sleep clinics have also been found to be different in autistic people, suggesting a possible biological cause for some of the sleep difficulties²⁰⁶.

A biological marker important for sleep that has been reported to be different in autism is melatonin levels²⁰⁷. Melatonin is the hormone released to control the sleep/wake cycle and is sensitive to changing light conditions²⁰⁸. Melatonin can be given as a supplement to those with sleep problems and RCTs (randomised control trials) have estimated that melatonin improves sleep time by 61 mins in autistic people and sleep onset latency by 29 minutes, but there were no significant benefits in terms of frequency of awakenings²⁰⁹. Despite reported benefits in sleep onset and duration, it remains unclear whether these lead to clinically significant changes in autism symptoms or improve family wellbeing²¹⁰.

The UK's health guidance on autism and sleep recommends a behavioural intervention before medication is considered²¹¹. The recommendations are to keep a sleep diary and to work with a specialist to develop a sleep plan; making environmental adjustments to identify the optimal sleep conditions. For example, one recent study suggested that bedroom access to a TV or a computer reduced sleep among autistic boys more than it did boys with ADHD²¹².

Programmes have now been developed to train parents to manage their autistic child's sleep. After five sessions in such programmes, parents have reported significant improvements²¹³. Treating sleep problems can significantly reduce parental stress²¹⁴. Given that parents of autistic children also report earlier wakening and less total sleep time²¹⁵, improved sleep for the whole family will likely improve quality of life.

Diet

Autistic people are known to have a more selective diet than non-autistic people^{216,217,218}. In the early developmental period (15–54 months) autistic children are classed by their mothers as being “picky eaters”, eating a restricted range of foods and as difficult to feed²¹⁹. Food selectivity is broadly classified as a tendency to eat a limited range of foods or being

restricted to eating a single food. It is reported to occur in approximately 70 % of young autistic people^{220,221,222} and may continue to be an issue into adulthood²²³. One of the factors that has been identified that leads to food refusal is the sensory components of the food (taste, texture, temperature etc)²²¹. Research has suggested that without intervention the frequency of food selectivity is relatively stable over childhood and when left untreated it may lead to health complications²²⁴. Evidence is emerging of the beneficial effects of parent training to reduce feeding problems, improve behaviours of concern and alleviate parental stress²²⁵.

The fact that autistic people have a more restricted diet has led some to predict that they must also have poorer intake of nutrients²²⁶ but the findings in this area have been inconsistent, with some researchers reporting no difference from controls²²⁷ and others reporting poorer intake of certain vitamins²²⁸ or dairy products²²⁹. Those autistic children who are on an exclusion diet (i.e. gluten and/or casein is purposefully removed from their diet) are more likely to have a different nutritional profile (in part negative, in part positive) than autistic children not on an exclusion diet²³⁰, showing the importance of getting nutritional advice before starting a specialist diet. Overall, there is no suggestion that any variation in nutritional intake has a negative impact on energy or physical growth in autism²¹⁹.

A limited diet, such as eating less fruit and vegetables²³¹, may be one reason why autistic people have a higher incidence of gastrointestinal (GI) problems^{232,233}. Reviews of the frequency of GI problems in autism have estimated rates ranging from 9–91 %; with abdominal pain ranging from 2–41 %, constipation from 6–45 % and diarrhoea from 3–77 %²³⁴. GI problems are reported to be more frequent in autism compared to non-autism control groups²³⁴ and have been correlated with higher rates of behaviours that challenge²³⁵ and poor sleep²³⁶. Children with higher rates of anxiety and sensory sensitivity have also been found to have higher rates of GI problems²³⁷.

The higher incidence of GI problems and speculation around food intolerances has led some parents to believe that removing gluten and casein from their child's diet will improve symptoms²³⁸. A large parental survey of 18 European countries showed that a quarter of respondents had used a dietary or supplement intervention within the last 6 months²³⁹ and from a UK survey 83 % of parents had tried a dietary intervention at some point²³⁸. A significant proportion of parents report that the diet

has a beneficial effect on their child's behaviour²⁴⁰ but independent research evidence has been harder to come by²⁴¹. A small-scale but methodologically rigorous study that looked at the efficacy of a gluten and casein free diet in 3–5yr old autistic children found no beneficial effects in the social, communication and sleep outcome measures after 12 weeks of autistic children being on the diet²⁴². Given the strength of the evidence, the associated costs of being on an exclusion diet and the additional family pressure of trying to stick to the diet, recommendations are to advise parents to seriously consider whether using this diet is the best use of their resources²⁴³.

One consequence of having a restricted diet and a less active lifestyle^{244,245} has been increased rates of obesity in autistic young people²⁴⁶ and adults²⁴⁷. Beyond reduced engagement with physical activity and increased interest in passive activities such as watching TV²⁴⁸, rates of obesity in autism have correlated with sleep problems, mental health difficulties, socioeconomic status of parents and medication use^{249,250,251}. There is now strong evidence to suggest that there are significant health, mental health and behavioural benefits from autistic people participating in an autism-specific exercise programme^{252,253}. Effective strategies in intervention programmes for fitness have been identified as: prompting; modelling; praise; structure²⁵².

Epilepsy

Epilepsy and seizures are broadly classified as abnormal neuronal activity that may or may not cause a physical response (e.g. convulsions). Classification of different types of epilepsy can be challenging and have changed over time²⁵⁴ and misdiagnosis is common²⁵⁵. Meta-analysis of previous research has estimated the prevalence of epilepsy in autistic individuals with ID to be 21.5 % and 8 % in individuals without ID²⁵⁶. Bolton et al²⁵⁷ reported that epilepsy had a later onset (mean age 13.3 yrs) than seen in the non-autistic epilepsy populations, general (whole brain) rather than partial (one brain region) seizures were more common and EEG (electroencephalography) didn't aid diagnosis or clinical management. Epilepsy has also been reported to be more common in autistic individuals who regress (a period during early development when autistic children lose social and/or communication skills²⁵⁸), leading to some terming this *autistic eleptiform regression*²⁵⁹, which may be more common in autistic women²⁵⁹.

The majority of autistic people with epilepsy take anti-convulsant medication²⁵⁹ and it is important that families, practitioners and autistic

people understand the reasons for taking this medication as epilepsy is a risk factor for early mortality in autism²⁶⁰. Expert opinion in the autism and epilepsy field has argued that more clinical trials need to be conducted to develop autism-specific medications, as well as to look at the efficacy of combined behavioural and pharmacological interventions²⁵⁶.

Concluding remarks

It is well recognised that the health, behavioural and psychiatric conditions that co-occur with autism should be priorities in terms of planning services for autistic people and for staff training programmes⁸³. Managing these conditions are priorities for autistic people and their families, and can lead to significant improvements in quality of life, as well as increasing societal participation. Co-occurring conditions should not be assessed and managed in isolation, but consideration should be given to how these different conditions interact. For example, improved sleep may make weight problems easier to manage²⁴⁶ and interventions for anxiety may lead to a reduction in GI problems²³⁷. Future research should focus on the relationship across co-occurring conditions and develop recommendations for service delivery.

PART 2:

Research related to practice

Signs and diagnosis

Early signs of autism

Because of the strong genetic influences on the development of autism, families who have had one child on the autism spectrum are much more likely to have a second autistic child. Researchers have taken the opportunity to conduct longitudinal studies of later born siblings in families who already have one autistic child in order to observe the behaviours that predate the development of diagnosable autism. These studies have shown that in the first year of life, later born siblings who subsequently receive a diagnosis of autism can show differences from those siblings who don't go on to develop autism^{262,263}.

In the first year of life children who go on to develop autism can show social attention and communication, increased repetitive behaviours and distinct body movements, as well as evidence of temperamental dysregulation²⁶². These signs are often subtle and rooted in processes outside the core domains of autism. In the second year of life delays or differences in use of gesture, eye contact, social attention, response to name, imitation, language and evidence of repetitive behaviours are more clear-cut, but the pattern of onset may be more complex than subsequent parental recall suggests²⁶⁴.

Although it is possible to diagnose autism in the second year of life, quite often this does not occur. For instance, across eight sites in the USA³³, 85 % of parents of autistic children had reported developmental concerns by 36 months but only 42 % of these children had been evaluated by that age, and the median age of diagnosis was four years and four months. Research in the UK has shown that between 2004–2014, the age of diagnosis did not decrease and was relatively stable at an average of 55 months of age²⁶⁵. Crane et al²⁶⁶ found that the time interval for UK families between initial expression of parental concern to a health professional and diagnosis was on average 3.6 years. In terms of factors that appear to influence the age of diagnosis, children with more autism symptoms appear to

be identified earlier, particularly if there is severe language delay²⁶⁷ or language regression²⁶⁵, whereas ethnic minority immigrants appear to be at particularly high risk for diagnostic delay²⁶⁸. There is increasing evidence that unusual behaviours observed outside the home, either in preschool²⁶⁹ or kindergarten²⁷⁰, can be a useful pointer to a possible diagnosis of autism.

One approach to improving the detection of autism is to undertake screening of a target population and then to conduct a comprehensive diagnostic assessment in individuals who are identified as possibly scoring high enough on the screen²⁷¹. In the context of autism, screening usually refers to general population screening of young children in order to facilitate earlier diagnosis and access to early intervention²⁶². One of the earliest attempts at screening was conducted by Baron Cohen's group, who devised the CHAT²⁷²: a questionnaire for the parents of 18-month-old children that focused on the skills which were thought to be precursors of the ability to understand that other people have thoughts and emotions (so called Theory of Mind). Subsequently the CHAT has been extensively revised and elaborated and its revisions have been widely used in different screening studies and translated into multiple languages²⁷³. There are numerous other screeners available, which are reviewed by Zwaigenbaum and Penner²⁷⁴ and as part of the UK's NICE Guidance review (<https://www.nice.org.uk/guidance/cg128>).

To be useful in clinical practise, a screener must show both high sensitivity (the ability to identify individuals who do have the disorder being screened for) and high specificity (the ability not to misidentify other children as having the disorder). Although intuitively screening seems a sensible idea, most countries have not adopted universal screening of young autistic children (see the American Academy of Paediatric Bright Futures guidelines [2016] and the USPSTF recommendation statement [2016] for contrasting viewpoints). In part that is because the sensitivity and specificity of screening instruments need to be extraordinarily high if they are to be used economically and effectively on a regular basis in large populations (e.g. 4 million babies are born a year in the USA). Nevertheless, this is a constantly developing field. The judgement of governments may change in the future as new evidence becomes available. In the meantime, educating parents, professionals and the public about the early signs of autism seems likely to improve identification^{275,276} (see UK Royal College of General Practitioners toolkit on autism). Much less attention has been paid to the screening of groups in whom the rate of autism is known to be increased,

such as individuals with ADHD, ID, eating disorders, gender dysphoria and individuals in the criminal justice system, and we anticipate that this will be an expanding area of research.

Diagnosing autism in children and young people

Since its initial description, autism and related disorders have been defined on the basis of a distinctive combination of behaviours, which are usually apparent from the second or third year of life onwards^{78,79}. Although the behavioural criteria for diagnosis have changed somewhat over the years, reflecting both scientific advances and an appreciation that the autistic spectrum extends more broadly than initially supposed, the focus of history taking and observation have proved remarkably stable.

The terminology attached to autism has changed over the years, in part because of how clinicians have classified and revised it in the World Health Organisation's International Classification of Diseases and the American Psychiatric Association's Diagnostic and Statistical Manual (DSM). ICD 10²⁷⁷ and DSM-IV²⁷⁸ characterized autism and related conditions as Pervasive Developmental Disorders (PDDs), a term that was initially contentious as some experts considered this description was more applicable to intellectual disability, but the phrase was chosen to highlight that this group of conditions affect many areas of functioning over and above the core diagnostic features. PDD's were conceptualized as categorical disorders (autism, atypical autism, Asperger's syndrome, PDD NOS); an approach that in part reflected periodic broadening of the diagnostic construct since Kanner's original description of infantile autism. Because it has been difficult to demonstrate that these conditions were meaningfully distinct, DSM-V¹ and ICD-11² have done away with separate categorical diagnoses and instead refers to Autism Spectrum Disorder (ASD), whose severity is specified. Additionally, the separate domains of social and communication difficulties in DSM IV have been collapsed into one domain in DSM-V and ICD-11, highlighting challenges in the social use of language rather than the previous strong emphasis on absence of language. Sensory hypersensitivities have also now been included in the stereotyped and repetitive behavioural domain.

Many diagnostic guidelines for autism have been produced by professional and national bodies (see Zwaigenbaum and Penner²⁷⁴ for a summary and critique; Baird et al., 2011²⁷⁹ for a summary of the UK's NICE Guidance on autism diagnosis and management in children and young people). A comprehensive diagnostic evaluation for autism will

usually involve several different components. Obtaining a developmental history of the child is the core component of an assessment and this approach becomes more not less important when assessing older children, adolescents and adults. That is because some features of autism may only be observed at early stages of development and children may either be taught behaviours (e.g. greeting during social interaction) or over time they may acquire compensatory strategies that mask diagnostically useful features. Additionally, an experienced clinician should undertake an interactive assessment with the individual in order to elicit characteristic differences in social-communication and examples of repetitive and stereotyped behaviours or speech. There are several standardised and semi-standardised assessment tools available to the clinician (see Zwaigenbaum and Penner²⁷⁴ for the most commonly used) which enable diagnostic information to be gathered in a uniform manner, although there is no agreement across the different diagnostic guidelines regarding the use of specific tools²⁷⁹.

There has been an increasing appreciation over the last 10 or so years that autism is more often than not co-occurring with other psychiatric disorders (particularly ADHD)^{280,281}. A comprehensive assessment should include a search for other psychiatric disorders. Recent studies suggest that commonly available screeners for psychiatric disorders also appear to be effective in individuals on the autism spectrum^{282,283}. Because autism is sometimes associated with intellectual disability and diverse learning difficulties, cognitive and language assessments can be particularly helpful during the diagnostic assessment, but often resource limitations mean they are not be routine. One important recommendation from professional guidance in the field is for decisions to be made as part of multi-disciplinary clinics (i.e. professionals from different background are included in the clinical decision making)²⁸⁴. NICE guidance for the UK recommends the core multidisciplinary team to include a paediatrician or psychiatrist, a speech and language therapist and a clinical psychologist. Additional support should be available from occupational therapists, specialist nurses and social workers. The use of multidisciplinary working may go some way to improving the reported low levels of confidence clinicians have when giving an autism diagnosis²⁸⁵.

With regard to testing of individuals with autism for potentially causal genetic changes, the American College of Medical Genetics guidelines²⁸⁶ suggests whole genome screening for all individuals, as well as Fragile X testing for boys and testing for PTEN gene in those individuals with large

head circumference. Nevertheless, in populations of individuals coming for a diagnosis, the yield of such testing is much lower than the guidelines suggest (see for instance Kalsner et al²⁸⁷). Others have pointed out that there is no economic data to support such a recommendation²⁸⁸. Given what we now know about the genetics of autism, the guidelines still seem applicable to individuals with ID (and those with a large head circumference), but it is less clear that testing should be routine in more cognitively able individuals. Although there have been attempts to diagnose autism using a number of different biological measures (e.g. Ecker et al²⁸⁹), it seems likely that even if the sensitivity and specificity of these approaches reach clinically acceptable levels, such biological diagnostic testing will as in most other areas of medicine remain an adjunct to the developmental history because test results will reveal nothing about the child's behaviour, which is key for developing an appropriate management plan.

Diagnosing autism in adulthood

Not all autistic individuals are diagnosed in childhood. In many countries specialist services have been or are being established to conduct adult diagnostic assessments. The principles of diagnosis are the same as in childhood, and usually a parent, caregiver or sibling will be available to provide information about the patient's childhood development. An observation of the individual can also be conducted¹⁸⁶. When the UK's NICE body systematically reviewed the research evidence for which diagnostic tools are useful in an adult autism diagnosis, none of them reached a high enough standard of evidence to be recommended (<https://www.nice.org.uk/guidance/CG142>). Despite the lack of evidence, the NICE Guideline Development Group still recommended the use of standardised diagnostic tools that have been developed for children. Future research will likely focus on how these instruments can be adapted for adult assessment, as well as the development of adult-specific diagnostic tools.

Most autistic individuals who reach adult life without an autism diagnosis will have intellectual abilities in the typical range and may be living independently. When adults come for a diagnostic assessment it is important to take into consideration aspects such as mental health and addiction issues, self-neglect, relationship problems and exploitation or abuse by others. Evaluation of cognitive strengths and weaknesses, including IQ, may also be helpful when there is either a history of learning disability or frequent job losses that may be a consequence of specific impairments.

When autistic adults and family members were asked about their experiences of the diagnostic process, they reported a number of issues, notably in terms of the lack of confidence shown by professionals to support and refer them, the need to create clinic environments adapted to the needs of autistic people and the limited post-diagnostic support offered^{290,291}.

Gender differences

Recently there has been increased attention on the differences between males and females with autism²⁹². Historically there had been suggestions that females had more marked difficulties; however, recent data^{293,294} suggest that these findings were a consequence of under-recognition of more able females on the autism spectrum. In fact, newer studies suggest that cognitive abilities are similar between autistic males and females^{295,293}. The findings from the standardised diagnostic assessments used for children²⁹⁶ and adults²⁹⁷ are overall also comparable, although girls with higher IQs are less likely to meet diagnostic criteria on the Autism Diagnostic Interview – Revised²⁹⁶. It does seem, however, that females show less repetitive and stereotyped behaviours in childhood and fewer externalizing and social problems than males²⁹³. Additionally, some girls and women report conscious attempts to fit in, either by copying the behaviours of non-autistic peers or by actively masking autistic traits²⁹⁸.

Interventions

Early interventions

In the context of meeting the needs of autistic individuals, there are many strategies, approaches, therapies, and psycho-educational programmes²⁹⁹. In fact, the website ‘Research Autism’ has evaluated over a thousand interventions in the field of autism¹¹. Many of these programmes employ a mix of behavioural, developmental and educational approaches, with the goal of enhancing cognitive, communication and social skills whilst minimising behaviours that challenge.

The definitions, criteria and classifications of these approaches have been categorised in different ways in the literature²⁹⁹. Comprehensive Treatment Models focus on many areas of development and on improving functioning across multiple domains. Examples include Early Intensive Behaviour Intervention (EIBI), or Social Communication Emotional

Regulation Transactional Support³⁰⁰. Developmental and educational programs include, but are not limited to, daily life therapy³⁰¹, the Denver Model³⁰², Floortime³⁰³, Son-Rise³⁰⁴ and TEACCH³⁰⁵. Some Intervention Packages cover fewer areas of functioning and behaviour. These include peer training and social skills packages. Focused Intervention Packages, on the other hand, target very specific skills in areas of functioning such as play, cognition, or behaviour. These include communication interventions, such as the Picture Exchange Communication System (PECS)³⁰⁶, and those that target early interactions between parents and children, such as Early Bird³⁰⁷ and Pre-Linguistic Milieu Therapy³⁰⁸, amongst others.

Applied Behaviour Analysis (ABA) encompasses a range of behavioural approaches in autism. Early Intensive Behaviour Intervention (EIBI) is largely based on ABA principles and is one of the most common used treatments for autistic children according to surveys of parents and service providers³⁰⁹. ABA is also the most comprehensively studied treatment model in research³¹⁰. This is partly due to a study by Lovaas³¹¹, which subsequently stirred much debate. Experimental studies in which different programmes for early intervention have been compared, have produced mixed results. Some studies have concluded that EIBI is an effective intervention, and that the average effects of EIBI appear to be strong, with increases in IQ and to a lesser degree in adaptive behaviour³¹⁰. Magiati et al³¹², for example, reviewed EIBI approaches, and found evidence that these are generally more effective in supporting the development of cognitive, language skills and to some extent adaptive behaviours than eclectic approaches. Eclectic approaches draw on a range of different strategies, approaches and interventions and implement them differently according to the needs of the individual child (Guldberg 2010). Other studies have reported limited or no clinically significant benefits to EIBI approaches compared with other forms of provision such as specialist nursery provision³¹³. Interventions that used EIBI techniques have been shown to be successful in teaching specific skills for some children, such as joint attention and play-related skills²⁹⁹.

Although studies have highlighted that EIBI appears to be effective for some children and in relation to specific domains, numerous studies have concluded that no treatment has been effective for all children³¹⁴. There are a number of reasons to why it is difficult to make strong claims about a specific intervention or educational programme³¹⁵. Firstly, reviews indicate that there is variation in inclusion criteria, inconsistencies in the actual intervention that is being implemented, different independent variables

being evaluated and a variety of research designs³¹⁰. There are also many variables that can influence outcomes³¹⁶. Secondly, very few studies have measured long-term effectiveness (after 4 years) and there have been no follow-up studies in adulthood. A further challenge relates to the fact that most research studies are based on efficacy studies in clinical settings using experimental research designs³¹⁷. Implementation in Early Years and school settings has been limited³¹⁸.

Moreover, within all comprehensive interventions, large individual differences are reported with wide variability in response to treatment³¹⁴. As individuals on the autism spectrum are very different from one another in terms of their profile of needs and strengths, variation in individual characteristics mean that more individualised approaches are often needed than can be delivered using manualised approaches³¹⁰. Families are also different in their aspirations, goals and personal qualities. Much more research is needed into factors related to family, child and intervention factors that moderate outcomes³¹⁸.

Research has nevertheless highlighted the potential value of interventions that focus on broader areas of development (such as communication and social understanding) rather than on specific skills. Many autistic children will have language delay and have limited nonverbal communication in terms of their use and understanding of gesture, facial expression and body language, for example³¹⁹. They often have delayed joint attention, do not point, and gaze-following is often absent or infrequent³²⁰. Crucial areas to focus upon therefore include communication and language that help the individual to function in day-to-day life, social understanding and joint attention, peer interaction and play³¹⁹. Research focusing on teaching early communicative behaviours (e.g. joint attention) could offer potential for the later development of social and communication skills and show promise regarding efficacy and outcomes for the child³²¹. Studies have shown that when parents interact with their children in ways that motivate, encourage and support their child's communication, they can make a significant difference to their child's social and communication development³²². Furthermore, early intervention approaches that directly target joint attention, imitation and play abilities appear to support the development of language and social skills for these children³²³.

The SCERTS® Model (Social Communication, Emotional Regulation, Transactional Support) is a person-centred comprehensive model focused on the critical priorities of developing communicative and socio-emotional

abilities³⁰⁰. It provides a framework for selecting educational objectives that are meaningful to the child and family, promotes the importance of parents and carers as social partners central to their child's development and coheres the educational team around the child³²⁴. Studies that have taken place so far have been promising. These include two randomized controlled studies showing significant effects on the participating children's social communication, adaptive behaviour and developmental level, and that interventions that focus on communication and joint social interaction can have a significant and positive impact on children's general functioning^{325,318}.

However, the process of deciding on an intervention is more complex than the results of individual research papers can tell us. This is because the choice of intervention needs to take into account the child's characteristics, parental preference, staff expertise and the goals selected³²⁶. While a diagnosis might give a signpost to the needs of a child on the autism spectrum, the identification of those needs should arise from a thorough assessment of the child and discussion about how best to address these with their parents and the services involved⁹. Interventions and approaches need to be tailored to meet the unique characteristics of each person³²⁷.

Expert views therefore indicate that a range of approaches is needed in order to suit individual needs and preferences. Guidelines from the National Institute of Clinical Excellence (NICE) in the UK point to the importance of making adjustments to the social and physical environment, to support families, and to focus on the development of life skills (<https://www.nice.org.uk/guidance/cg128>). The NICE guidelines pinpoint that interventions need to be developmentally appropriate, that there should be a focus on increasing the understanding of caregivers, teachers and peers, and on anticipating and preventing behaviours that challenge. They also emphasise the importance of enabling environments, augmented communication, person and family-centred work, as well as collaborations and multidisciplinary work (i.e. professionals from different backgrounds working toward shared targets)³²⁸. There is evidence that an organised environment with visual cues can enable access to the learning environment. The importance of taking into account sensory processing difficulties and the social demands of working with other CYP has also been emphasised.

Interventions for adults

Despite the fact that the outcomes for autistic adults (e.g. in employment, accommodation) are reported to be frequently negative and needs are great^{329,330,331}, there has been very little intervention research conducted to alleviate these challenges. It has also been generally assumed, but is open to debate (see alternative opinions from Howlin³³² and Dawson³³³), that by investing greater resources in early intervention we allay the need for intervention in adulthood. This point is somewhat mute, however, given the growing number individuals who were missed in childhood and are receiving a diagnosis as adults.

When the UK body NICE conducted a review of the adult autism intervention literature, the quality of research was found to be very limited¹⁸⁶. The NICE team looked at interventions for communication, self-help and independence skills, and social learning programmes but because of the weakness in evidence they needed to fall back on the recommendations of experts. The suggestions put forward by NICE included the use of programmes to train social skills³³⁴, leisure activities that build on the interests of the individual³³⁵ and programmes to manage anger and behaviours that challenge (see earlier section on behaviours that challenge and PBS). There is also limited research on the use of medications in adult autism populations. Most recommendations are based on studies of autistic children and non-autistic adult populations¹⁷⁶.

In terms of service use, there are different experiences depending on the autistic person's level of IQ and how services are configured within the country or region in question. For example, the 2009 UK National Audit Office report *Supporting People with Autism Through Adulthood* (<https://www.nao.org.uk/wp-content/uploads/2009/06/0809556.pdf>) estimated that around 200,000 autistic adults with no intellectual disability were not receiving services because of limited availability. Autistic adults with a typical or middle range IQ often “fall through the cracks” in terms of accessing diagnostic and support services. As a consequence, they are less likely to be active in their daily lives³³⁶, which may lead increased mental health difficulties and pressure on services³³⁷.

Technology

Given the ubiquity of technology at home, in schools, hospitals and on one's person, it is understandable that the last fifteen years has seen a significant

increase in the amount of autism technology research³³⁸. One reason why technology and autism has been of particular interest is the belief, with some evidence, that autistic people especially enjoy and may have an affinity with technology that may not be seen so readily in non-autistic people^{339,340}. This may also be reflected in the finding that the prevalence of autism is higher in regions where there is a larger number of people working in the IT field³⁴¹.

Autistic children show a preference for using non-social media (such as video games or television) than social media³⁴² and their excessive playing of video games is reported as a problem by parents³⁴³ and may impact on the quality of their child's sleep³⁴⁴. The preference shown by autistic children for using non-social media may in part be related to an increased risk of cyberbullying³⁴⁵ and, as with all people who may be more vulnerable to the risks of engaging online, additional support may be needed. Guidance on this issue has been developed by UK Charity Cerebra³⁴⁶.

There have been a number of challenges for the technology and autism research field, including the quality of study designs and lack of randomised control trials³³⁸. It has also been challenging to match the expectations of technology users, researchers and developers³⁴⁷ and there have been concerns as to whether individuals will generalise learnt skills to "real-world" situations³⁴⁸. The growing belief that technology has an important role to play in transforming the lives of autistic people has not just been seen in the increase in research output but also the adoption of technology tools in educational settings³³⁹ and the interest of large companies (e.g. Samsung)³⁴⁹.

A range of technologies have been tested in the technology and autism field, including virtual reality, robotics, wearable devices, mobile technologies and apps, telemedicine and training, computer programmes, virtual agents and the application of medical technology (see^{338,350,351}). These technologies have been tested in different environments (e.g. school, workplace, home) with a number of beneficial outcomes reported, including in social cognition³⁵², communication³⁵³, planning³⁵⁴ and emotional health³⁵³. An important feature of autism technology research has been the focus on the need to include a range of opinions (e.g. end-users, engineers and researchers) in the successful design of tools^{356,357}.

A meta-analytic review of technology-based intervention studies³³⁸ reported an effect size (akin to the strength of evidence) of 0.47 (0.3 is a medium effect and >0.5 a large effect). This effect was seen independent of the age or IQ of individuals tested. The authors of this review argue for the need to grow this field of study, improve the quality of research

methodologies and recommend that technology can be a future tool for intervention. Nevertheless, there have been few research studies that have demonstrated efficacy for a technology and then moved that product into homes or services. One example, of where this has been achieved is the Transporters DVD to help children recognise emotions³⁵². Another example is TeachTown: software to instruct pupils through a curriculum to develop language and cognitive skills³⁵⁸. Unfortunately, it is the case then many of the technology solutions available for autistic individuals and families have been developed by companies, not researchers, and come with almost no research evidence.

Pharmacology

A large-scale study in the US of autistic children reported that 56 % were using at least 1 psychotropic medication and 20 % were prescribed three or more³⁵⁹. In the same study almost a fifth of children in the 0–2year old range were prescribed medication, with the most commonly prescribed drugs being neuroleptics, antidepressants and stimulants³⁵⁹. Studies of autistic adults have also shown very high prescription rates (60–80 %) ^{360,261}. A US longitudinal study found that individuals were not coming off medication as they aged but instead rates increase from adolescence into young adulthood³⁶⁰. A worrying trend is the frequency of multiple medications being prescribed, with little knowledge of how these medications work in combination³⁶².

Despite these high rates of prescribing, when autistic people and parents are asked about medication use they often report feelings of reticence to take them or previous negative experiences³⁶³. Wallace et al³ found that half of autistic adults and a third of parents in the UK disagreed with the statement “I would choose to use medication to reduce the difficulties associated with my/my child’s autism” and almost two thirds of autistic and parental respondents expressed concerns about using medications. The typical concerns reported were regarding the negative side effects and the lack of beneficial effect³. As a result of these concerns, and the lack of research evidence, there is an increasing emphasis in autism guidelines to explore behavioural and therapeutic approaches prior to prescribing medications^{186,284}.

Many of the drugs that are prescribed have not been tested with autistic people but have been shown to be effective in other populations and repurposed for use in autism³⁶⁴. This obviously raises concerns about

the safety and suitability of using these medications with, often very young, autistic people. Most of the pharmaceutical efficacy research in autism has been with children and young people, whereas adults, the intellectually disabled and those with co-occurring conditions are often excluded from treatment trials¹⁷⁶. Therefore, the field is in a position where there are no medications recommended for core symptoms of autism. Risperidone and aripiprazole are recommended for some behaviours that challenge and there are medications recommended for use with specific co-occurring issues (e.g. melatonin for sleep and methylphenidate for ADHD symptoms). Clinicians are encouraged to explore non-pharmacological options first, consider the adverse effect profile and review prescriptions on a regular basis¹⁷⁶.

Education and adult services

Schools and higher education

In autism education, current debates emphasize the need for educators to ground their work in evidence-based practice (EBP)³⁶⁵. However, the notion of EBP is complex in the field of autism, where there are a number of possible interventions and different theories about autism. Although the field has made attempts to identify the evidence base for different educational models, there remain real difficulties in implementing interventions in naturalistic environments³¹⁷. Reasons for this include that there are barriers to effective implementation of different psycho-educational interventions. These barriers include the fact that those implementing the interventions need high levels of training, interventions can be intense and they tend to require high ratios of staff to children³⁶⁶. In addition, they are rarely implemented in the way they are designed³⁶⁷, and do not take into account the school context³⁶⁸. Practitioners rarely alter their practice by drawing on the evidence base from research³⁶⁹ and many continue to use practices that are unsupported by research³⁷⁰. Educators tend to be more interested in the needs of individual children³⁶⁷ than in EBP. There is therefore a disparity between what the research evidence may prescribe and what happens in practice³⁷¹, policy or service provision. Given that long-term educational and work-related outcomes for individuals with autism are poor, practical solutions for education and life skills are clearly needed.

As a result of this, the need to move EBPs into daily educational practice for learners with autism has been identified as a research priority³⁷¹.

Educational researchers have highlighted that there has been a notable lack of empirical evidence to inform practice and policy with regard to what ‘best practice’ means in real-world classrooms and how effective and appropriate practice can best be achieved for autism-specific schools and services. There is therefore a need to build a stronger evidence base regarding what good teaching is within the context of each individual setting and how it leads to learning³⁷². This includes developing better insights into how teachers view good teaching, as well as how they eclectically sample from a variety of instructional or teaching models³⁷³. There is also growing recognition of the need for interventions to be tested in the settings they will be delivered³⁷⁴.

In fact, the range of sources when developing good autism practice in classrooms needs to include the perspectives of autistic pupils and their families, practitioner experience, research, school data, and the views of stakeholders³¹⁷. Studies have indicated that good autism practice should be based on the integration of the best available research and practitioner expertise within the context of a pupil’s individual characteristics, as well as cultures, values and preferences³¹⁴. Such an approach starts with the individual and what is best for the pupil and their family, takes account of the context and looks at the evidence for different approaches whilst integrating consultation with autistic pupils and their families⁹.

As autism is a complex condition which impacts daily functioning, pupils with autism require specialised supports and assistance to be successful in their local schools. Many autistic pupils will be educated in mainstream schools. In these settings, teachers often apply their knowledge of general education to autistic learners, rather than basing teaching on the needs of the autistic learners³⁷⁵. A number of studies have suggested that a lack of autism knowledge in teaching staff can negatively impact on the school experiences of autistic children and their opportunities to succeed³⁷⁶. Yet in the education of autistic pupils, full inclusion in education relies on staff having knowledge of the specific needs of pupils with autism as well as the distinctive teaching approaches, tasks and outcomes that are important to take into account³²⁷. There is therefore a need to increase school practitioner’s knowledge of appropriate educational practices in autism and also do so in culturally sensitive ways.

A consultation with teachers about strategies for creating an effective inclusive environment identified a number of key recommendations from staff. These include more resources and greater training; teaching

methods tailored to each child; greater teamwork within the school; building a rapport with the autistic child; and whole-school awareness of disability and acceptance of differences³⁷⁷. The design of classrooms is particularly important in terms of enabling learning and modifications to the environment may be related to the frequency of behaviours of concern³⁷⁸ and increased participation³⁷⁹. Guidance on elements to consider when designing a school or classroom include proper placement of the visual timetable, reducing visual distraction and controlling lighting, as well as using a space to create a sense of calm, a quiet space and adequate storage³⁸⁰. The opinions of Children and Young People (CYP) on the autism spectrum are imperative when considering school design.

Given that the variety and extent of profiles of autistic pupils is notable³¹⁴, it is crucial that educators individualize assessments of the CYP they work with in order to identify a profile of relative strengths and weaknesses that can inform educational programming³⁸¹. This should include assessment tools that can measure wellbeing and family quality of life³⁸². Jones et al⁹ found that researchers, policy makers and education staff need to know more about how to effectively consult with children and young people, in particular those with significant learning or communication difficulties⁹. Practitioners need to ensure pupils on the autism spectrum are effectively engaged in decision-making and in planning for after the school years. Further exploration is also needed of the implications of ‘strong interests’ and how these affect learning interactions³⁸³. Wood³⁸³ found that CYP with autism benefitted from being able to pursue their interests. These benefits included improved communication, greater independence, and better motor skills.

All cultures, races, ethnicities and genders are represented within the population of pupils diagnosed with autism. These factors influence both the expression of autism in individuals and also the educational needs of the population. Research on the needs of culturally and linguistically diverse pupils with autism and their families has found that minority populations are underrepresented in research studies (see³⁸⁴). As a consequence, there is little understanding of how different cultures and beliefs influence the unique educational needs of autistic pupils from diverse backgrounds³⁸⁵. In addition, culturally and linguistically diverse families find it difficult to access the information, help and resources they need and to navigate the education system³⁸⁶.

Recent research on the implications of gender on autism indicates that females often do not receive accurate diagnosis or appropriate supports in

educational settings³⁸⁷. This can lead to different school experiences and decreased school engagement³⁸⁸. The last few years have seen an increase in studies of gender identity and gender self-esteem in autism. It has been found that autistic people identified less with a gender group and perceived specific gender more negatively compared to non-autistic individuals³⁸⁹. There is also some evidence to suggest that autistic females have higher masculinity and lower femininity compared to non-autistic females³⁸⁹. It is important for educators to be aware of the rights of an autistic person who changes how they identify their gender and assist others in understanding this aspect of their life³⁹⁰. Friendships and peer relationships are a way to promote social and emotional development³⁹¹. This is crucial as pupils on the autism spectrum may have the lowest rates of friendships compared to both non-autistic children and other disability groups. They meet friends less outside of school and friendships are not maintained beyond school³⁹². The evidence for promoting social interaction is strong, and beneficial effects of this generalise to other areas as well³⁹³. However, it is important to note that the majority of this research is conducted with individuals in mainstream settings³⁹⁴.

Pupils on the autism spectrum experience a higher frequency of bullying than non-autistic peers³⁹⁵. Pupils who are included in mainstream settings without specialist support, who show a high number of autistic traits and co-occurring difficulties are at the highest risk of experiencing bullying³⁹⁶, as are those CYP on the autism spectrum who are seeking out social interactions³⁹⁷. Research indicates that education staff should receive training on how to reduce bullying³⁹⁸ whilst facilitating quality and lasting peer relationships. Attention needs to be focused on playground supervision, classroom management and being consistent in enforcing anti-bullying rules, as well as carefully restoring relationships between pupils when bullying occurs³⁹⁸. A comprehensive approach including peers, teaching and support staff and the broader ethos of the school are needed in order to support CYP on the autism spectrum who are experiencing bullying at school.

Given the mental health needs of autistic people, the curriculum for students on the autism spectrum should be diversified to work on emotional competence and mental health. Practitioner reports identify the need in schools to teach students on the autism spectrum about their emotional state and to use appropriate coping strategies, whilst promoting a calm, caring and positive whole-school environment³⁹⁹. This approach is aligned with the work of authors promoting the use of a low-arousal approach, as they

suggest that individuals on the autism spectrum have extreme reactions to their sensory environment⁴⁰⁰. Mindfulness is another technique that has been used effectively to help manage physiological stress responses to daily challenges⁴⁰¹. There are a number of classroom strategies and technology tools (e.g. Brain in Hand) that students on the autism spectrum can use to identify and regulate their emotional state⁴⁰² but there is little research currently on the effectiveness of these approaches.

Practitioners and parents can find planning transitions (such as between home and school, from setting to setting and from school into adult life) with young people on the autism spectrum stressful, with the lack of future options often being their greatest concern⁴⁰³. This highlights the need for transition planning and the importance of multi-agency working to lead to improved outcomes for autistic adults^{403,404}. More could be done in preparing students for leaving education. The lack of employment support and options has been shown to be a significant worry⁴⁰³. Research shows that some of the strategies to assist with person-centered planning for transition include adapting communication, building a rapport, individualized preparation for meetings and adjusting the meeting design⁴⁰⁵. Parent reports of their children's transitions to secondary school suggest that there are a number of factors that impact on how successful this is. This includes the parents' level of anxiety, the quality of their social experience and the level of support they received⁴⁰⁶.

In countries where there has been a broadening of the autism spectrum, there has also been an increase in the number of autistic people attending further and higher education institutions^{407,408}. Research focussed on the experiences of autistic students has been consistent in highlighting the challenges in terms of the social, academic, environmental and organisational pressures^{409,410,411} as well as the risks of significant mental ill-health issues and failure to complete courses as a result of a lack of support^{411,412}.

Research has identified a number of key issues autistic students who are in Higher Education report (see⁴¹²). By giving clearer instructions, breaking tasks down and assisting with planning, lecturers can support students in overcoming difficulties in planning, scheduling and organisation. Academic pressures can be addressed by flexibility with deadlines, extra time with exams and alternatives to group tutorials. Communication issues can occur in busy lecture rooms or when an autistic student is stressed, which can be addressed by asking the student his/her preferred means of communication

and checking that instructions have been understood. Sensory sensitivities can be managed by discussing with the student their particular needs and conducting a sensory assessment of the teaching or living environment. Those students who are living away from home can be supported with independent living, self-help, cooking and financial management. Lastly, for those students who are interested in socialising, strategies can be explored in terms of peer support, mentoring and facilitating access to clubs and societies (an important way to meet likeminded individuals). Before a student completes their course of study, plans should be put in place to transition out – including career advice and facilitating work experience. Mentoring, where a trained individual provides guidance and support to access academic, social and daily living activities, has been used in some educational settings to good effect⁴¹³ and a more structured programme of support has been delivered at one US university to guide autistic students about social life, navigation around campus, time management, hygiene etc.⁴¹⁴.

Employment

Rates of employment in autism are low and are not improving over time³³⁷ (see UK NAS campaign *I'm not Unemployable, I'm Autistic*). When asked, autistic young people and autistic adults both have a strong desire to be employed^{404,415} and studies have shown that employment leads to improvements in quality of life and a sense of independence^{416,417}. Furthermore, there are significant benefits for employers, given that supervisors who work with autistic people report them to be methodical, punctual and working to a high standard⁴¹⁸. Increased employment will alleviate the significant economic costs associated with autism in adulthood (see the earlier section on economics and autism). Therefore, not supporting adults on the autism spectrum into work would seem to be a lost opportunity all round.

There are many stages of the employment process that can be challenging for autistic people, from organising themselves to complete job applications, having the self-confidence to apply, “performing” in interview situations, transitioning from one stage of life to the next, dealing with the new work environment and managing the social pressures of being with colleagues⁴¹⁹. Autistic adults are more likely to switch jobs because of issues with the new environment, undertake employment that is different from their training, receive lower incomes than non-autistic peers and have lower job satisfaction^{329,420,421}.

When asked about their employment prospects, young autistic people spoke positively about getting a job but requested that employment was based on their aspirations and strengths⁴⁰⁴. Recommendations are that schemes to support employment should provide help with writing CVs, explore opportunities for work experience, focus on individual strengths, prepare the employee with training and support, train employers to make reasonable adjustments to the work environment and continuation of support after starting a new job¹⁸⁶. Mawhood and Howlin⁴²² looked at the outcomes from a supported employment programme in London and found that compared to autistic individuals who didn't have vocational support, trainees were more likely to find employment, their jobs were of a higher quality, they maintained work and had higher wages. Reviews that have looked at employment programmes for individuals with an ID or behaviours that challenge have recommended supported employment (in the open job market) over sheltered workshops^{423,424}, based on greater financial compensation, social inclusion and impacts on esteem.

Although most studies have looked at the experiences of diagnosed autistic people, there is a larger number of undiagnosed autistic adults currently in work who may be struggling with the social and occupational demands. Some of these individuals may be referred to services because of their deteriorating mental health or they may have experienced a crisis situation at work and there has been a recommendation for them to go to an autism diagnostic assessment. Given research has suggested that autistic people may be more likely to undertake STEM (science, technology, engineering and mathematics) subjects⁴²⁵, future research may look to explore the benefits of “light touch” social and emotional support for all staff within these companies.

Social care

The UN Convention on the Rights of Persons with Disabilities⁴²⁶ specifies that dignity, autonomy and freedom to make choices should be central to the lives of disabled people. Progress has been made as a result of this UN Convention but there have been significant challenges in the field of adult learning disability social care (e.g. the UK Winterbourne View scandal), including how staff are recruited and trained, how services are commissioned, safeguarding and clinical governance⁴²⁷.

Social care services are those that provide personal care, protection or social support services to adults in need or at risk (e.g. Social Care Act, UK).

The estimated prevalence of autistic adults in residential learning disability services is between 23–50 % depending on the study and among users of mental health services for people with learning disabilities it is 38 %⁴²⁸. One of the reasons for such a high proportion of autistic individuals in these services is the association between autism and behaviours that challenge⁴²⁸. For those autistic adults attending non-residential intellectual disability services, parents have called for more autism-specific interventions and activities that engage their children's interests, as well as staff trained on how to work with autistic adults⁴²⁹.

Recent years have seen an increased awareness that there is a growing elderly population with autism and that there is a need to make adjustments to their health and care needs⁴³⁰. Consideration needs to be given to how older autistic people understand the world around them as patterns of cognitive decline appear to be different in autistic and non-autistic populations⁴³¹. There are a range of psychiatric and health conditions that elderly intellectually disabled individuals experience but symptoms are often missed and treatments not available⁴³².

Research is lacking in terms of demonstrating evidence for interventions or supports in social care settings and much of the recommendations have focussed on practical guidance to manage behaviours that challenge¹⁸⁶. Positive Behaviour Support (PBS) interventions grew from a growing recognition that many behavioural approaches to manage behaviours that challenge were ineffective and used aversive techniques⁴³³. Despite there being a limited amount of research in social care and autism, there have been a number of reviews that have concluded with practice recommendations for staff working in the intellectual disability field (see⁴³⁴). Two areas that are consistently recommended are the importance of autism-specific provision within social care services and the need to upskill staff so they understand the specific needs of the autistic individuals they work with⁴³⁴.

Advocacy and ethics

There is increased recognition of the importance of grounding practices and research in the lived experience of autistic people⁴⁰⁴ as there is a huge gap between the type of knowledge being produced by current autism research and the stated priorities of the autism community²². There is increasing recognition amongst researchers that autistic people and their families are not sufficiently involved in making decisions that shape their lives⁴³⁵ and should be involved in identifying research priorities²². Many autistic people

have expressed frustrations at the current research landscape. They state that they are often passive participants in research and are ‘frequently frozen out of the processes of knowledge production’ (Milton and Moon⁴³⁶ p. 794).

This highlights the importance of research, services and practitioners becoming better at developing ‘interactive expertise’ in caring for and working with autistic people, as well as becoming ‘more able to engage and interact with autistic language and communications’ (Milton¹¹ p 796). The autism field needs to draw on the experiences of autistic people, as well as on the research evidence so that a positive relationship between research, the perspectives of autistic people and practice is generated³⁶⁸.

Although the last ten years have seen a growing recognition that strengths and differences associated with autism are central to a person’s identity⁴³⁷, there is still a need to develop knowledge about how to meaningfully consult and involve individuals on the autism spectrum around lesson planning, approaches and learning what they want to achieve in terms of outcomes from education⁴⁰⁴. More broadly, the voice of autistic people should be central in terms of the successful design and delivery of services^{317,438}. Positively reframing thinking around autism can help autistic individuals and their parents manage their difficulties and provide a more resilient outlook of what is ahead⁴³⁹.

What does the future hold?

The last 10–15 years has seen an increase in the amount of research funding for autism and increases in research outputs, but we still remain in the dark about a number of key questions and have not developed definitive models of support and intervention. It is likely that the voice of autistic people and their parents will be important in holding funders to account in terms of how research investments are spent, and they will increasingly lead the research agenda. It remains unclear as to whether there is an appetite for funders and the community at large to continue investing heavily in autism research for another 10–15 years unless outputs have clinical, educational or practical relevance. One can imagine that the current research trend to detail the specific health, educational and adult service needs of autistic people will continue and service delivery will be built around these areas of need and their effectiveness researched.

In terms of the biology of autism, researchers have expressed some certainty about what may cause a small percentage of the autism population

but this could be regarded as the low hanging fruit. The more complex task will be to understand how the likely numerous genes for autism interact both with each other and with environmental factors in generating an individual's specific type of autism. For those genes or microscopic structural genetic differences that seem to increase someone's chances of being autistic, we still know very little about how they function, and whether being a "carrier" always equals autism, or how and why de novo (non-transmitted) genetic events occur. Given the complexity of the autism phenotype and the overlap with other disorders, it is likely that identifying the genetics of autism will be an extremely arduous and costly task. The research community needs to be clearer as to what the ultimate goals are and how they fit with the priorities of autistic people and their families. One can imagine that the significant sums of money spent on genetics research with limited success may lead to a shift in the emphasis of research toward environmental causes. However, in this field we currently have a growing number of association studies (correlating factors) and too few models of causation, which is imperative if this area of research is to be successful.

Genetics of autism research suggests that many putative neurobiological differences are at the cellular level⁴⁴⁰ but the technologies we currently use in humans visualise many thousands of cells (e.g. MRI). There has been a recent initiative to organise the collection of brain tissue of deceased autistic people (Autism BrainNet), which allows us to investigate differences at a cellular and molecular level, but it remains to be seen whether this initiative will lead to large enough collections of brain tissue. There are consortia actively looking to increase the sample size of brain imaging cohorts but these researchers are still to report on their success in identifying sub-types based on a profile of brain structure (see⁴⁴¹). For many researchers the ultimate aim is to develop personalised medicines based on neurobiological and genetic markers but there is little evidence to suggest that autistic people and families have an appetite for this approach³, with concerns centred around what behaviours are being targeted and side effects, as well as a preference for behavioural interventions. Additionally, designing drugs for which there may be only a tiny market is likely to not be economically viable.

Large-scale genetic, neurobiological and phenotypic data collections have not produced the answers they originally promised but these efforts continue to be funded (e.g. Simons Foundation's SPARK⁴⁴²). One goal is to identify genetic and neurobiological markers that could be used to assist in

the early detection and diagnosis of autism. Given the state of the science, the complexity of the autism spectrum and the accompanying noise in many datasets it is likely that well-trained clinicians working from behavioural descriptions will continue to be the mainstay in clinical practice, but this is a fast-moving area of research that needs to keep pace with technological advances.

Early intervention research has seen a significant uplift in funding and data from a larger number of more methodologically rigorous interventions have been published. Nevertheless, there remain a number of key issues that need to be addressed in the future. Firstly, the sample sizes of these studies need to be larger as to date they lack the statistical power to demonstrate reasonable effects given the heterogeneity of the autism spectrum. Secondly, there needs to be more independent replication studies as too often those who are authors of the intervention are also conducting the research study. Thirdly, we need good outcome measures or expert consensus on what intervention studies should be aiming to achieve. Fourthly, there needs to be greater investment in longitudinal research of the potential benefits of early intervention. Fifthly, there need to be more effectiveness studies (how the intervention performs in community settings by regular staff) than efficacy studies (conducted in controlled settings often by extremely well-trained staff). Lastly, the ultimate aim for many researchers will be to know why some autistic children respond well to some interventions and others do not, so that we can tailor interventions to children with specific profiles.

As has already been stated, autistic people and their families prioritise research to focus on services across the lifespan (health, education and adult services) but this is an area which comes with specific challenges in conducting research. Forming partnerships between academics and service providers has been identified as an area to develop agreed research programmes and to deliver meaningful research for specific settings. Knowing what service design is most effective for local populations will be extremely important as well as which are the most cost-effective. Autistic children spend most of their formative years in education settings and not intervention services but we are still not certain about how effective the mixture of approaches used in schools is. Much has been done to capture our understanding of best practice in service delivery but future research may want to look at the impact that disseminating this has had.

Despite a welcome recent shift, a very small proportion of autism research focuses on the needs of adults. Four broad research areas stand out in terms

of future focus. First, the strong associations between autism and diverse co-occurring mental health conditions is now well documented. Arguably it is the association with anxiety disorders that causes the greatest overall impact on individuals and families. Secondly, success in higher education or the workplace still eludes many autistic adults. Both entry into higher education and graduation rates are relatively low compared to the general population and there appear to be multiple barriers to employment, but little guidance from the current research literature as to which of these deserve most attention. Thirdly, adult relationships are protective for both psychological and physical health but in the context of autism, we simply do not know the number and quality of extra-familial relationships that are sufficient for good health. Lastly, there is a growing number of elderly people with autism and it remains to be seen whether they show an atypical pattern of cognitive decline that requires specialised healthcare planning.

There are a number of under-researched areas that need addressing in the future, as well as emerging research trends. Firstly, the intellectually disabled are often not included in research despite the fact that in many countries they still make up the largest proportion of the autism population. Within this population, more research needs to focus on genetics, overcoming diagnostic challenges, ways to include them in research design and how to manage their own and their parents' end of life care. Secondly, gender and autism has been an area of interest for a while and future research may look to focus on how to overcome identification and diagnostic challenges, whether autistic females have adaptive skills not seen in males, the relationship with co-occurring difficulties (e.g. anorexia nervosa) and differences in forming and maintaining relationships. Thirdly, there is emerging evidence of different prevalence rates in migrant populations and of there being cultural differences around beliefs about autism and access to services. As migration becomes more commonplace and a political hot topic, how to safeguard these populations should be a research priority. Fourthly, epilepsy in autism is still common but we know very little about its nature, there are no recognised autism-specific assessment tools and it is a major cause of early death; hence, it should be a priority in terms of clinical management. Fifthly, autistic people and parents have asked for better mental health services and in particular help with anxiety, so researchers need to develop autism-specific diagnostic tools and individualised interventions. Sixthly, research has shown higher rates of gender dysphoria (identifying as a different gender to the one assigned at birth) in autistic

young people⁴⁴³. Future research will need to investigate whether similar patterns are seen in autistic adults and what combinations of cognitive, hormonal and environmental factors are at play. Lastly, during a long period of austerity for much of the world's economy, what has been the impact in terms of access to autism services, irregular staffing and cutbacks to provision.

As the prevalence of autism has increased, so autism has figured more in the minds of society and politicians. Compared to twenty or thirty years ago, autism in many countries now features regularly in the media. Annual campaigns (such as the UN designated World Autism Awareness Day) are a way of bringing the community together, many governments and international organisations have strategies on autism and the voice of autistic people is central in reframing our thinking. One can only hope that increased awareness and acceptance of autism will continue and that countries from emerging economies will be the ones that see the greatest advances. Researchers have a role to play in partnering with and supporting these countries as they begin to conceptualise autism and look to develop suitable interventions and systems for training⁴⁴⁴. Partnering with countries of emerging economies may also allow researchers to ask specific questions that they may not be able to pose elsewhere (e.g. the high level of within-family marriage in the Middle East⁴⁴⁵) and increase the scale of data collections in highly populated countries. Broadly speaking, research has not focussed on the role that society plays in negatively impacting autistic people and its potential for improving their lives. The research community can look to reframe its own message so that there is a greater focus on the positive contributions autistic people make and what has in the past been regarded as a deficit or a problem can in the future be seen as part of the lived experience of being autistic.

Conclusion and recommendations

The last fifteen years will be seen as a period of significant growth in the autism research field, with greater funding and autism becoming a priority for many institutions. There have been advances in our understanding but other than a small number of examples there has been little impact on practice or improvements in the welfare of autistic individuals and families. Researchers have become energised to advance the field but there has been a lack of clarity in terms of what they are trying to achieve and what is achievable. There have

been significant challenges, not least the heterogeneity of individuals who share an autism diagnosis, but there has been a need for greater coordination of resources, agreement around long-term objectives and management of progress.

In many ways autism research can be seen as being at a junction. The lack of definite answers to many research questions has led autistic people, families, funders and members of the research community to reappraise what the objectives of research should be. There is a sense of impatience with the length of time research takes to affect lives and also that many promising research leads do not come to fruition. The response has been for autistic individuals and their families to become more vocal about the direction of research, which has already begun to result in more practice-focussed research and autistic individuals shaping research programmes.

Autism research has historically been focused in the US and Europe. The efforts of organisations such as the International Society for Autism Research and the World Health Organisation has meant that many more countries have become involved in the field. Extending collaborations beyond traditional borders will mean that the pace of research will increase and we can share experiences of how services are delivered in a broader range of contexts. These new emerging trends in terms of priorities and partnerships, and the continuation of significant funding, presents positive opportunities for autism research in the coming years.

Recommendations that have come from this review include:

1. There should be a shift in priorities to fund research that will provide practical benefits for autistic individuals and their families. This may include more effectiveness research (how interventions work in the settings they were intended for), more partnerships between researchers and practitioners (health and education) and creating research infrastructure (e.g. clinical networks of paediatric services) where research outputs can be tested and scientific findings can be disseminated.
2. Strategic planning for research should be improved. Initiatives like the Interagency Autism Coordination Committee (<https://iacc.hhs.gov/>) in the US should be more common, so national stakeholders (including government agencies) can agree on long-term strategies. Monitoring long-term objectives should be properly managed, a consensus should be reached on what “success” looks like and long-term funding secured.

3. There are groups of autistic individuals who have been under-researched and should be a priority for the future. The methodological barriers leading to autistic individuals with an intellectual disability being included less in research should be overcome. Autistic adults and females with autism should also be prioritised in research.
4. Co-occurring issues (in particular stress and anxiety) are a clear research priority for autistic individuals and families. Ways of optimising the mental and physical health of all autistic individuals and their families should be researched.
5. Autistic individuals and their families report a number of barriers to them being included in society. It is important that research continues to identify these barriers and produces interventions and guidance on how to overcome them. Science dissemination has a role to play in terms of accurately informing the public about autism and dispelling myths. Autism awareness training should be provided to frontline health staff working with children and adults to improve access to diagnosis. It will also be important for future research to identify those individuals who one would regard as having a successful outcome (e.g. employment, financial stability) and what factors helped them achieve this.
6. Much more research needs to focus on improving our understanding of autistic adults. Advances should be made in terms of diagnosis and providing interventions. Key research areas in terms of management include what social care interventions are most effective, evidence-based models of employment, support services in higher/further education and old-age/end-of-life care.
7. Technology, as with all aspects of modern life, has an important role to play in autism. This is a field where partnerships are especially important. Engineers, researchers, service providers and IT companies must work closely together and with autistic individuals to produce products that will be potentially transformative.
8. One of the factors that has helped guide and advance autism research has been the views of autistic individuals. It will be important to learn more about the lived experience of autistic people and our role as individuals working with them.



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