Frith, U. and Hill, Elisabeth L.

Editorial. Autism: Mind and Brain

Originally published in Philosophical Transactions of The Royal Society Series B Copyright The Royal Society. Please cite the publisher's version.

THE ROYAL SOCIETY

Published online 8 January 2003

Introduction

Although we know much more now than we did 50 years ago about autism, the nature, origin and even the definition of the condition are still debated and remain largely unknown. This special issue begins with a review of the facts about autistic disorders, as they are known at present. In their introduction, Elizabeth Hill & Uta Frith (2003) remind the reader that autism is no longer regarded as a rare disease. They provide examples of genetic and brain research that targets the biological causes of autism and they review the three major cognitive theories that are currently used to explain the core signs and symptoms of autism. Much more is known now about autism than was known only a few years ago, and there is justified hope that our understanding of autism will continue to accelerate at a fast pace. This issue contains examples of the cutting edge of research and highlights some of the most burning questions. Some of these relate to the diagnosis of Asperger syndrome (AS), the identification of subgroups in the autism spectrum and early signs of autistic disorder. Other questions relate to the brain abnormalities that underlie the putative cognitive deficits and whether these can be made visible through magnetic resonance imaging. The shared assumption among the contributors is that autism is a neurodevelopmental disorder that gives us a unique window on the relationship between mind and brain. The research reported elaborates the key theories that have been put forward to explain the signs and symptoms of autism. These theories try to explain the selective impact of brain abnormality on some of the most high-level mental functions, such as social insight, empathy and information processing style.

One of the puzzles presented by the autistic disorders (which we will term 'autism' for short) is that the inability to communicate with others can coexist with high intellectual function. This puzzle has been part of the core description of autism since the beginning, and particularly so in Hans Asperger's early descriptions. When he first described a handful of cases of what he termed 'autistic psychopathy', little could he have imagined the impact on theory and practice. The criteria for AS are currently the subject of hot debate. It is ironic that the present definition of AS, as an autism spectrum disorder without early language and cognitive delay, may be based on a misunderstanding of Asperger's own definitions. However, Asperger's own definitions have been shrouded in obscurity. Kathrin Hippler & Christian Klicpera (2003) retraced the clinical case records of 74 of Asperger's original cases. For the first time, we have available the catalogued information detailed in these case reports. One finding is that while many of the cases that Asperger diagnosed would still be classified in the same way, a quarter of his cases would now be diagnosed with autism, according to the criteria adopted by both the World Health Organization and the American Psychiatric Association. Furthermore, Hippler and Klicpera's findings suggest that it may be the high verbal abilities of those with AS that allow them to achieve an apparently greater degree of social awareness than is achieved by those diagnosed with autism. However, then, as now, it is clear that high intelligence does not preclude severe impairment in everyday social adaptation, and that the social impairment typical of autism is largely independent of intelligence and surprisingly independent of language ability.

How productive is it to continue with research aimed at explaining the whole of the autism spectrum? Given the enormous heterogeneity of the spectrum, perhaps the time is ripe to reconsider the possibility of new subgroups. Ideally, such groups do not just capture relatively superficial distinctions in terms of overt behaviour, but distinctions that relate to distinct neurological causes. Whether new subgroups confirm historical distinctions is another question. Helen Tager-Flusberg & Robert Joseph (2003) used the profile of performance on cognitive tests to establish neurocognitive phenotypes, which, in turn, they have related to brain size and organization. They show how it is now possible to strengthen our understanding of autism by integrating the use of several sensitive neuropsychological techniques at our disposal. By drawing on similarities with children with specific language impairment, which is diagnosed in the presence of significant language difficulty and in the absence of other cognitive impairments, Tager-Flusberg and Joseph identified one autistic subgroup with overlapping specific language impairment. Furthermore, a group of boys with autism had reversed brain asymmetry similar to that reported previously in boys with specific language impairment. The other distinct subgroups identified by Tager-Flusberg and Joseph showed a large discrepancy between verbal and non-verbal IQ. In cases where the discrepancy was in favour of verbal IQ, the condition tended to be milder. In cases where it was in favour of non-verbal IQ, autism was more severe, and only this group was characterized by larger head size. Larger head size in autism has recently emerged as an important finding, and correlates with brain size and weight. This difference suggests that different aetiologies may be revealed in the two subgroups.

Impairments in the domain of social communication are the most striking feature of autism, and language impairments would be expected to aggravate these difficulties. However, impairments in gaze-following could be even more fundamental and provide the common denominator between children with both high and low language abilities. It is already known that children with autism do not necessarily look towards the same direction that another person is looking. Normal children tend to do this because they seem to wish to share another person's attention. This behaviour is referred to as 'joint attention' and

One contribution of 14 to a Theme Issue 'Autism: mind and brain'.

develops rapidly from 6 to 12 months of age. Joint attention involves the triadic coordination, or sharing, of attention between the infant, another person and an object or event. Looking at another person and pointing to a cup to request a drink, or looking at another person and pointing to a toy to share enjoyment, are examples of this skill. Lack of joint attention is one of the earliest signs of autism. Tony Charman (2003) highlights the crucial role that joint attention plays in autism, delineating its component parts further in the youngest longitudinal cohort yet studied. He discusses the psychological and neurological processes that might underlie the impaired development of joint attention and confirms that it is one of the earliest manifestations of mentalizing failure. One of Charman's most important findings is that impaired joint attention does not predict repetitive behaviour at later ages. By contrast, individual differences in joint attention ability are associated with language gains and social and communication skills at later ages. Thus, it may be futile to search for a unifying account for all of the currently specified behavioural criteria of autism, which include repetitive behaviour as well as social and communication impairments.

Following another person's direction of gaze is a voluntary action, but there is also an involuntary tendency to follow eye gaze, a kind of reflex. One highly interesting hypothesis is that this reflex is absent in autism. This hypothesis has been tested by John Swettenham *et al.* (2003) with clear and negative results. These authors investigated whether an observer would be affected by the direction of moving eye gaze of a face. Would the observer be induced to look into the same direction as the face when this gaze did, in fact, give no useful information as to the location of a target that the observer was instructed to look at? The direction of seen eye movement provided an involuntary cue even for children with autism. This new finding suggests that a missing attentional reflex is not the reason why individuals with autism fail to follow eye gaze voluntarily and fail to engage in joint attention.

In blind children, the absence of the visual modality would certainly preclude the use of eye gaze to monitor another person's direction of attention. The importance of the visual channel for developing this ability is shown by the fact that congenital blindness is associated with a raised incidence of autism, and tends to produce some social impairments that are reminiscent of autism. Peter Hobson & Martin Bishop (2003) report on their long-standing investigations of a group of children with congenital blindness but without the diagnosis of autism. They pose the question of whether visual impairment is a source of the social difficulties and to what extent these difficulties (however they originate) have an intrinsic connection with other autistic features in these children. Intriguingly, autistic features are much more pronounced in some children than in others, and it is the comparison between these groups that is the major concern of Hobson and Bishop's paper. By directly observing the social interactions of blind children, Hobson and Bishop suggest that one reason why congenital blindness may predispose an individual to autism lies in the nature of the experience of two-way interactions.

However, there is another low-level perceptual process that could be at fault: the normally innate preference for faces and eyes may be missing in autism. This hypothesis is developed and tested in the paper by Ami Klin *et al.* (2003). There is good evidence that even well-compensated individuals with autism experience difficulty with everyday social interactions in a variety of ways, even when their performance on laboratory tests of social cognition appears flawless. These individuals still experience difficulties in peer interaction and are unlikely to have close friends. Klin *et al.* (2003) ask what it is about social situations that high-functioning individuals with autism find difficult to process. They answer this question in a novel attempt to investigate naturalistic performance. Klin *et al.* synthesize the findings of their recent studies in which they have adopted a new technique—eye tracking—to monitor the approach of individuals with autism to finding meaning in naturalistic social scenes. While being able to produce, verbally, the rules of social interaction (such as explaining what a pointing gesture means), the individuals with autism studied in this paper were unable to translate this information into spontaneous social interaction. Such findings lead the authors to propose an alternative way of viewing social cognition, which they term 'embodied cognition', an emerging neuroscience approach to cognitive development.

Possible deficits in very high-level cognitive processes are considered by Simon Baron-Cohen *et al.* (2003). Successful social interaction involves a need to empathize (the term 'empathizing' is here used to include mentalizing) and this is contrasted to an ability to 'systemize'—a drive to analyse or construct systems. Having developed two scales to assess empathizing and systemizing, Baron-Cohen *et al.* contrast the performance of adults with high-functioning autism or AS and a normal population on these two measures. Not only does a male–female difference exist on these measures in their normal sample (favouring males on their systemizing quotient and females on their empathizing quotient), but individuals with autism also showed an unusually strong drive to systemize. These findings reflect the different pattern of interests of individuals with autism. Could these different interests arise because the normal preference for social stimuli in the environment cannot be presumed? This would correlate well with Klin *et al.*'s hypothesis. The approach provided by Baron-Cohen *et al.* starts to provide methods for the much-neglected area of adult assessment and, with further development, these questionnaires could be useful tools for wide population screening. Furthermore, the systemizing and empathizing quotient instruments could have potential importance for the broader phenotype. It is still an empirical question whether empathy and mentalizing ability correlate strongly with the degree of social interest and whether low social interest is a necessary, if not sufficient, prerequisite for a diagnosis of autism.

Of course, it is not just areas of social interaction that are unusual in the individual with autism. Aside from a cognitive explanation of autism relating to these difficulties, two further cognitive theories of autism—central coherence and executive function—are also widely acknowledged. Clinically, children and adults with autism often show a preoccupation with details and parts, while failing to extract gist or configuration. This cognitive style of weak central coherence has been used to refer to a number of processes including perception, attention, semantic

and linguistic processes. In an original and methodologically rigorous attempt to elucidate the mechanisms that can give rise to weak central coherence effects, Kate Plaisted *et al.* (2003) postulate that these mechanisms may be perceptual and examine these through the use of visual configural and feature discrimination tasks as well as an auditory filter task. Their findings of enhanced feature discrimination and abnormally broad auditory filter widths in autistic children suggest that while perceptual processing in autism is abnormal, this abnormality does not impact on the postperceptual processes responsible for integrating perceptual information to form a configural representation. Their work identifies areas in which the central coherence account requires modification, and suggests the potential for integrative studies of peripheral perceptual processes, central cortical processes and computational studies to identify the mechanisms underlying the abnormalities of stimulus processing associated with autism.

The relationship between weak central coherence and a third cognitive theory of autism, executive dysfunction, remains unclear. Rebecca Booth *et al.* (2003) provide an incisive investigation of their relationship by comparing boys with autism with boys from another clinical condition that is also believed to be associated with executive dysfunction: attention deficit hyperactivity disorder. Participants were asked to draw objects with specific items included (e.g. a house with four windows). These drawings were analysed in such a way that it was possible to see whether they focused on a small detail, and whether they showed lack of planning. Booth *et al.* found evidence that both groups of boys showed planning impairments in comparison with a normally developing control group. However, only the boys with autism showed a detail-focused drawing style, as predicted by the theory of weak central coherence. These results indicate that weak coherence may be a cognitive style that is specific to autism and not secondary to deficits in frontal functions.

A new and valuable approach to the neuropsychological impairments in autism may be through the study of motor coordination. Individuals with autism show delays in achieving motor milestones, soft neurological signs and difficulties with motor imitation, among other motor difficulties. Very little is known about the extent of such difficulties within the autistic population. Having developed an innovative reach-to-grasp movement paradigm, Morena Mari *et al.* (2003) show differences in movement planning and execution in what they term low-ability children with autism in comparison with normally developing control children. Their paradigm provides evidence that movement disturbances may play an intrinsic part in abnormal neurophysiological processes in at least a subgroup of individuals with autism. The movement abnormalities that these authors found show striking parallels to Parkinsonism. Given the apparent heterogeneity of the autistic condition and the difficulties that this presents for unifying explanations of the disorder, Mari *et al.*'s paradigm may make it possible to identify a particular neurocognitive subtype of the disorder in the future.

Research on the brain in autism is currently undergoing a rapid phase of development and very little is currently known about brain development in autism. One of the more prominent theories about the brain in autism is the amygdala theory, although the evidence to date is equivocal. Claire Salmond *et al.* (2003) have investigated this theory by comparing the presence of structural neuroanatomical abnormalities in the amygdala with behavioural evidence for amygdala dysfunction. They tested the emotional modulation of the startle response in children, a response known to be dependent on the amygdala in adults, but found no significant group differences. Surprisingly, only half of the children with autism showed structural abnormalities in the amygdala, whereas, in all children, abnormalities in a variety of other brain regions were identified. This highlights the heterogeneity of the disorder and may pave the way to subtyping at the brain level.

In the final paper of this issue, Robert Schultz *et al.* (2003) provide a vital contribution to an understanding of the network known as the social brain. In a study in which they focus on the fusiform face area (FFA)—an area of the brain that has previously been shown to be involved in the processing and discrimination of faces—Schultz *et al.* show that this is not the only role of the FFA. Rather, it is engaged in social processing in general and is part of a well-established set of brain regions that are specific to social cognition. These include the amygdala, superior temporal sulcus and medial prefrontal cortex. Critically, in their study, the strength of activity across normal participants in the region of the FFA during social attribution was related to the accuracy with which they performed the task. This suggests that hypoactivity of the FFA in autism may be a reflection of a core social brain network underlying the disorder. Clearly, in the future we can look forward to further studies correlating structural and functional brain activity with the behavioural signs and symptoms of autism.

In the past ten years, research on autism has undergone a period of consolidation, with empirical work guided by the three major cognitive theories—theory of mind, central coherence and executive function—and with cognitive explanations of the core features of autism providing a vital interface between brain and behaviour. The varied papers in this issue demonstrate that new ideas on how to link mental dysfunctions and brain abnormalities are emerging, facilitated by the use of new techniques. More is becoming known about the brain basis of autism and the nature and variability of its behavioural symptoms. We are also becoming more aware of the earliest signs of autism and about persistent difficulties, even in well-compensated adults. Last, but not least, the cognitive strengths of individuals with autism are finally being recognized and seriously examined.

We are very grateful for the support of the following for reviewing papers in this issue: Truett Allison, Simon Baron-Cohen, James Blair, Sarah-Jayne Blakemore, Dermot Bowler, Tony Charman, Hugo Critchley, Emily Farran, Chris Frith, György Gergely, Patrick Haggard, Paul Harris, Claire Hughes, Charles Hulme, Knut Kampe, Simon Kilcross, Ami Klin, Sue Leekam, John Morton, Laurent Mottron, Sally Ozonoff, Josef Perner, Trevor Robbins, Michael Rutter, Rebecca Saxe, Jim Stevenson, Michael Thomas, Michael Tomasello, Patrik Vuilleumier and Lorna Wing.

Uta Frith
Elisabeth L. Hill *October 2002*
Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London WC1N 3AR, UK

REFERENCES

Baron-Cohen, S., Richler, J., Bisarya, D., Gurunathan, N. & Wheelwright, S. 2003 The systemizing quotient: an investigation of adults with Asperger syndrome or high-functioning autism, and normal sex differences. *Phil. Trans. R. Soc. Lond.* B **358**, 361–374. (DOI 10.1098/rstb.2002.1206.)

Booth, R., Charlton, R., Hughes, C. & Happé, F. 2003 Disentangling weak coherence and executive dysfunction: planning drawing in autism and attention-deficit/hyperactivity disorder. *Phil. Trans. R. Soc. Lond.* B **358**, 387–392. (DOI 10.1098/rstb.2002.1204.)

Charman, T. 2003 Why is joint attention a pivotal skill in autism? *Phil. Trans. R. Soc. Lond.* B **358**, 315–324. (DOI 10.1098/rstb.2002.1199.)

Hill, E. L. & Frith, U. 2003 Understanding autism: insights from mind and brain. *Phil. Trans. R. Soc. Lond.* B **358**, 281–290. (DOI 10.1098/rstb.2002.1209.)

Hippler, K. & Klicpera, C. 2003 A retrospective analysis of the clinical case records of 'autistic psychopaths' diagnosed by Hans Asperger and his team at the University Children's Hospital, Vienna. *Phil. Trans. R. Soc. Lond.* B **358**, 291–302. (DOI 10.1098/rstb.2002.1197.)

Hobson, R. P. & Bishop, M. 2003 The pathogenesis of autism: insights from the study of congenital blindness. *Phil. Trans. R. Soc. Lond.* B **358**, 335–344. (DOI 10.1098/rstb.2002.1201.)

Klin, A., Jones, W., Schultz, R. & Volkmar, F. 2003 The enactive mind, or from actions to cognitions. Lessons from autism. *Phil. Trans. R. Soc. Lond.* B **358**, 345–360. (DOI 10.1098/rstb.2002.1202.)

Mari, M., Castiello, U., Marks, D., Marraffa, C. & Prior, M. 2003 The reach-to-grasp movement in children with autism spectrum disorder. *Phil. Trans. R. Soc. Lond.* B **358**, 393–404. (DOI 10.1098/rstb.2002.1205.)

Plaisted, K., Saksida, L., Alcantara, J. & Weisblatt, E. 2003 Towards an understanding of the mechanisms of weak central coherence effects: experiments in visual configural learning and auditory perception. *Phil. Trans. R. Soc. Lond.* B **358**, 375–386. (DOI 10.1098/rstb.2002.1211.)

Salmond, C. H., de Haan, M., Friston, K. J., Gadian, D. G. & Vargha-Khadem, F. 2003 Investigating individual differences in brain abnormalities in autism. *Phil. Trans. R. Soc. Lond.* B **358**, 405–414. (DOI 10.1098/rstb.2002.1210.)

Schultz, R. T., Grelotti, D. J., Klin, A., Kleinman, J., Van der Gaag, C., Marois, R. & Skudlarski, P. 2003 The role of the fusiform face area in social cognition: implications for the pathobiology of autism. *Phil. Trans. R. Soc. Lond.* B **358**, 415–428. (DOI 10.1098/rstb.2002.1208.)

Swettenham, J., Condie, S., Campbell, R., Milne, E. & Coleman, M. 2003 Does the perception of moving eyes trigger reflexive visual orienting in autism? *Phil. Trans. R. Soc. Lond.* B **358**, 325–334. (DOI 10.1098/rstb.2002.1203.)

Tager-Flusberg, H. & Joseph, R. M. 2003 Identifying neurocognitive phenotypes in autism. *Phil. Trans. R. Soc. Lond.* B **358**, 303–314. (DOI 10.1098/rstb.2002.1198.)