

INVITED REVIEW

The neuropsychology of autism

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Summary

In this review, we aim to bring together major trends in autism research at three levels: biology, behaviour and cognition. We propose that cognitive theories are vital in neuropsychology, which seeks to make connections between brain abnormality and behavioural symptoms. Research at each of the three levels is incomplete, but important advances have been made. At the biological level, there is strong evidence for genetic factors, although the mechanism is, as yet, unknown. At the behavioural level, diagnosis and education are becoming more coherent and less controversial,

although the possibility of autism subtypes has provoked new debate. At the cognitive level, three major theories are proving fruitful (mentalizing impairment, executive dysfunction and weak central coherence), although the relation and overlap between these is uncertain. Rapidly advancing technology and methodology (e.g. brain imaging, gene mapping), as tools of cognitive theory, may help to make autism one of the first developmental disorders to be understood at the neuropsychological level.

Keywords: autism; Asperger's syndrome; cognitive development; neuropsychology

Abbreviations: DSM = Diagnostic and Statistical Manual; ICD-10 = International Classification of Diseases; SPECT = single photon emission computerized tomography

Introduction

Neuropsychology is the study of how brain systems and pathways mediate behaviour. Cognition forms the natural intermediate level of description in this study, at once explaining behaviour and providing clues to the mapping between brain function and mental function. Autism, as a developmental disorder with a biological basis and a behavioural definition, serves as a model to put into practice the notion of cognition as the key element linking brain to behaviour. In order to structure our review and critique of the literature on autism, we shall use the three levels of description biological, cognitive and behavioural in the framework originally devised for autism, and subsequently applied to other developmental disorders (Morton and Frith, 1995). A full explanation requires causal links between the available facts at the three levels. With the discipline imposed by this framework a unifying cognitive theory of the biology and behaviour of autism may emerge.

Our aim in this review is to see how far we can take the available evidence in the direction of such an explanatory account. This forces an interdisciplinary approach which has

sometimes been missing in the field. Clinical work on autism has often ignored theories of normal development, neuropsychological accounts have tended to focus narrowly on single symptoms at the cost of the full clinical picture, and psychological accounts have frequently ignored biological research. Our review attempts to integrate some of this considerable body of work in order to examine possible neuropsychological conceptions of autism. We have not attempted to be exhaustive in our discussion of current work, and instead refer the reader to recent reviews of each area covered, as well as a comprehensive field review by Bailey *et al.* (1996).

Behaviour

Issues of diagnosis

Autism, although a biologically caused disorder, continues to be diagnosed on the basis of behaviour. Since its first description (Kanner, 1943; Asperger, 1944), there have been

various changes in the diagnostic criteria, with the emphasis on different clinical features shifting from time to time. However, the core elements of 'extreme isolation and the obsessive insistence on the preservation of sameness' (Eisenberg and Kanner, 1956), have remained the same and persist in diagnostic systems today. Specifically, the latest edition of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-IV; American Psychiatric Association, 1994) describes autistic disorder as 'the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interests' (p. 66). The main criteria for the diagnosis in DSM-IV (American Psychiatric Association, 1994) and in the International Classification of Diseases (ICD-10; World Health Organization, 1993) can be summarized as qualitative impairment in social communication and restricted and repetitive patterns of behaviour and interests. These features must be evident before 3 years of age, although diagnosis is often made much later.

Autism has formed a recognized diagnostic category since 1978, when it was included in DSM-III. This definition was based in turn upon epidemiological work which validated the clinical consensus that children with autism could be identified as presenting a coherent and consistent syndrome (Rutter, 1978). Following Kanner's first description and labelling of the disorder in 1943, autism (then also referred to as childhood schizophrenia or childhood psychosis), quickly became recognized as an important clinical entity in child psychiatry.

In the absence of knowledge of biological causes, and prompted perhaps by the normal physical appearance of these children, the first interest in autism focused largely on psychogenic explanations. However, psychological and epidemiological work in the 1960s and 1970s established autism firmly in the discipline of mental handicap studies (Hermelin and O'Connor, 1970), separating it from mental illness in general and from schizophrenia in particular (Kolvin *et al.*, 1971). With the finding of reliability in IQ assessments over time (Freeman *et al.*, 1985; Lord and Schopler, 1989), and the demonstration of widespread mental retardation (Lockyer and Rutter, 1970) and epilepsy (Rutter, 1970), the search for a biological basis for autism became respectable. This change of focus also allowed researchers to think of life-course and prognostic issues, and prompted follow-up studies which showed that autism persisted throughout adult life (Rutter *et al.*, 1967).

A major impetus to a reconsideration of diagnostic criteria was provided by Wing and Gould's (1979) epidemiological study. These researchers looked at the associated impairments of children with social handicap, and demonstrated for the first time that autistic disorder formed a true syndrome. The study introduced the notion of a triad of co-occurring impairments in socialization, communication and imagination, which marked out children already diagnosed by Kanner's criteria for autism, but also applied to a wider sample of children. This wider autistic spectrum included

not only children who were withdrawn or aloof (like many of Kanner's cases) but also children who showed their social impairment in unusually passive, or in 'active-but-odd', social behaviour. In the same way, the communication impairments may vary from muteness to inappropriate verbosity. Wing's triad formed the basis for the diagnosis as set out in DSM-III-R (American Psychiatric Association, 1987), and raised awareness that the manifestation of the social impairment in autism could vary with age and ability.

Prevalence

The first epidemiological study of autism, using Eisenberg and Kanner's (1956) criteria, estimated the incidence at four in 10 000 (Lotter, 1966) a figure for nuclear autism which has remained remarkably constant over the years (Wing, 1993). The wider spectrum of autistic disorders, taking Wing's triad as definitional, has a somewhat higher incidence, ~1 per 1000, and appears to be responsible for apparent increases in numbers of cases of autism reported in recent years (Gillberg and Coleman, 1992).

The sex ratio varies according to severity, with males more often affected, especially in intellectually unimpaired cases. Males outnumber females by 3 to 1 in nuclear autism, and by perhaps 5 to 1 at the more able end of the spectrum (Lord and Schopler, 1987). Although autism can occur at all IQ levels, three-quarters of individuals with autism also have mental retardation (i.e. IQ below 70), and autism is increasingly common as groups of lower IQ are sampled (Lockyer and Rutter, 1970; Wing, 1993). Epilepsy is present in approximately one-third of all cases, and a number of different medical disorders are occasionally associated with autism (Gillberg and Coleman, 1992). At present it is unclear whether the association with disorders such as fragile-X syndrome and tuberous sclerosis is mediated by the associated mental retardation, or whether these disorders have some specific link with autism (Fisch, 1992; Smalley *et al.*, 1992). While autism can occur in individuals with such syndromes but without mental retardation, it remains to be seen whether incidence of autism is raised above population norms in fragile X or tuberous sclerosis individuals of normal IQ.

Early signs

Current diagnostic instruments (ICD-10, World Health Organisation, 1993; DSM-IV, American Psychiatric Association, 1994) specify that the onset of the disorder must be prior to age 3 years. At present, autism is usually diagnosed in the third or fourth year for nuclear cases, and often much later for atypical or mild cases. Diagnostic instruments [e.g. Childhood Autism Rating Scale (Schopler *et al.*, 1988) and Autism Diagnostic Interview—Revised (Lord *et al.*, 1994)] are based on intensive clinical interview of the care-givers and history taking, focusing on early childhood. These instruments may be used retrospectively, and early

abnormalities may be recognized in cases where diagnosis occurs late.

The most recent development in early diagnosis is the use of experimental screening questionnaires, aimed at identifying autism at 18 months. Preliminary studies, both with genetically at-risk infants (Baron-Cohen *et al.*, 1992) and with population screening (Baron-Cohen *et al.*, 1996b) suggest that failure to show pretend play and joint attention at 18 months marks out children diagnosed at 30 months as autistic (Charman, 1994). Other work, both prospective and retrospective, suggests that before 18 months children with autism do not show easily recognized social or cognitive abnormalities (Johnson *et al.*, 1992; Lister, 1992). Interest in this area continues, with analysis of home videos forming one source of information (e.g. Osterling and Dawson, 1994).

Prognosis

From the first follow-up studies onwards it has been clear that autism is a life-long handicap (Kanner, 1973; Lotter, 1978; Rumsey *et al.*, 1985). Markers of relatively good prognosis and adaptation appear to include higher IQ and the presence of useful language by age 5 years (Lockyer and Rutter, 1970). Estimates of adult functioning and independence vary according to ability level and type of educational provision (Rumsey *et al.*, 1985). Lord and Venter (1992), in their review of follow-up studies, concluded that adaptation in adulthood can range from poor to good in subjects with near normal IQ, but tends to be very poor for those with an IQ below 50. Among high-functioning individuals with autism, verbal skills emerged as the strongest predictor of social-adaptive functioning (Venter *et al.*, 1992). Claims for a cure for autism have so far failed to find objective support, although significant improvement and compensation can occur. Programmes of behavioural management can be successful in controlling problem behaviour, and educational approaches which give structure and use concrete prompts in a stepwise programme are demonstrably effective (Howlin and Rutter, 1987).

The picture which autism presents in adulthood can sometimes resemble chronic schizophrenia in that both conditions show poverty of action, speech and thought (Frith, 1992). Thus diagnosis in adulthood can be difficult, and always necessitates information about early history.

Asperger's syndrome

Research has recently focused on the distinction between autism and 'Asperger's syndrome' a disorder taking its name from Hans Asperger who described children similar to Kanner's cases contemporaneously (Asperger, 1944, translated in Frith, 1991). The status of this syndrome, which shares many features with autism, is somewhat contentious. However, present consensus is that Asperger's syndrome falls within the autistic spectrum, but deserves its own label because the course of the disorder, and consequently prognosis

and management, diverge from nuclear autism. Whether aetiology is different from that for autism, remains an open question. In both cases a genetic cause is likely (*see below*), and indeed the two disorders frequently co-occur in the same family (Gillberg and Coleman, 1992). People with Asperger's syndrome tend to be less aloof, more socially interested, more verbal in a pedantic style, and tend to have special interests to the point of obsession. Clumsiness has been described as characteristic of Asperger's syndrome in contrast to autism (Gillberg, 1992). However, recent experimental work suggests that clinically significant levels of motor impairment are common in both groups (Manjiviona and Prior, 1995).

The DSM-IV and ICD-10, which introduce Asperger's syndrome as a diagnostic category for the first time, stipulate that cases must show social impairments and restricted interests as for autism, but should not show significant delay in language or cognitive skills. This latter criterion is problematic, in that many authors (e.g. Wing, 1981) insist that a Kanner-type early history (including aloofness and language delay/abnormality) may give way to an Asperger-type picture in later life. Since the diagnosis of Asperger's syndrome is often given in late childhood or even adulthood, clinicians find it hard in practice to establish whether or not early language developed on time. The only epidemiological study to date (Ehlers and Gillberg, 1993) reflects this difficulty in using DSM-IV or ICD-10 criteria, but estimated the prevalence of Asperger's syndrome (including individuals with presumed language delay) as between 3 and 7 in 1000 school-age children. The sex ratio of boys to girls in Asperger's syndrome is estimated to be 8:1 as fits its position at the high ability end of the autism spectrum.

The DSM-IV currently places autistic disorder within the category of pervasive developmental disorders; disorders characterized by severe impairments in more than one area of development. As well as Asperger's disorder, pervasive developmental disorders also include Rett's disorder, childhood disintegrative disorder and pervasive developmental disorders not otherwise specified. Other diagnoses from which autism is distinguished include specific disorder of receptive language (with its secondary emotional/social consequences), and early onset schizophrenia. Additional descriptive categories, whose validity remains controversial and whose relationship to autism is as yet unknown, include nonverbal learning disabilities (Semrud-Clikeman and Hynd, 1990), schizotypal personality disorder (Wolff and Chick, 1980) and semantic-pragmatic disorder (Rapin and Allen, 1983; Bishop, 1989).

Summary

Autism is a well-established diagnostic category and, although the diagnosis has been widened by the spectrum notion, many of the children diagnosed with autism today closely resemble those described by Kanner 50 years ago. The core features of autism are captured by the triad of social,

communication and imagination impairments, with restricted repetitive activities. Over and above the core symptoms, individual children may show other behavioural features (e.g. self injury, pica, hyperactivity), due, in some cases, to additional medical conditions and/or mental retardation.

Biology

Genetic studies

Because autism (at least in its nuclear form) is such a rare disorder, and because people with autism so rarely have children, the familial clustering of autism was at first overlooked. The repeat occurrence of autism in siblings is low in absolute terms (2–3%; Smalley *et al.*, 1988) but high in comparison to incidence in the general population (at least 20–50 times greater risk). Although stoppage lowers the rate of multiple occurrence somewhat, a large number of multiplex families have now been studied. In particular, studies of monozygotic and dizygotic twins (Bailey *et al.*, 1995) have shown a concordance rate for monozygotic pairs of between 36 and 91%, compared with zero concordance in same sex dizygotic pairs. In addition, perhaps as many as 92% of monozygotic twin pairs are concordant for a broader phenotype of ‘cognitive and/or social abnormalities’ compared with 10% of dizygotic pairs (Bailey *et al.*, 1995). These ‘social and cognitive’ abnormalities are also more common in the non-twin siblings of children with autism, compared with siblings of children with Down’s syndrome (Bolton *et al.*, 1994). Bolton *et al.* (1994) include among cognitive impairments (also referred to as communication deficits), difficulties and delays in language, reading and spelling (the latter not typical of children with autism themselves). There are suggestions, also, from other studies that parents and siblings may show certain mild features of autism; performance–verbal IQ discrepancy (Minton *et al.*, 1982; Freeman *et al.*, 1989), mildly impaired performance on a test of planning (Tower of Hanoi; Ozonoff *et al.*, 1993), less coherent narrative (Landa *et al.*, 1991) and better spatial ability (Smalley and Asarnow, 1990).

Although more data are needed in order to understand the genetic mechanism involved, some authors have speculated on the type of genetic transmission which might be implicated. Szatmari and Jones (1991) conclude on the basis of a review of IQ- and sex-effects in existing studies that three types of transmission may be involved: exogenous, autosomal recessive and X-linked recessive. Bailey *et al.* (1995) concluded, on the basis of the large difference between the concordance rates in monozygotic and dizygotic twins, that autism is likely to be a complex genetic trait involving more than one gene locus. Support for a multilocus model comes from the family study of Bolton *et al.* (1994) in which the rate of disorder in relatives was related to the severity of disorder in probands. Bailey *et al.* (1995) favour a multiplicative multilocus model of inheritance, perhaps involving only a small number (estimated at between three and seven) of genes.

The reports from many mothers that the pregnancy of their autistic child was affected by various negative events (rubella, anoxia, etc.), has led to considerable research on pre- and peri-natal problems. Results of such studies have typically shown a significantly raised incidence of nonoptimal factors, as compared with nonautistic sibling controls (Lord *et al.*, 1991) and with other types of disorder (e.g. schizophrenia; Green *et al.*, 1984). The causal status of such adverse factors is uncertain (Goodman, 1990). Various infectious agents have been implicated in the aetiology of autism, e.g. cytomegalovirus, herpes simplex and a range of vaccines, although it appears that such agents could account for only a small number of cases (Stubbs *et al.*, 1984). Autistic-like behaviour has been documented in children with congenital rubella, although these problems may disappear with age (Chess *et al.*, 1971; Chess, 1977). Other environmental pathogens have also been suggested (e.g. dietary factors, immune deficiency; Todd, 1986), but so far no strong evidence for a causal role for any such agent has been adduced. Further, the season of birth and its possible link with viral illness during pregnancy has not yielded concrete clues (for review, see Bolton *et al.*, 1992). The problem that bedevils the behaviourally based diagnosis of autism in cases where an additional medical disorder is identified, is the apparently ubiquitous presence of significant mental retardation. Although the existence of severe mental retardation as such does not preclude autism, the behavioural repertoire in severely retarded individuals is restricted, making diagnosis contentious.

Previous studies seemed to suggest that genetic predisposition for autism and environmental causes interact; Folstein and Rutter (1977) and Steffenburg *et al.* (1989) found that in non-concordant monozygotic twin pairs, the affected child was the one who had suffered significant perinatal complications. They concluded that in order for autism to be manifest, an additional adverse factor (i.e. brain injury) had to compound the genetic predisposition. This conclusion was later modified, by both groups of authors, because the obstetric complications seen were relatively minor. Bailey *et al.* (1995) found that more complications were found in those twins who also had congenital physical anomalies, whose origin dated to the early stages of gestation. This finding has suggested the possibility of reversed causation: pre-existing congenital anomaly in the foetus causing obstetric complications.

Physical signs

Autism is typically described as a disorder without physical stigmata; indeed the normal or attractive appearance of children with autism stands in stark contrast to other forms of mental handicap. There has been great interest, however, in relatively minor physical anomalies in autism, which might give clues to the timing of the developmental abnormality. Bailey *et al.* (1995) collecting evidence from a British twin study, noted significantly raised incidence of dysmorphic

facial features (increased inter-pupillary distance and meeting of the eyebrows in the mid-line), and increased head circumference. Since facial development and mid-brow patterns are thought to be largely established by 16 weeks gestation, this might suggest very early origins for autistic disorders.

Bailey *et al.* (1993) report from autopsy of four mentally handicapped individuals with autism, that three brains were abnormally heavy: 1.53 kg in one 4-year-old, and 1.60 and 1.81 kg in two young adults in their twenties (normal range 1.25–1.49 kg for the ages covered). This report of megalencephaly is supported by results from a twin-study in which 42% of the 19 subjects with autism had head circumference above the 97th centile (Bolton *et al.*, 1994; Bailey *et al.*, 1995). The pathological basis of this brain enlargement is not known, but may be due to an excessive number of neurons, in the absence of any report of decreased neuronal density. Of course, most individuals with megalencephaly are not autistic, and it is unclear whether this abnormality should be considered a contributory factor, a consequence or merely a marker of the key pathology in autism.

Aitken (1991), among others, has suggested that what may be common to all cases of autism is the timing of the insult, with many different causes (genetic, organic, viral, etc.) interfering with neural development at the same key stage. It may well be that multiple aetiologies may lead to autism, converging on a 'final common pathway'.

Anatomical studies

The localization of the brain abnormalities in autism has been sought via *in vivo* imaging and post-mortem autopsy studies. Both macro- and microscopic levels have been explored. As is the case for other biological studies, the correct comparison groups have not always been used, nor has the documentation of the subjects studied always been complete. With these limitations in mind, what has emerged from recent work?

Neuropathological studies to date have been limited by the small numbers of brains studied; with such small numbers, the co-occurring features of the individuals involved may obscure the important specific abnormalities. Most studies have used brain tissue from individuals who are also mentally handicapped, and some have used subjects who were epileptic and/or on medication. The causal role of discovered abnormalities is not clear; the effects on brain tissue of a lifetime of autism (including, for example, stereotyped behaviour, self-injury) are unknown. However, no gross anatomical abnormalities have been shown to be specific to autism.

Perhaps the most solid finding, given these concerns, is of cytoarchitectonic peculiarities in the limbic system and cerebellum. Bauman and Kemper (1985, 1994), using whole brain serial sections, reported increased cell packing, reduced cell size and reduced connections, in many parts of the

limbic system. Additional abnormalities were found in the cerebellum and inferior olive of the brainstem (lower Purkinje cell counts). Since this picture resembles that typically seen during an early stage of normal brain maturation, the authors suggest its presence in autism may indicate a curtailment of development. In addition, the preservation of neurons in the principal inferior olive is taken as suggestive of cerebellar cortical lesions with onset at or before 30–32 weeks of gestation (Bauman, 1991).

Most brain imaging studies to date have involved structural, rather than functional, techniques, using MRI, PET and single photon emission computerized tomography (SPECT). Early CT scans in the 70s revealed some hemispheric asymmetries, in particular ventricular enlargement in the left hemisphere (Hauser *et al.*, 1975). This abnormality has only been found in a minority of autistic subjects studied in subsequent research (Caparulo *et al.*, 1981), and does not appear to discriminate autism from mental retardation in general (Gillberg and Svendsen, 1983).

Structural MRI studies have also had equivocal results; not all subjects with autism show abnormalities, and no single abnormality characterizes all subjects with autism. Courchesne *et al.* (1988) have reported hypoplasia of the cerebellum to be common in autism: 14 out of 18 nonretarded autistic subjects showed a 25% decrease in the vermis of the cerebellum and lobules VI and VII. However, other authors have reported nonreplications (Garber *et al.*, 1989). A recent study by Hashimoto *et al.* (1995) showed morphological abnormalities (size reduction) of the cerebellum and brainstem. This paper is notable for its inclusion of extremely young children (for whom diagnosis was confirmed at later ages), which rules out the possibility that similar abnormalities shown in adults with autism are late appearing or secondary consequences of autism. Piven *et al.* (1990) found a variety of cortical malformations in 54% of high-functioning individuals with autism, suggestive of neural migration defects during the first 6 months of gestation.

In an early structural PET scan study, Rumsey *et al.* (1985) showed elevated glucose utilization in widespread brain regions, although the 10 autism subjects showed considerable overlap with the 15 age-matched normal controls. Herold *et al.* (1988), on the other hand, found no differences in resting blood flow and oxygen consumption, measured by PET, in people with autism compared with controls. These contrasting findings have not been clarified by later results, which have been equally inconsistent. For example, using SPECT, Zilbovicius *et al.* (1992) found no cortical regional abnormalities in 21 children with autism. However, in 1995 the same group reported a transient (at 3–4 years but not at 6–7 years) frontal hypoperfusion, which the authors suggest indicates delayed frontal maturation (Zilbovicius *et al.*, 1995). The results of two SPECT studies, carried out in different centres, have shown reduced regional cerebral blood flow in the temporal lobes (George *et al.*, 1992; Gillberg *et al.*, 1993).

Although extensive work has been carried out using EEG recordings in autism, the results have not contributed

independent evidence concerning the nature of the biological basis of this disorder (for review, *see* Dunn, 1994). On a clinical and individual level, however, EEG has been useful for establishing seizure abnormalities (*see* section on epilepsy). New work is underway, focusing on event related potentials in combination with cognitive tasks, which carries more promise.

Clinical signs indicative of neurological disorder

In addition to the above investigations, there are clinical reports and research explorations of diverse neurologically relevant signs and symptoms shown by many individuals with autism.

Epilepsy is perhaps the best studied of these associated abnormalities. Of individuals with autism, 35–45% are affected (Gillberg and Steffenburg, 1987; Olsson, *et al.*, 1988), with seizures beginning in puberty in about half of these cases (Volkmar and Nelson, 1990). Mental retardation alone cannot, it seems, account for this strong association; although similarly high rates of epilepsy are found among severely mentally handicapped nonautistic persons, epilepsy is common in even high-functioning individuals with autism (Gillberg *et al.*, 1986, 1987; Ritvo *et al.*, 1990). From a sample of 28 individuals with autism and mental retardation, Elia *et al.* (1995) concluded that the tendency to develop seizures was not correlated with severity of autism (as measured by the Childhood Autism Rating Scale).

Infantile spasms, in particular, are shown at a higher rate in autism than in severe mental retardation (Riikonen and Amnell, 1981). The effects of such early seizures on the development of cognitive functions are as yet unknown (Deonna, 1993). Recently, a number of cases have been described where preschool children with 'autistic-like behaviour' were found to suffer from an unusual type of partial complex seizures (Deonna *et al.*, 1993). The seizures and correlative EEG changes were atypical in terms of age of onset and complex movements and might easily have escaped notice. In one case, at least, recovery was well documented following specific pharmacological treatment for the seizures (Deonna *et al.*, 1995). The pattern of recovery and relapse over the 2-year period studied suggested a close link between the abnormal electrical activity and the autistic symptoms (as measured by the Childhood Autism Rating Scale).

Other possible indications of neurological abnormalities that have been reported in autism include toe walking, nystagmus, motor posturing, hypotonia and spasticity, and abnormal persistence of infantile reflexes (Minderaa *et al.*, 1985). Raised incidence of left handedness or mixed handedness differentiates autistic samples from normal, but not from other mentally handicapped groups (Lewin *et al.*, 1993).

Biochemistry

The success story of phenylketonuria has shown that serious developmental disorder can be averted by dietary restrictions which take account of identified biochemical abnormalities. This has given rise to the hope that a similar treatment could be found for autism if key biochemical abnormalities were identified (*see* review chapter in Anderson, 1994). Taking a lead from schizophrenia research, a whole range of neurotransmitters has been explored. For instance, serotonin levels were found to be elevated in blood samples from people with autism (Anderson *et al.*, 1990; Cook, 1990). Elevated levels have also been found in relatives of some autistic individuals (Cook *et al.*, 1988; Piven *et al.*, 1991). However, the level of serotonin in the brain, and its effects, are unknown. In addition, it should be borne in mind that elevated levels of serotonin are also found in other groups (e.g. nonautistic mentally handicapped, Williams syndrome; August and Realmuto, 1989).

The dopaminergic system, which has also been implicated in schizophrenia, has been explored in autism with some, but not robust, evidence of abnormality (Narayan *et al.*, 1993). Observations of self-injury have led to a hypothesis of reduced pain sensitivity, due to production of endogenous opiates or increased reactivity to opiates (Panksepp, 1979). All of these hypotheses have held out the promise of effective pharmacological treatment, which has so far proved illusory; to date drug treatments (e.g. fenfluramine, haloperidol, naltrexone) have been ineffective against the specific features of autism, and of debatable value for the associated problems (e.g. hyperactivity, self-injury; Sloman, 1991). This appears to diminish the causal importance of the biochemical abnormalities, although it remains possible that intervention at key stages early in development is necessary for successful biochemical treatment.

Summary

Definite associations may be found between certain neurological signs and symptoms and autism, independent of mental retardation. This is the case, for example, for epilepsy. However, the causal status of even strongly associated factors remains uncertain. These factors are neither specific nor universal to autism and as yet, therefore, no complete picture of the biological basis of this disorder has emerged [for comprehensive reviews, *see* Gillberg and Coleman (1992) and Bailey *et al.* (1996)].

The associated features studied may, however, be markers of autism and give clues indirectly to the brain basis and genetic mechanism. To date it is unclear which of the many associated biological disorders and signs are simply coincidental. In addition, the specificity to autism of many of the features must still be in doubt, since appropriate control groups equated for degree of mental retardation, are often missing. Even features specific to autism may be linked at the biological level without necessarily having a causal role in the psychological impairments.

Cognition

'A claim such as the following is unhelpful: limbic system abnormality causes social impairment. Even if the statement were true, in that it pinpointed correctly a critical brain structure, we would still have an insufficient account of social impairment . . . We need plausible links in the causal chain from origin to signs and symptoms.' (Morton and Frith, 1995, p. 359).

While it is often thought that cognitive theories of autism would be rendered redundant by a fully fledged biological account, our framework argues strongly against this. Cognitive theories differ from other theories in bridging the gap between brain and behaviour, and can give explanatory and predictive accounts of the complex behavioural pattern in developmental disorders such as autism.

By the term 'cognitive' we do not mean to exclude emotions, which decidedly lie at the interface of brain and behaviour, nor do we intend to deny the vital role of environment in interaction with mental development. This wider notion of cognition, encompassing all that lies between brain and behaviour, is well suited to the integrative role of neuropsychology.

Rather than survey at length the various aspects of cognitive functioning and their peculiarities in autism, this section will focus on cognitive theories. Before discussing these, however, we shall highlight a few challenging observations on cognitive assets and deficits in key areas which must constrain current hypotheses.

Preserved and impaired cognitive functions

Autism has attracted a great deal of research largely because it is not a homogeneous disorder; while some functions are notably impaired, others are spared or even superior. One striking example is the now well-established spiky profile across the subtests of the Wechsler IQ scales. More than a dozen studies (for review, see Happé, 1994a) have shown that most subjects with autism show peak performance on the block design subtest of the performance scales and worst performance on the comprehension subtest of the verbal measures. This pattern appears to hold true across age and ability levels. The pattern is not simply due to verbal-nonverbal discrepancy: where measured, digit span (a verbal test) is also found to be a common peak of ability, and picture arrangement (a nonverbal test) tends to be poor. Although this characteristic pattern is not universal, it does appear to be specific (Lincoln *et al.*, 1988); other types of mental handicap or developmental disorder do not share this profile (Dudley-Marling *et al.*, 1981; Greenblatt *et al.*, 1991).

From the beginning, autism has been linked with so-called 'islets of ability'. These include good rote memory and skill at completing jigsaw puzzles, as well as the savant abilities in calendar calculation, drawing, music, prime number calculation, and mnemonism (O'Connor, 1989). Such savant abilities, superior to the individual's other functioning or

even to normal performance, occur in ~1 in 10 people with autism (Rimland and Hill, 1984). The incidence of savant skills in autism is therefore much higher than in other disorders, and might be even higher if skills such as hyperlexia and simple rote memory were included. These skills are not yet fully understood, nor is the link to autism explained. However, Hermelin and O'Connor (1986) have shown that these skills are based not on mere rote learning, but on implicit recognition of inherent patterns and rules (e.g. improvisation in the style of certain composers is possible for some savants). The skills are not taught and may emerge suddenly and spontaneously (Selfe, 1977). Typically the individual cannot explain their feats of, for instance, calculation, and the application of the skills is remarkably circumscribed (e.g. calculating only dates, while not being able to multiply two given numbers).

Alongside the excellent rote memory and short-term recall shown by many people with autism, some striking memory deficits have been reported. Boucher and Warrington (1976), drawing parallels with the amnesic syndrome, found that autistic children (compared with verbal and nonverbal ability-matched controls) showed impaired free recall but unimpaired cued recall, and learning of non-related word pairs. Boucher (1981) and Boucher and Lewis (1989) found that memory for recent events, i.e. autobiographical memory, was poorer than that of control children.

Attention, too, shows assets and deficits; on the one hand children may show narrowing of attention, perseveration and resistance to distraction. On the other hand, the same children may be described as hyperactive and unable to concentrate (attention deficit) (Dawson and Lewy, 1989). While simple 'overselectivity' is unlikely to be specific to autism (Lovaas *et al.*, 1979), there has recently been a renewal of interest in attention deficits in this disorder. For instance, Courchesne *et al.* (1996) have shown that individuals with autism are impaired on tasks requiring rapid shifting of attention following a cue, either between or within modalities.

Language

Like memory, language in autism shows both preserved and impaired functions. Some cases of autism will, of course, have additional language impairment over and above the autism. However, the idea that language might be the core deficit, and language impairment might be the major cause of social and communication failure in autism (e.g. Rutter, 1968), is no longer held (Rutter and Bailey, 1993).

In perhaps a quarter of cases of autism, especially among those with severe mental retardation, useful language is absent (Bryson *et al.*, 1988). What is more striking, however, is that such individuals are not only mute, but more generally uncommunicative: they do not use gesture or facial expression to stand in for absent spoken language, as do language impaired or deaf children.

There is evidence that young children with autism do not preferentially orient to intelligible speech versus a jumble of

voices (Klin, 1991). An early study by Ricks and Wing (1976) established that preschool children with autism used idiosyncratic vocalizations, which were recognized as meaningful signals by their own parents, but not by parents of other autistic or normal children. By contrast, normally developing infants showed a range of vocalizations elicited by four standard situations (pleasant surprise, frustration, greeting, requesting) which could be decoded readily by naive listeners.

Lack of communication, rather than language, seems to characterize autism; even those individuals who have language seem to fail to use it for intentional communication. Indeed, many cases of autism appear to present instances of an intact 'Language Acquisition Device' (Chomsky, 1980) in the absence of higher-order communicative intent (Frith and Happé, 1994a). Certainly, the presence of echolalia, which may involve delayed repetition of whole phrases or even conversations, demonstrates that phonological processing is not specifically impaired in autism. Development of syntax, too, appears to follow the normal course, and in a longitudinal study of young autistic and Down's syndrome children, no specific differences were noted (Tager-Flusberg, 1981, 1993).

While language delay is the norm in autism, this may be due, in many cases, to attendant mental retardation. In other cases, however, it may be secondary to the failure of communicative understanding (Frith and Happé, 1994a). Normal acquisition of the agreed names for things seems to rely on recognition of communicative gestures, eye gaze and joint attention (Tomasello, 1992; Baldwin, 1993, 1996) all of which are impaired in young children with autism leading inevitably to delays or mismatches in language learning through ostention (i.e. the teaching of labels by pointing and naming). The existence of neologisms in autism (Volden and Lord, 1991) may be related to such mismatches in word acquisition.

Pronoun reversal (confusing 'you' and 'I') may be explained in terms of echolalia in some cases, and in others by the failure of the automatic monitoring of speaker-hearer roles that is characteristic of normal conversation (Frith, 1989a).

Semantics has been relatively little explored. Some people with autism acquire extensive and erudite vocabularies, although use of these words may be limited. A study by Tager-Flusberg (1985) suggests that category knowledge is broadly normal in autism.

Impairments in pragmatics, the use of language, appear to be a universal feature in autism, encompassing the various observations of intact and impaired functions (Frith, 1989a). Prosody and intonation, normally used to convey emotional content or to highlight new/important information, are notably deviant in autism (Baltaxe, 1977; Baltaxe and Simmons, 1992). Eye gaze, which is normally used unconsciously to control conversational interchange, is abnormal in autism, often giving the impression of being avoidant, merely fleeting or else fixedly staring (Mirenda *et al.*, 1983). Gestures, body

language, and facial expression are poorly co-ordinated and often appear grossly abnormal to the listener, even in high-functioning individuals with autism who may have fluent spoken language (Tantam, 1988; Macdonald *et al.*, 1989; Yirmiya *et al.*, 1989). Comprehension of nonverbal cues accompanying communication, including body language and intonation, also appears to be impaired (Hobson, 1986a, b; Macdonald *et al.*, 1989).

Figurative language (e.g. 'I'm boiling!') is notably absent from the speech of individuals with autism, and is poorly understood when encountered in the speech of others. Where communicative intent differs from the literal form of the words used (e.g. indirect requests, irony, etc.), even able adults with autism may make striking errors of comprehension (Happé, 1994b). The tendency to take things literally is also shown in pedantic, over-exact, comprehension and production.

By contrast with pragmatic deficits, the acquisition of literacy is often an islet of ability. Indeed some children with autism learn to read before they use meaningful spoken language. Reading and spelling show evidence of excellent decoding skills, while comprehension of text lags behind (Frith and Snowling, 1983). High-functioning individuals with autism have written autobiographies (Grandin, 1984; Williams, 1992) which clearly demonstrate their intact language skills (Happé, 1991), while the same individuals may have much greater difficulties of expression in on-line conversational settings.

Cognitive theories

The rise of cognitive accounts can be traced back to Hermelin and O'Connor (1970), who first contrasted autism with other forms of mental handicap, and sensory handicap (blind and deaf). One of the important assumptions these authors made was that there could be specific impairments over and above the general lowering of IQ attendant on brain damage. Their work showed that neither general retardation, nor a peripheral input problem, could explain the specific pattern of impairments in autism. Innovatively, they applied information processing models to the study of developmental disorders, distinguishing central processing from input and output processes; O'Connor and Hermelin's data suggested that possibly all, but in particular the central processes, were abnormal in autism.

Subsequent theoretical approaches to autism followed O'Connor and Hermelin in looking for what is specific to autism, and in using control groups to subtract out the general effects of mental retardation and developmental delay. At present, there are perhaps three major cognitive accounts which have attracted widespread interest [for more exhaustive reviews, see Baron-Cohen *et al.* (1993), Happé (1994 c, d) and Bailey *et al.* (1996)]. We will discuss these briefly under the following headings: theories of impaired social cognition; theories of impaired executive functions; and theories of

weak central coherence. The first of these broad topics covers the most research, and will be discussed first.

Theories of social impairment

The idea that autism is, at root, a disorder of social insight, has been the most successful cognitive account to date. This central idea has been discussed by many authors and a number of current theories deal with this in differing ways. To a large extent there is disagreement only concerning the developmental sequence and fundamental cause of the social cognitive impairment. Three core areas of very early social interaction, presumed to mediate later social development in the normal child, have been suggested to be innately disturbed in the child with autism: interpersonal relatedness, joint attention and imitation.

Hobson (1986a, b, 1993) suggested that children with autism lack interpersonal relatedness. This failure to co-ordinate affective perspectives (how self and other feel towards the target of shared attention) is assumed to be basic to the most striking, later appearing, social impairments of autism. Hobson argues that in normally developing children it is this emotional relatedness which lies at the root of social understanding; that basic to the child's social skills is a realization that others are like him/her, based on observation and mirroring of 'bodily-expressed psychological states'. This hypothesis postulates impairments in the earliest months of the autistic child's life, which have yet to be explored experimentally. Since autism is rarely diagnosed before the third year, questions of causal precedence have not been tested. However, work is underway (Hobson, 1993), to investigate the causal role of early social perception deficits, by investigating autistic-like behaviour in congenitally blind children.

Abnormalities in recognition of emotional expression have been explored in older children with autism. Hobson *et al.* (1988) found, for example, that children with autism were impaired relative to controls at cross-modal matching of emotions (e.g. face to voice), but not of non-emotional stimuli (e.g. sound to picture of waterfall). Similar deficits have been found in a number of different paradigms, although recently it has been suggested that such deficits may not distinguish autistic children from nonautistic children of equivalent verbal ability (Ozonoff *et al.*, 1990). Perhaps the most important findings concern not how well but how children with autism recognize expressions of emotion. For example, Hobson *et al.* (1988) found that progressively blanking out portions of photos of faces disrupted the processing of identity in similar ways for autistic and control subjects, but affected emotion recognition more abruptly for the autistics. Whether such data are best accounted for in terms of interpersonal relatedness is, however, unclear.

The second early social skill which normal children show and children with autism appear to lack, is joint attention: the sharing of a focus of attention through alternating eye gaze (and sometimes pointing), between an object and another

person. A similar type of behaviour, social referencing, also involves the child in relating another person's emotional expressions to novel objects in the world (e.g. if the mother expresses fear, the child will not approach a new object; see Bretherton, 1992). Sigman, Mundy and their colleagues, in a substantial body of work (for review, see Mundy *et al.*, 1993), have explored the impairments in preverbal social interaction, focusing especially on joint attention. Failure to share eye gaze in a communicative way, co-ordinate eye contact and emotional expressions, take information from another's reactions, and respond to negative expressions, all appear to be characteristic impairments in children with autism (Kasari *et al.*, 1993). By contrast, Sigman and Ungerer (1984) have shown that children with autism are not markedly different from other mentally handicapped children in their attachment style, as tapped by the Ainsworth 'strange situation' paradigm. Strikingly, failure of joint attention (showing and pointing, or following a point) appears to be one of the earliest specific markers of autism, according to current screening studies (Baron-Cohen *et al.*, 1992). The causal status of these deficits, however, is still uncertain and it remains an important question whether all children with autism lack such abilities, whether any other children do so, and whether these are causes or simply early manifestations of later emerging social deficits.

Imitation is the third early behaviour which has been thought to play an important role in laying the foundations for later social development. Meltzoff (1988) and Meltzoff and Moore (1977) have shown that even newborns will imitate a posed facial expression (e.g. mouth open, tongue out), an ability which is presumably innately specified. Meltzoff and Gopnik (1993) have suggested that, for the normal child, such imitation is effectively a tutorial in social understanding. For instance, imitation may underlie emotional contagion; by assuming the same facial expression the infant may come to share the emotion felt by the other. A failure of early imitation, then, might severely affect the course of social development. Meltzoff and Gopnik hypothesize that autistic children lack early imitation, the so-called initial starting state for later social insight. Rogers and Pennington (1991) also suggest that a basic biologically caused deficit in imitation could be the underlying cause of the later failure to share affect with care-givers. They have reviewed empirical evidence on imitation in autism and report some difficulties in complex voluntary imitation shown in later childhood and adulthood (see also review by Smith and Bryson, 1994). On the other hand, Charman and Baron-Cohen (1994), for example, found intact gestural and procedural imitation in children with autism, of mean mental age 3 years 10 months. There is no evidence to date, however, that children with autism lack neonatal imitation. Nor is it clear that neonatal imitation relies on the same cognitive capacities as later voluntary imitation.

Theory of mind

In the 1980s, following Wing and Gould's (1979) epidemiological work, interest swung from the investigations

of language, perception and memory, to explorations of the social impairments in autism (Fein *et al.*, 1986). The task for psychological theories became to explain the concurrence of imagination, communication and socialization impairments: Wing's triad. Perhaps the most influential of these attempts has been the 'theory of mind' deficit account; the hypothesis that people with autism are unable to represent the mental states (beliefs, desires) of themselves and others, and to understand and predict behaviour in terms of these states. Baron-Cohen *et al.* (1985) proposed such a deficit on the basis of failure on a simple false belief task; children with autism, unlike normal 4-year-olds or children with Down's syndrome, were unable to predict where a protagonist would look for an object moved in his absence. Instead of taking into account the character's mistaken belief about the object's location, the children with autism answered on the basis of the real state of affairs. This failure to attribute mental states independent of reality and of the child's own belief, has now been replicated in a number of studies (for review, see Happé, 1994d). Importantly, children and adults with autism have been shown to succeed on closely matched tasks not requiring this ability, which has been given the term 'mentalizing'.

The notion of a deficit in mentalizing seems to account well for the triad of impairments described at the behavioural level. It makes sense of the particular pattern of socialization impairments, which are most striking in the lack of sensitive social reciprocity, yet leave intact general social desire and simple physical contact (Frith *et al.*, 1994). So, while children with autism may enjoy rough and tumble play with their parents, they typically lack joint attention behaviours, which seem to involve affecting the mental state of another.

The communication difficulties in autism also show a particular pattern of strengths and weaknesses: coded communication is possible, but ostensive-inferential communication (which displays the intention to communicate information) is impossible without mentalizing ability (Happé, 1993). So, for example, the person with autism may accurately transmit a message, verbatim, but fail to recognize who does and does not already possess the information (Perner *et al.*, 1989). In addition, mind blindness may account for difficulties and delays in language acquisition (Frith and Happé, 1994a), due to failure to learn words through ostention (Baron-Cohen, *et al.*, 1996a) and by reference to the speaker's intention.

The impairment of imagination was documented in the study of Wing and Gould (1979) by the absence of pretend play shown by the socially impaired group. Pretence, as argued by Leslie (1987) is a striking manifestation of mentalizing ability; it depends on the ability to distinguish between a real state of affairs and a playfully pretended state. Other types of play (e.g. skilfully manipulating mechanical toys), do not depend on this ability and are notably intact in children with autism. A theory-of-mind deficit thus accounts neatly for the core features of the syndrome of autism, while

allowing for the normality of certain activities in the spheres of social interaction, language and object manipulation.

The notion of a deficit in theory of mind has also been of clinical significance, inspiring investigations of possible screening measures and even educational interventions. The screening instrument for autism at 18 months of Baron-Cohen *et al.* (1992) drew on theoretical ideas about connections between early joint attention and pretend play and later explicit attribution of mental states. A number of authors (e.g. Ozonoff and Miller, 1995; Swettenham *et al.*, 1996) have attempted to teach individuals with autism an appreciation of rules such as 'seeing leads to knowing, not seeing to not knowing' with some success but typically a lack of generalization to other theory of mind challenges in tests or in real life. Above all, however, this cognitive theory has given teachers and carers a new insight into the world of the child with autism.

Despite these successes, the theory of mind account of autism faces several apparent limitations. First is the finding that between 15 and 55% of experimental groups with autism do pass first-order false belief tasks. These individuals still appear to be autistic, although they are, in general, somewhat more verbal (and older) than those who fail (Happé, 1995). While it is possible to explain their success in terms of task-specific strategies which do not, in fact, rely upon the attribution of mental states, there is evidence that at least some who pass such tasks do possess the ability to think about thoughts and feelings. Some individuals show evidence of mindreading skills in everyday life (Frith *et al.*, 1994), and perform well across a range of different social and communication tasks (Happé, 1993). Whether this subgroup is of different aetiology is an interesting question which has not yet been explored. It appears that individuals with Asperger's syndrome are distinguished by rather better social insight (Ozonoff *et al.*, 1991b; Happé, 1994d). However, even these individuals are socially impaired in everyday life; this may be a consequence of delay in acquiring social insight or, alternatively, may be due to some other persisting impairment which restricts the usefulness of the theory of mind abilities demonstrated in simple tests. No child with autism has yet been documented to demonstrate normal attribution of mental states at the appropriate age/mental age. Thus a hypothesis of an impairment in mentalizing, involving at least a delay, is still tenable for all cases of autism.

A second problem for the theory concerns basic social abilities which are normally present very early in life, and which appear to be missing in some cases of autism. Impairments in primitive social abilities are not easily explained as the result of impaired mentalizing, which is commonly assumed to rely on a later maturing mechanism. In particular, Klin *et al.* (1992) found deficits in early social skills, such as reaching in expectation of being picked up, in a group of children with autism. Such findings have led to increased interest in possible precursors to full blown theory of mind, which might be missing in autism, leading to mindblindness as a knock-on effect (Baron-Cohen, 1995).

The work on early socio-emotional development and joint attention (discussed above) is also pertinent to this issue.

The third major limitation of the theory of mind account, and of other accounts focused on social impairment, has to do with the nonsocial aspects of autism. Clinical features such as the restricted repertoire of interests (specified as a diagnostic criterion in DSM-IV and ICD-10), stereotypes of word and action, and pattern of cognitive abilities, have, as yet, received little research attention. A recent study by Turner (1996) showed that the degree of repetitive behaviour in autism is not related to theory of mind ability nor to IQ. Indeed, some types of repetitive behaviour (e.g. tics and motor problems) were more severe in those with high verbal ability, many of whom pass theory of mind tasks. These data suggest that repetitive behaviours cannot be dismissed as merely secondary to other cognitive problems (i.e. a coping response), and require explanation in their own right. Furthermore, at least some of the nonsocial deficits and skills described are specific to autism, as demonstrated by early experimental work on learning and memory (Hermelin and O'Connor, 1970).

A last question, not yet fully explored, is whether the theory of mind problem so characteristic of autism is actually specific to this group. While some (nonautistic) people with mild or moderate learning disabilities do fail experimental false belief tasks, this seems to bear little relation to their everyday social insight (Frith *et al.*, 1994). Other developmental disorders, such as conduct disorder and attention deficit hyperactivity disorder, or phenylketonuria have still to be explored. In a recent study, intact attribution of false beliefs in adult psychopaths, in the presence of impaired discrimination of different types of social transgressions (i.e. hurting a victim versus breaking a conventional rule; Blair, 1995; Blair *et al.*, 1996) has been reported. Children with conduct disorder appear to show some peculiarities in attributing mental states in tests and in real life, perhaps showing a negative attribution bias (Happé and Frith, 1996). In adults with Tourette syndrome, a disorder in which an executive function deficit has been shown, theory of mind appears to be intact at least at first-order (4-year-old) level (S. Baron-Cohen, J. Moriarty, C. Mortimore and M. M. Robertson, unpublished data).

Executive function deficits

Apart from the triad of impairments in socialization, communication and imagination, a feature that all diagnostic criteria of autism include, is restricted, repetitive and stereotyped patterns of behaviour. The parallel, in terms of perseverative and repetitive behaviour, seen with patients who have suffered frontal lobe injury, has given rise to a second major cognitive theory of autism. This theory draws on the link between brain and behaviour established from neuropsychological studies (for a review of stereotyped behaviour and neurological disorders, *see* Ridley, 1994). In this way a range of tests of executive function (Wisconsin

card sorting task, extra-dimensional shift, Tower of Hanoi, working memory, fluency) have been applied to individuals with autism, who appear to show substantial impairments when compared with mental age matched handicapped controls (Pennington and Ozonoff, 1996).

Executive function is an umbrella term covering a wide array of higher cognitive processes; the ability to disengage from context, inhibition of inappropriate responses, planning sequences of willed actions, staying on task, monitoring performance and using feedback, and shifting attentional set (Duncan, 1995). To date, these different areas have not been specifically disentangled. There is some evidence, however, that individuals with autism, even those of normal IQ, have problems in planning and organization (Prior and Hoffman, 1990; Ozonoff *et al.*, 1991a; Hughes *et al.*, 1994), switching set and perseveration (Rumsey and Hamburger, 1988; Hughes *et al.*, 1994). Turner (1996) found markedly impoverished generativity (e.g. generating words in a category, uses for objects, geometric designs) in both high- and low-functioning individuals with autism. Ozonoff *et al.* (1991b) found that executive function deficits were also characteristic of people with Asperger's syndrome, and suggested that these impairments are therefore basic to the whole spectrum of autistic disorders. Interestingly, while failure on traditionally executive tasks such as the Wisconsin card sorting task and Tower of London/Hanoi has been taken as suggestive of frontal damage, there is also evidence that performance on these tasks is disrupted by lesions in other areas [e.g. basal ganglia (Robbins *et al.*, 1994) hippocampus (Upton and Corcoran, 1995)].

Executive function impairments are not specific to people with autism. A variety of other groups with developmental disorders also show these difficulties; attention deficit hyperactivity disorder, phenylketonuria, Tourette syndrome, conduct disorder (Welsh *et al.*, 1990; Pennington and Ozonoff, 1996). How these disorders differ in their executive impairment from autism which is so different in clinical presentation is, as yet, unclear [but *see* Pennington and Ozonoff (1996) for an attempt to distinguish executive problems in these disorders]. Another question concerns the relationship of executive functions to IQ. The higher cognitive functions concerned (e.g. planning) are clearly tapped by many IQ assessments (Duncan, 1995), and would be expected to be compromised in general mental retardation. The choice of appropriate control groups, and the correct matching measures, therefore, become imperative issues. As interest in frontal functions increases, some contrary evidence is emerging. For example, Barth *et al.* (1995) found unimpaired performance by young able autistic children, on a delayed-match-to-sample task known to be sensitive to frontal damage. They conclude that their findings are more consistent with the possibility of temporal (e.g. amygdala) rather than frontal dysfunction in autism. So far no direct evidence of structural frontal damage has been shown in autism.

Problems in executive functions cannot explain all aspects of the nonsocial impairments in autism and more importantly,

cannot, on the face of it, explain the intact and superior skills. The spiky IQ profile is a case in point; block design, which is so often a peak in autism, is considered a good test of 'fluid' intelligence, which in turn relies on executive abilities (Duncan, 1995).

Central coherence

The notion of weak central coherence is different from other theories of autism, in that it does not present a deficit account. Frith (1989b) reviewed and reinterpreted the earlier work on language, memory and perception. The most striking results concerned the superior processing by normal children and mentally handicapped people of meaningful and patterned information over random and meaningless stimuli. People with autism appear to show a reduction or absence of this benefit from meaning or central coherence. For example, while normal and mentally handicapped children recalled meaningful sentences better than random word strings, children with autism were almost as good at recalling the latter as the former (Hermelin and O'Connor, 1967; Tager-Flusberg, 1991). In the same way, it seems that while normal subjects typically extract the gist of a passage or story while forgetting the surface form (Bartlett, 1932), children and adults with autism may retain the actual words used but fail to extract the meaning.

The idea that people with autism make relatively less use of context and pay preferential attention to parts rather than wholes, can go some way towards explaining the assets seen in autism, as well as some of the deficits. So, for example, Shah and Frith (1993) explored the well-established block design skill in autism, and found that this superior performance was largely due to an advantage in segmenting the original design. Presenting pre-segmented designs to normal or mentally handicapped controls significantly improved performance, and removed the autistic group's advantage while not aiding them in the task, as if the autistic subjects already saw the design in terms of its constituent blocks. In the same way, subjects with autism are better than controls at judging visual illusions; controls, by contrast, succumb to the effects of the figure context and are aided by a segmented condition (Happé, 1996a).

Frith and Happé (1994b) reviewed the available evidence for the notion of weak coherence in autism. They suggested that this cognitive style may be an additional and independent feature of autism, quite apart from theory of mind deficits. Thus even bright adults with autism who can pass theory of mind tasks, continue to show patterns of performance characteristic of weak coherence [e.g. peak block design performance (Happé, 1994a); poor sentence-specified pronunciation of homographs, e.g. 'In her eye a big tear . . .' versus 'In her dress a big tear . . .' (Happé, 1996b)]. Since it seems that weak central coherence has benefits as well as disadvantages, it is an interesting possibility that this is an aspect of autism which is genetically transmitted, and which characterizes the extended phenotype of autism, marking out

some of the non-autistic relatives. Findings of superior block design and less coherent narrative in relatives are consistent with this idea (Smalley and Asarnow, 1990; Landa *et al.*, 1991). In combination with a specific deficit such as lack of mentalizing, however, weak central coherence may have damaging consequences, for example limiting compensation and the ability to apply late-acquired social skills in everyday life.

Summary

The idea that there might be only a single cognitive deficit in autism has faded somewhat in recent years, although there are still strong claims about primacy and parsimony of explanation. Clearly the consequences of weak central coherence and of executive function deficits may overlap, and each will, in turn, interact with other specifically social deficits. Attempts, however, to reduce theory of mind deficit findings to problems in executive function or central coherence alone appear to be unfruitful. The pattern of 'fine cuts' between tasks requiring theory of mind and those which do not, is not easily explained by these alternative theories (*see* discussion by Bishop, 1993). It remains to be seen, however, to what extent a purely nonsocial deficit could lead to social impairment or, alternatively, how widespread the effects of a purely social impairment would be in terms of general understanding of the world.

One aspect of recent psychological thought which has not yet influenced the study of autism, is connectionist modelling. This approach, with its special relevance to development, may be particularly useful. For example, the cognitive effects of a failure of neuronal pruning have yet to be fully explored and may be of relevance to autism, given the finding of megalencephaly (*see* above). Connectionist modelling, then, represents a promising way in which (future) cognitive theory may link brain to behaviour.

Psychological research has refined our notions of the social and communication impairments in autism (for a recent review of theories, *see* Happé, 1994c). In this way, it has, perhaps, made the job for biological, and especially neuropsychological theories harder. Models which would lead to global deficits in these areas are no longer tenable. The nonsocial impairments in autism have, so far, been less well explored. The existence of characteristic nonsocial assets and skills, poses a special challenge to neuropsychological models of this disorder.

Neuropsychology: linking the three levels

A still influential neurological model of autism was suggested by Damasio and Maurer (1978). Their analysis of the behavioural features of autism (failure to develop normal relationships, ritualistic and compulsive behaviours, stereotyped movements, and abnormal attention) suggested analogies with acquired damage (in humans and animals) to the frontal lobe, or to the closely related structures of

the basal ganglia, mesial temporal lobes and thalami. The neurotransmitter dopamine has a major role in this system. According to the model, mesocortical structures relay limbic system information back to the neocortex, allowing affective labelling and recognition of stimuli. It is impressive that Damasio and Maurer's attempt at localization is still topical. Indeed all the areas they highlighted are current targets of biological investigation in autism (*see* chapters in Bauman and Kemper, 1994). However, taking into account plasticity of the developing brain, a model where all these regions are simply failing to function would appear unlikely. On the other hand, damage to a neural pathway connecting these areas, might result in a pattern which resembles failure of all these regions. Given the intact abilities in many domains in autism, and absence of gross anatomical abnormalities, some form of disconnection(s) along a crucial pathway is a distinct possibility. The extent or form of disconnection may explain some of the heterogeneity of the clinical picture of autism.

The brain basis of current cognitive theories

Damasio and Maurer's (1978) model was based on analogy at the behavioural level. Have more recent cognitive accounts brought us any closer to a useful understanding of the neurological basis of autism? One attempt to connect cognitive aspects and biological data in autism comes from Courchesne *et al.* (1993). They suggest that those individuals with autism who show bilateral abnormalities (nine out of 21 studied), mainly volume loss in the parietal lobes, performed poorly (performance more variable, inaccurate, poorly timed and effortful) on tests of attention shifting, which are sensitive to acquired parietal damage. Courchesne *et al.* (1996) have directly combined cognitive assessments and electrophysiological and behavioural data. Attention problems are hypothesized to underlie the social difficulties, through narrow focus of attention and the supposedly greater requirement for shifting attention in social (versus nonsocial) situations. It is not clear, however, that the precise pattern of intact and impaired social behaviour can be explained as sequelae of such a general deficit. It is possible to speculate that an inability to shift attention is relevant in the well-documented impairment in joint attention, considered to be important in the development of later social understanding. It remains to be seen, however, to what extent such attention-shifting difficulties are universal in young children with autism, and whether other groups with attentional difficulties are necessarily socially impaired.

In reviewing work on cognition we have highlighted three main accounts which go beyond single symptoms and suggest underlying impairments which must, at some point, be mapped onto brain pathways. Theory of mind, executive functions and central coherence are, on the face of it, very high level, complex cognitive constructs, which do not map straightforwardly onto cortical regions (as would peripheral handicaps). What progress has there been, as a result of these

three theories, in linking cognition to biology in autism? In what follows we will attempt to review evidence for the brain basis of each of the three major types of theory of autism. The executive function account is somewhat different from theory of mind or central coherence in this respect, since much of the substance of the theory is itself a claim about brain pathology.

In principle, evidence could be available from three major areas of study: from animal models (through precise lesions and subsequent loss of functioning), from the study of acquired disorders (brain pathology associated with loss of cognitive functions), and finally from brain scan studies (exploring the normal brain basis of cognition). What information from these areas bears on the social cognition, executive function, and central coherence accounts of autism?

Animal models

The classic Harlow studies of the effects of maternal deprivation in rhesus monkeys (Harlow and Harlow, 1962) have established the existence of a critical period for certain areas of social development. Peer contact also appears to be important, and deprivation of such social contact has long-term consequences. These studies fuelled the now-discredited psychogenic theories which claimed that environmental causes (e.g. mothering failure) might underlie autism. These theories grew from a conception of autism as primarily a problem of social withdrawal. Tinbergen and Tinbergen (1983) saw in autism a parallel with the approach-avoidance conflict demonstrated, for instance, by herring gulls. This ethological and behaviourist conception of autism addressed surface features of the disorder alone, and failed to take account of the quality and range of manifestations and underlying cognitive functions.

Investigators presenting animal models of autism have more commonly used lesion methods. Impairments of social and emotional behaviour have been studied in relation to limbic system lesions. The amygdala and orbitofrontal cortex have been implicated in normal social and emotional competence; lesions in macaques in these brain areas have been shown to be associated with changes in social behaviour including withdrawal, decreased aggression, and failure of maternal behaviour (Bachevalier, 1991; Kling and Brothers, 1992). The studies by Bachevalier and colleagues (for review, *see* Bachevalier and Merjanian, 1994) focused on minute neonatal lesions of the hippocampus and amygdala complex in rhesus monkeys, raised with unoperated monkeys and studied as infants and later in life. While memory deficits were surprisingly mild in comparison with the effects of similar lesions in adult animals, Bachevalier and colleagues report that the lesioned monkeys, when observed in pairs with a normal animal, showed abnormal avoidance of social contact, and increased object manipulation and locomotor stereotypies. In addition, the control animals are reported to have treated the lesioned monkeys somewhat differently. While these studies are interpreted as evidence of strong

parallels to autistic behaviour, and suggestive of a particular causal theory, they are open to criticism. The social effects reported appear rather general and nonspecific. They might be accounted for by increased inactivity or passivity of the operated animal, which does not capture well the complexity of autism. In addition, the absence of comparison groups with lesions in other brain areas renders this study somewhat inconclusive.

It is as yet unclear whether autism is a disorder for which an animal model can be found. At the heart of this disorder lie abnormalities in higher cognitive systems which may not be present in other mammals. To date there is no compelling evidence that any nonhuman primate or other species possesses a theory of mind (Byrne and Whiten, 1988; Povinelli *et al.*, 1990). Animal models thus appear better able to address precursor theories than to find the brain basis of mental state attribution itself. Brothers and Ring (1992) discussed the possible circuitry for the social brain in animals, involving the orbitofrontal and temporal regions including the amygdala. More specifically, Baron-Cohen (1995) has suggested an 'eye direction detector' which he sees as an important stepping stone to theory of mind. He suggests that eye direction detection may require intact amygdala and superior temporal sulcus; lesions in the latter region in monkeys lead to inability to discriminate gaze direction (Campbell *et al.*, 1990). Nevertheless, while children with autism have difficulty using eye gaze communicatively, and fail to orient preferentially to eyes, they appear able, in simple tasks, to detect where someone is looking.

Non-social features of autism have also been explored with animal models. Adult lesions of amygdala and hippocampus together have been shown to lead to severe and specific memory problems (Mishkin, 1978). For example, monkeys were unable to perform delayed nonmatching to sample tasks which are hypothesized to depend upon an intact 'cognitive memory' system. By contrast, the 'noncognitive habit' system was unaffected by such lesions and is hypothesized by Bachevalier (1991) to explain the pattern of good rote memory and poor memory for meaning in autism. Note, however, that Barth *et al.* (1995) have recently reported good performance on delayed-match-to-sample tasks by young children with autism.

A parallel has been drawn between the social and nonsocial deficits in autism and the 'lack of recognition of the significance of persons' objects or events' seen in Kluver-Bucy syndrome in monkey and man (Hetzler and Griffin, 1981). Likewise, hippocampal dysfunction has been suggested by Delong (1992) as the source of memory and social difficulties in autism, by analogy with clinical cases (including amnesia) and animal lesion models. The hippocampus, in this model, is assumed to be the brain centre necessary for flexible multidimensional association and integration. Difficulties with integration of meaning at different levels is an issue explored by the theory of weak central coherence in autism. Of potential relevance for the central coherence account, is the suggestion from animal

work (Rudy, 1991) that separate neural systems support elemental and configural associations in learning, the latter being disrupted by hippocampal-formation damage. This is similar to Ridley and Baker's (1991) suggestion that hippocampal damage impairs conditional learning but not simple discrimination learning.

Other nonsocial features seen in autism have also been studied in animals. For example, motor stereotypies can be induced through activation of the dopaminergic system with amphetamine (Ridley and Baker, 1983). Effects of early frontal damage in animals should be highly relevant for executive function theories of autism, but have not, as yet, been fully explored. However, so far, there is no evidence that such lesions result in a picture resembling autism.

Animal studies have, in the past, worked with a somewhat simplistic notion of autism; autism is no longer considered a syndrome of social avoidance, but rather one of failure of social understanding. Two particular challenges for this area are (i) how to model higher cognitive functions in animals, and (ii) what type of lesion might lead to superior performance in certain areas.

Brain damage in adulthood

To date, no clear case has been reported of autism acquired late in life following brain insult. However, there are cases with symptoms reminiscent of autism. Some cases of marked social impairment following herpes simplex encephalitis, have been reported in adults and older children (e.g. Gillberg, 1991). However, in these cases such severe handicap results from the encephalitis that a diagnosis of 'autism' is not unambiguously appropriate; no case of 'pure' autism (i.e. autism without general mental handicap) following a late acquired lesion has been found.

An interesting case of acquired social impairment but preserved intellectual ability was described by Eslinger and Damasio (1985). Patient E.V.R. suffered damage to orbital and lower mesial frontal lobes, following which he was unable to make appropriate social judgements or assessments of the character and motivations of others. Grattan *et al.* (1994) compared the effects of frontal and non-frontal lesions on cognitive flexibility and empathy. They found evidence to distinguish patients with lesions in mesial, dorsolateral or orbital regions; the latter two groups showed impaired empathy as measured by a self-rating questionnaire. Patients in the mesial group showed reduced cognitive flexibility only, while the dorsolateral group showed impairments in both functions. In general, however, it is notable that patients with acquired frontal lobe lesions, although suffering from socio-emotional impairments and specific memory problems, are not recognizably autistic.

Patients with acquired right hemisphere damage show some impairments in social communication which are strongly reminiscent of similar failure in high-functioning individuals with autism. In particular, right hemisphere patients fail to understand metaphorical remarks (Brownell *et al.*, 1990),

inferred meaning (Bryan, 1988), nonconventional meaning (Hirst *et al.*, 1984), indirectly stated material (Brookshire and Nicholas, 1984), indirect requests (Weylman *et al.*, 1989; Foldi, 1987) and the emotional-prosodic quality of utterances (Ross, 1981). Despite the common report of social and emotional problems following right hemisphere damage (e.g. in two cases reported by Ross and Mesulam, 1979), these patients' problems with pragmatics have not been investigated in terms of a breakdown of the understanding of speakers' intention. Nothing is known about the state of such patients' theory of mind, although such work is currently underway.

So far, relatively little work exists on the converse question: how do people with autism perform on right hemisphere tasks? One study, by Ellis *et al.* (1994), reported poor performance on the Warrington Recognition Memory test in six out of seven subjects with Asperger's syndrome. Klin *et al.* (1995) have suggested strong similarities between Asperger's syndrome and 'nonverbal learning disability'. This disorder is also referred to as 'developmental learning disability of the right hemisphere', although the connection to brain basis is indirect and based on behavioural parallels (Weintraub and Mesulam, 1983; Rourke, 1985). Klin *et al.* (1995) found a neuropsychological and IQ profile similar to nonverbal learning disability (visuo-motor impairment, social difficulties, good verbal skills) in 18 out of 21 Asperger individuals, but only one out of 19 subjects with high functioning autism. The verbal-performance IQ discrepancy typical in autism (verbal relatively impaired) appears to be reversed in the Asperger population. However, it is not clear to what extent this pattern is a result of motor clumsiness which is often included in the clinical criteria for Asperger's syndrome.

Autism is, of course, a developmental disorder; even if exactly the same brain system were damaged in adulthood, the resultant picture might not closely resemble autism. Frith and Frith (1991) have suggested that, taking into account this effect of difference in onset, autism and schizophrenia may provide some interesting behavioural parallels. Common behaviours include emotional flattening, social withdrawal, perseveration and stereotypies, as well as failure to initiate action and speech (Frith, 1992). It is important, of course, to remember that similarities at the behavioural level (especially of single symptoms) may not reflect underlying similarities at the cognitive level and this is especially so when comparing adult and child disorders. However, initial studies of cognitive impairments in patients with schizophrenia, suggest that those with paranoid symptoms show abnormal attribution of mental states, and those with negative symptoms may fail to use mentalizing in simple social tasks (Corcoran *et al.*, 1995; Frith and Corcoran, 1996).

Brain damage in childhood

Lesions at early stages in development, by their very nature, appear to be fairly nonspecific in their effects. Considerable plasticity exists for at least certain functions (Bach-y-Rita,

1990). For example, language acquisition is commonly preserved even following extensive left hemisphere damage early in life. On the other hand, lesions which have persistent effects (e.g. ongoing seizure disorders) tend to cause widespread impairments (Vargha-Khadem *et al.*, 1992). Clearly the effects of lesions are complex, and depend, in large part, on timing, affected projections, and relative rate of maturation of different brain areas.

What evidence is there for early damage to specific brain regions leading to later social impairment? A number of cases of early frontal damage, with resulting problems in social adaptation and executive functions, have been reported. For example, Pennington and Bennetto (1993) review nine cases of childhood focal frontal damage in relation to later conduct disorders, including difficulties in social relationships. Useful discussions are provided in Eslinger and Grattan (1991) and Segalowitz and Rose-Krasnor (1992). Despite detailed case studies, it is unclear whether the nature of the social impairment in these acquired cases are similar to that in autism. Since such lesions are rarely well localized or discrete, it is not possible from the current evidence to make strong claims about specific brain pathways. It is, as yet, unknown whether children with lesions in other areas also have social impairments, and whether they have impaired theory of mind.

At present, then, there is relatively little evidence of the specific early lesions which might impair the key cognitive functions implicated in autism. The exploration of theory of mind ability following early and later frontal lesions is an obvious task for future research. The effects of non-frontal lesions early in development will also be of interest: there is one report of unimpaired performance on theory of mind tasks by two siblings with callosal agenesis (Temple and Vilaroya, 1990).

Functional brain imaging

Perhaps the most exciting advance in localizing cognitive activity and cognitive impairment is the development of sophisticated brain scanning technology. PET, SPECT and now functional MRI allow the mapping of regional blood flow indicating differential brain activity during cognitive tasks. Some methodological and conceptual limitations exist which must be taken into account in the interpretation of resulting data (Nadeau and Crosson, 1995). This technology has just begun to be used in the study of autism, and there are, to date, two functional brain scan studies of theory of mind in normal volunteers, prompted by interest in autism.

In one study (Baron-Cohen *et al.*, 1994), using SPECT and a 'regions of interest' approach, adult volunteers listened to a list of words and were asked to decide which words 'described the mind or things the mind can do' (e.g. think, remember). The comparison task involved discriminating from foils those words which 'described the body or what the body can do'. During the mind-word task there was increased blood flow in the right orbitofrontal cortex relative

to the left frontal polar region. The argument for the relevance of the task comes largely from the finding that children with autism performed poorly on a similar mental word judgement task (and well in judging body terms). A number of questions remain concerning this study; it is unclear, for example, whether this task actually taps the ability to attribute mental states, and whether the regions of interest analysis precluded significant findings in other brain regions.

A PET study by Fletcher *et al.* (1995) used stories which involved mental state attribution, and for comparison physical stories without the mental element, as well as a base line control involving unconnected sentences. The mentalizing stories (concerning double bluff, white lie, misunderstanding, etc.) had been used previously with high functioning children and adults with autism, and proved sensitive to even quite subtle difficulties in mental state attribution (Happé, 1994b). In this brain scan study, the standard subtraction method of functional brain imaging was used and statistical parametric mapping, rather than a regions of interest approach. Brodmann area 8 (left medial frontal) was isolated as active during mentalizing over and above other areas of the brain engaged in the task of story comprehension. The results therefore back the idea that a separable brain system may underlie the innate capacity to mentalize, damage to which would lead to autism. The area pinpointed in this study was also activated in an independent study which aimed to investigate processes involved in story comprehension (Mazoyer *et al.*, 1993) using stories which, in fact, had a strong theory of mind component (e.g. deception). While little is known about the neuropsychological function of Brodmann area 8, it is known (from animal and human brain imaging research) to be involved in conditional learning tasks where context must be taken into account in order to assess the significance of a particular stimulus.

Future work on functional brain imaging in autism

Functional brain imaging studies will undoubtedly play an important role in linking brain to behaviour through cognition in our understanding of autism. Future studies will involve not only normal volunteers but also individuals with autism and Asperger's syndrome, as well as clinical control groups. We note that the logic of testing impaired individuals is complex. It is, for example, necessary to equate rate of responding and, ideally, level of performance between normal and clinical groups. The fine cuts technique (discussed above) is well suited to inform the choice of tasks, and should allow the separation of components underlying successful performance. Since the same performance level can be achieved by different routes, it may be possible to see activation of different brain regions during tasks performed equally well by different clinical groups.

In exploring the brain basis of theory of mind, it will be important to scan those high functioning individuals who

show some ability to mentalize, but who may use a different cognitive route and a different brain basis to solve such tasks. A first example of this sort of study has recently been completed, using the story materials and paradigm described above (F. Happé, S. Ehlers, P. Fletcher, M. Johansson, C. Gillberg and R. Frackowiak, unpublished results). Five volunteers with Asperger's syndrome, who were able to understand the test stories, were scanned. Unlike normal volunteers, these subjects did not activate Brodmann's area 8 in the left medial frontal cortex when required to think about mental states. Instead, the Asperger's syndrome subjects activated neighbouring left medial areas 9 and 10, and overall showed much reduced differences in activation between the three conditions. This suggests these individuals may have developed different cognitive routes, using different brain regions, to solve problems requiring mentalizing. Unfortunately, we do not yet know what functions areas 9 and 10 subserve in the normal brain.

It is important to note that even if the same pattern of brain activation were seen in autistic and control groups during any particular cognitive task, this does not rule out the possibility that there was developmental delay in maturation of these cognitive mechanisms and brain regions. For this reason it will be important to scan younger children; scanning throughout development may allow us to map how the neurological underpinnings of cognitive functions change with age, independently, perhaps, of behavioural changes.

As yet, subjects with autism have not been scanned using functional brain imaging during executive function tasks. Scans with other populations have been performed to explore brain activity during tasks requiring so-called 'frontal' or executive functions (e.g. in schizophrenia; Weinberger *et al.*, 1986). Certain tasks traditionally associated with the frontal lobes, such as the Wisconsin card sorting task and Tower of London, have shown widespread brain activity, in normal volunteers, involving not only the frontal lobes (Weinberger *et al.*, 1986). Such findings remind us that failure on traditionally 'frontal' tasks may be the result of damage to other parts of the brain or brain pathways. Clearly the executive function theory of autism is particularly vulnerable to changing conceptions of the brain basis of the critical tasks. This is, perhaps, a result of the way in which this theory links brain localization directly to behaviour, rather than to underlying cognitive mechanisms. The demands of functional brain imaging, including the requirement for appropriate subtraction tasks, may aid the further development of the executive dysfunction account of autism. Designing appropriate and contrasting tasks may, at the very least, advance a task analysis of these complex tests, and the principled fractionation of executive functions into meaningful and dissociable cognitive components.

Functional scanning has also not yet been used to explore central coherence. This seems a fruitful area for future work, in particular because this theory predicts good performance by people with autism on certain tasks (e.g. embedded figures test and block design). The usual problem of equating

performance level for scanning purposes in patients and normal volunteers is therefore circumvented. Current psychological work suggests that coherence may be weak at a number of different levels (perceptual, semantic, etc.), and it is not, on the face of it, easy to see how these different levels could map on to a single brain region or pathway. It may be, however, that one neurochemical transmitter, or one high level control system, modulates the balance of part-whole information processing in different brain areas associated with different tasks on which weak coherence has been demonstrated.

Summary

Cognitive neuropsychology has provided some promising avenues for linking brain abnormality and symptoms in autism [reviewed by Rumsey (1992); issues of localization (Minshew, 1992)]. However, research on neuropsychology is still far from presenting a coherent picture. Compared with other developmental disorders, a great deal of research and interest is evident, and autism may be one of the first developmental disorders to be understood at the neuropsychological level. This would be due as much to well-specified cognitive theories of the disorder as to advances in scanning technology. This area of autism research is likely to show the greatest advances and a wealth of interest in the coming decade.

Conclusions and outlook

Our aim in this review was to bring together recent research at three levels: biology, behaviour and cognition. Careful documentation of the special pattern of deficits and preserved abilities in autism, has led to a better understanding of this behavioural diagnosis, and especially of the range of its manifestations. Investigators presenting cognitive theories have sought to explain this constellation and its variation throughout the autistic spectrum. Biological accounts have, in the main, looked for aetiology on the basis of behaviour. Biology has had a privileged status among these three levels. Because autism is biologically based, it has been a common claim that if only we knew the brain basis of this disorder we would know 'what autism is'. It is clear, however, that not only do we not know the biological basis for autism as yet, but that even if we did, it would not tell us everything we want to know about this puzzling developmental disorder.

The three major cognitive theories, theory of mind, executive function and central coherence, all have a role to play in future neuropsychological investigations. It is quite possible that studies guided by the different accounts will result in different brain pathways being pinpointed. This evidence will not necessarily be contradictory, and may even further our understanding of the disorder by highlighting the existence of different subgroups defined at the cognitive and biological levels. More interestingly, such apparent contradictions might be resolved through incorporating the

three theories in one; disruption at different points of one and the same brain system might conceivably result in breakdown well characterized by each of the theories.

Cognitive theories appear to be vital for a full understanding of this syndrome. We believe that they can inform the behavioural intervention (diagnosis, management and education), and the search for the brain basis. Through better definition of the extended phenotype of autism, cognitive theory may also help to identify the genetic mechanism in autism and Asperger's syndrome. Advances in cognitive theory, including connectionist modelling of brain development, in combination with current technological progress in functional imaging and genetic studies, hold out exciting promise for the future.

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