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Early intervention and brain plasticity in autism

Geraldine Dawson and Kathleen Zanolli

Autism Center, Center on Human Development and Disability, University of Washington, Seattle, WA 98195, USA

Abstract. Autism is associated with impairments in brain systems that come on line very early in life. One such system supports the development of face processing. Dawson and colleagues found that 3 year old children with autism failed to show differential event-related potentials (ERPs) to photographs of their mother's versus a stranger's face. Since differential ERP activity to familiar and unfamiliar faces is typically present by 6 months, this represents early brain dysfunction. McPartland and colleagues found that the face-specific ERP component ('N170') is atypical in older individuals with autism. N170 is typically larger to faces than non-faces, and prominent over the right hemisphere. In individuals with autism, N170 was larger for furniture than faces and bilaterally distributed. Biology and experience contribute to the development of face-processing systems. Newborns are capable of recognizing faces. Early face recognition abilities are thought to be served by a subcortical system, which is replaced by an experience-dependent cortical system. Development of a neural system specialized for faces may depend on experience with faces during an early sensitive period. Because children with autism fail to attend to faces, they might not acquire the expertise needed for a specialized face processing system to develop normally. Early interventions that enhance social attention should result in changes in brain activity, as reflected in ERPs to face stimuli, with those children showing the greatest social improvement exhibiting more normal brain activity.

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Studies have shown that behavioural intervention during the preschool period can be effective for many children with autism, presumably because of the plasticity of neural systems during that time. Such studies raise several important questions: What brain systems might be affected by early behavioural intervention? How might such effects be measured in young children? Are there sensitive periods in development during which behavioural intervention is likely to have its greatest impact on brain development? This paper briefly considers these questions.

Early behavioural intervention

Several studies suggest that early intensive behavioural intervention (EIBI) can result in dramatic improvements for some children with autism (e.g. Anderson et al 1987, Fenske et al 1985, Lovaas 1987, Smith et al 2000). As reviewed by Dawson & Osterling (1997) and Rogers (1998), although intervention models have varied across studies, most of these intervention models had several common features including (1) a curriculum that is comprehensive and includes core domains of attention, imitation, language, toy play and social interaction, (2) sensitivity to normal developmental sequence, (3) highly supportive teaching strategies, most often based on applied behaviour analysis, (4) behavioural strategies for reducing interfering behaviours, (5) involvement of parents in the intervention process, (6) gradual and careful transition from a highly-supportive environment to more complex, naturalistic environments, (7) intensive intervention consisting of about 25 hours a week of structured intervention lasting for at least 2 years, and (8) onset of intervention by 2–4 years. When these features are present, results have been impressive for a subgroup of children including robust gains in IQ, communication and educational placement.

Although previous studies have examined the efficacy of EIBI for improving behavioural outcome, no published studies have examined the effects of EIBI on brain development. Because autism involves core impairments in language and social relatedness, of particular interest is how EIBI affects the early development of social and language brain circuitry and function. This paper focuses specifically on how EIBI might affect the development of brain systems specialized for social processing, and in particular, face processing.

Autism involves a basic impairment in face processing

Evidence suggests that autism involves a fundamental impairment in processing information from faces. Indeed, one of the first recognizable symptoms of autism involves a failure to attend to faces. In a study of home videotapes of 1st birthday parties of infants with autism, a failure to attend to others' faces was the single best discriminator between one-year-olds with autism vs. typical development (Osterling & Dawson 1994). Face recognition impairments have been found in several studies of older individuals with autism (e.g. Boucher et al 1998, Klin et al 1999). Older individuals with autism fail to show the 'face-inversion effect' that has been demonstrated in normal individuals (i.e. superior ability to recall upright as compared to inverted faces; Hobson et al 1988). In fact, individuals with autism recognized inverted faces *better* than normal individuals, suggesting that they may be using a different information processing approach. In fMRI studies, the fusiform gyrus is activated during face processing, typically more on the right than left (McCarthy et al 1997). Schultz and colleagues found that high-functioning individuals with autism spectrum disorder failed to activate the fusiform face area during face processing (Schultz et al 2000). A study by Dawson et al (2002) using EEG recordings found that children with autism as young as 3–4 years of age exhibit atypical brain activity to faces, whereas they showed normal brain activity in response to objects. In this study, 64-channel event-related potential (ERP) recordings to digitized photos of mother's versus a stranger's face and photos of a favorite versus unfamiliar object were collected from 3–4 year old children with autistic spectrum disorder, CA-matched children with typical development, and MA- and CA-matched children with developmental delay without autism. Typically developing children showed significant ERP amplitude differences in all three components measured (P400, Nc, Positive Slow Wave) to familiar versus unfamiliar faces, and differences in P400 and Nc components to familiar versus unfamiliar objects. Developmentally delayed children showed significant ERP amplitude differences in the positive slow wave for both faces and objects. In contrast, children with ASD did not show differential ERPs to familiar versus unfamiliar faces, but like the typically developing children, they did show P400 and Nc amplitude differences to familiar versus unfamiliar objects. Increased P400 latency to faces was associated with greater joint attention impairment in the children with autism ($r = 0.63$, $P < 0.0001$). Because face recognition ability emerges very early in infancy, this impairment likely reflects a very early brain abnormality.

In an ERP study of adolescents and adults with autism, Dawson and colleagues (McPartland et al 2001) found that the ERP face-specific component ('N170') differed between participants with autism and normal participants. This ERP component is found in response to face stimuli in normal individuals as early as 4 years of age, and shows reliable increases in amplitude and decreases in latency throughout childhood (Taylor et al 1999), making it a sensitive neural marker of the developmental course of face processing. Consistent with previous research (e.g. Bentin et al 1996), typical subjects demonstrated a pattern of negative electrical activity over the posterior scalp at ~ 170 ms that was right-lateralized and larger in amplitude in response to faces than furniture. In contrast, participants with autism failed to show hemispheric lateralization, showing equal activity in right and left hemispheres. Whereas typical participants showed the expected shorter right hemisphere latency to upright faces than furniture, individuals with autism exhibited the opposite pattern, i.e. longer latency to faces. Typical participants also exhibited longer N170 latency to inverted than upright faces, whereas participants with autism did not.

The role of experience in the development of face processing

The neural systems that mediate face processing appear to exist very early in life. A visual preference for faces (Goren et al 1975) and the capacity for rapid face recognition (Walton & Bower 1993) are present at birth. By 4 months, infants recognize upright better than upside down faces (Fagan 1972). By 6 months, infants show differential ERPs to familiar versus unfamiliar faces (de Haan & Nelson 1997).

Studies of face recognition in adult human and non-human primates have been informative in describing the neural systems that mediate face processing. In monkeys, face selective neurons have been found in inferior temporal areas, TEa and TEm, superior temporal sensory area, amygdala, ventral striatum (which receives input from the amygdala), and inferior convexity (Desimone et al 1984, Rolls 1992, Williams et al 1993). Face recognition impairment results from damage to fusiform gyrus and the amygdala (e.g. Damasio et al 1982). Neurons that respond to faces have been found in the amygdala (e.g. Rolls 1984). The anterior inferior temporal cortex and the superior temporal sulcus project to the lateral nucleus of the amygdala (Amaral et al 1992). Parts of the inferior and medial temporal cortex may work together to process faces (Nelson 2001). The amygdala is important for assigning emotional relevance to faces, and the emotional arousal that results from amygdala activation may affect both attention and memory for faces. The amygdala is activated during eye-to-eye gaze and has been suggested to play a role in the emotional responses evoked during eye contact between persons (Kawashima et al 1999).

Morton & Johnson (1991) have hypothesized that early face processing abilities are mediated by subcortical systems which are replaced by cortical systems at about 6 months of age. These neural changes in the face processing system reflect 'experience expectant developments' (Greenough et al 1987, Nelson 2001). In other words, a sensitive period might exist during which there is a readiness of the brain to receive experience with faces. Such input is a reliable experience for most human infants, and Nelson (2001) has argued that this experience is important for the development of a specialized face processing system. Nelson and colleagues (Pascalis et al 2002) found human infants superior to adults in discriminating monkey faces, suggesting that experience with human faces results in a 'perceptual narrowing' similar to what is observed with speech perception (Doupe & Kuhl 1999). They demonstrated that younger infants, 6 months of age, were better at discriminating individuals of both human and monkey species, compared to older infants and adults. They argue that this is due in large part to the cortical specialization that occurs with experience in viewing faces. Based on the similarity in timing of perceptual narrowing for both face and speech perception (by about 6 months), these systems may develop in parallel and mutually influence one another.

Role of experience in abnormal face processing in autism

Experience may also play a role in atypical development of the face processing system in autism (Carver & Dawson 2002). As mentioned above, by 3–4 years of age, there is evidence of atypical brain activity in response to faces in young children with autism. In adolescents and adults with autism, there is evidence of slowed neural speed of face processing, as reflected in N170 latency, and atypical cortical specialization for faces in autism. *We hypothesize that the abnormalities in face processing found in autism may be related to abnormalities in social attention, and more specifically that the neural mechanisms that normally draw an infant's attention to others' faces are dysfunctional in autism.* As mentioned above, the amygdala is important for assigning affective significance to faces, and is activated during eye to eye contact. Such neural mechanisms normally facilitate mutual gaze and the acquisition of knowledge about others' faces, including their familiarity and expressions. Beginning early in life, in autism there may be a deprivation of critical experience-driven input that results from a failure to pay normal attention to faces.

What might be the impact of early intervention on the development of brain systems related to face processing? One goal of early behavioural intervention is to teach children to pay attention to social information, including faces, by rewarding them for doing so. Although prompting strategies and selection of skills to be taught vary among EIBI programs, the interaction between adult and child always includes two features (Anderson & Romanczyk 1999). First, the child emits a behavioural skill that is prompted or facilitated by the adult in some way. In the early stages of EIBI, nearly all these skills include eye contact, either in isolation or in conjunction with joint attention, imitation, language, cognitive and social skills. Second, contingent on the child's use of the skill (eye contact), the therapist immediately provides a reinforcer. Because reinforcers are defined functionally, in terms of their effect on the child's behaviour, the specific reinforcer used varies widely depending upon the child's momentary preferences. In practice, most children with autism receive access to a highly preferred non-social stimulus, typically related to the child's sensory or restricted interests. Often, at the same time, the child receives social feedback, such as praise, touch, smiling or applause.

There are several potential effects of this behaviour–reinforcer interaction. First, the ostensible and intended effect is that the skill (e.g. eye contact) is more likely to be repeated. Increased use of eye contact may improve the facial processing system simply by increasing the child's experience with faces.

This experiential input alone, however, may or may not affect the emotional arousal, or motivational, component of facial processing. Another second potential effect of behaviour–reinforcer interactions, which may influence the motivational significance of faces, is conditioned reinforcement. When a previously neutral stimulus (face) is frequently associated with a reinforcer (e.g. access to toy), the neutral stimulus can acquire reinforcer value, that is, it can function as a reinforcer for that individual's behaviour in the future. In EIBI, neutral social stimuli, including the face, facial gestures and language, frequently co-occur with reinforcing non-social stimuli. This could result in faces and social stimuli acquiring reinforcer value (see Fig. 1). Factors that enhance the acquisition of reinforcer value by a previously neutral stimulus are (1) temporal contiguity of the behaviour, neutral stimulus, and reinforcer; (2) consistent association between the neutral stimulus and reinforcer, such that one is never or rarely presented without the other; (3) similarity or overlap between the neutral and reinforcing stimuli; and (4) the presence of a contingency which requires the child to do more than simply attend to the reinforcer and neutral stimulus (Williams 1996, Mazur 1994, Silverstein & Lipsitt 1974). All of these factors are present in EIBI.

Thus, it is possible that EIBI might facilitate the development of the face processing system in two ways: (1) by providing enhanced early exposure to faces by increasing the child's

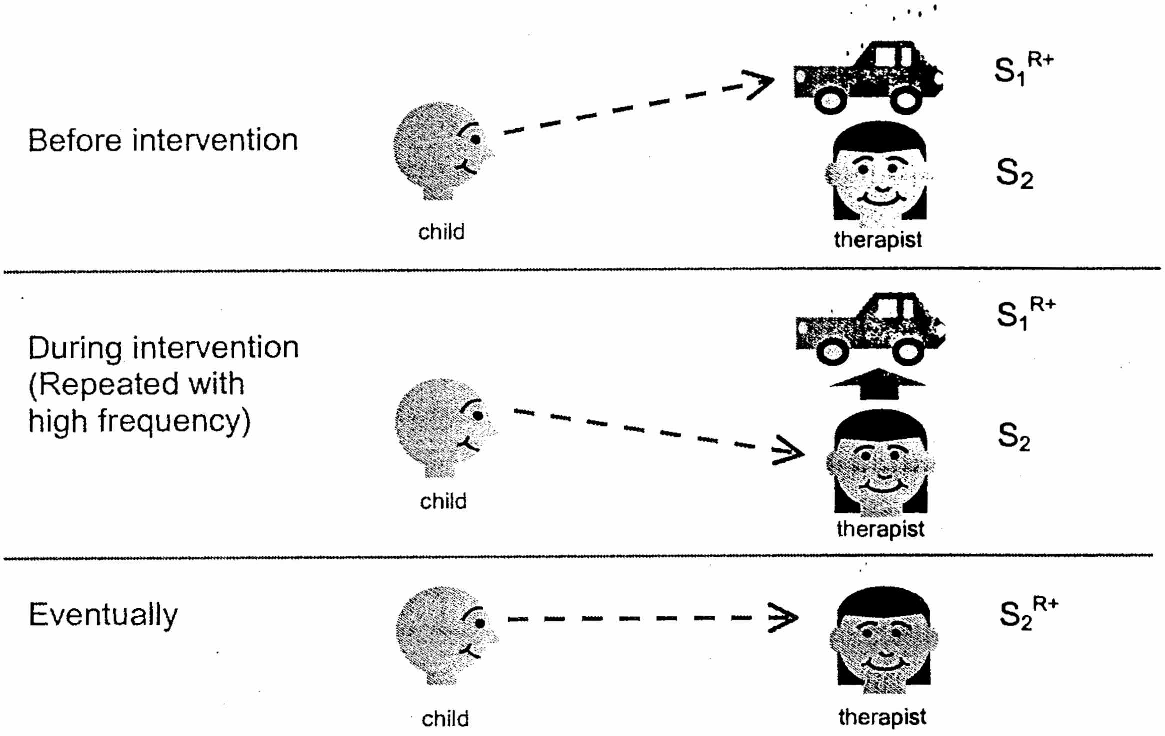

FIG. 1. Acquisition of conditioned social motivation in autism. Before intervention, child does not attend to therapist's face, a neutral stimulus which lacks reinforcer value. During the intervention, the therapist requires child to make eye contact in order to have access to highly preferred object or activity. Through conditioned reinforcement, the previously neutral stimulus, i.e. the face/eyes, eventually begins to function as a reinforcer itself. Through such interventions, brain regions responsible for encoding face stimuli, such as the fusiform gyrus and superior temporal sulcus, receive increased input and stimulation. Furthermore, brain regions responsible for 'affectively tagging' face stimuli, such as the amygdala, are activated through conditioned reinforcement. S, stimulus; R, positive reinforcement.

attention to faces, and (2) by altering the child's motivational preferences, such that engaging in face-to-face interaction becomes more rewarding, and more frequent. The latter mechanism may be important in explaining the robust and durable clinical effects of EIBI in some children, who seem to engage in social interaction and to learn new skills in social contexts after EIBI therapy is discontinued (Smith 1999).

It is possible that EIBI may result in improved *behavioural* performance on tasks related to face processing, but this improved performance may occur via alternative, atypical brain systems. Alternatively, early intervention may facilitate a more normal trajectory of brain development and thus have a fundamental impact on early developing brain systems. In the case of face processing, this might be reflected in more normal patterns of brain activity, as in electrophysiological and fMRI measures, e.g. a normal hemispheric specialization for faces.

The question of whether there might exist a sensitive period during which early intervention is most effective for altering the course of brain systems related to face processing is an important one. It has been shown that adult-level expertise in face processing develops gradually over years and is evidenced by increasing reliance of configural processing strategies (Carey & Diamond 1994). Le Grand et al (2001) found that deprivation of patterned visual input from birth until 2–6 months (due to bilateral congenital cataracts) results in permanent deficits in configural face processing. These results indicated that visual experience during the first few months of life is necessary for normal development of the face processing system. It is unknown whether the early abnormal experiences of young children with autism — i.e. reduced experience actively attending to faces co-occurring with normal or even accentuated experience with nonsocial patterned visual experience — has long-term effects on the development of the face processing system. It is clear, however, that the face processing system comes on line very early during infancy and is sensitive to experiential effects. Thus, very early intervention that enhances attention to faces and social interaction by making faces more rewarding may be optimal for best outcome in autism.

Early behavioural intervention may impact neural systems related to a wide range of domains, such as language. Given that electrophysiological measures of brain activity, such as high-density ERP, can be used with very young children to assess neural processing of a wide range of stimuli, such as speech and faces, this methodology can be useful for assessing whether and how early intervention affects brain development in young children with autism and other disabilities.

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References

Amaral DG, Price JL, Pitkanen A, Carmichael T 1992 Anatomical organization of the primate amygdaloid complex In: Aggleton J (ed) The amygdala. Wiley, New York, p 1–66

Anderson S, Romanczyk R 1999 Early intervention for young children with autism: continuum-based behavioral models. J Assoc Pers Sev Handicaps 24:162–173

Anderson SR, Avery DL, DiPietro EK, Edwards GL, Christian WP 1987 Intensive home-based early intervention with autistic children. Educ Treat Children 10:352–366

Bentin S, Allison T, Puce A, Perez E, McCarthy G 1996 Electrophysiological studies of face perception in humans. J Cogn Neurosci 8:551–565

Boucher J, Lewis V, Collis G 1998 Familiar face and voice matching and recognition in children with autism. J Child Psychol Psychiatry 39:171–181

Carey S, Diamond R 1994 Are faces perceived as configurations more by adults than by children? Vis Cogn 1:253–274

Carver L, Dawson G 2002 Development and neural bases of face recognition in autism. Mol Psychiatry 7:S18–S20

Damasio AR, Damasio J, Van Hoesen GW 1982 Prosopagnosia: anatomic basis and behavioral mechanisms. Neurology 32:331–341

Dawson G, Osterling J 1997 Early intervention in autism. In: Guralinick MJ (ed) The effectiveness of early intervention. Brookes Publishing Company, Baltimore, MD, p 307–326

Dawson G, Carver L, Meltzoff AN, Panagiotides H, McPartland J 2002 Neural correlates of face recognition in young children with autism spectrum disorder, developmental delay, and typical development. Child Dev 73:700–717

de Haan M, Nelson CA 1997 Recognition of the mother's face by 6-month-old infants: a neurobehavioral study. Child Dev 68:187–210

Desimone R, Albright TD, Gross CG, Bruce C 1984 Stimulus-selective properties of inferior temporal neurons in the macaque. J Neurosci 4:2051–2062

Doupe AJ, Kuhl PK 1999 Birdsong and human speech: common themes and mechanisms. Annu Rev Neurosci 22:567–631

Fagan J 1972 Infants' recognition memory for face. J Exp Child Psychol 14:453–476

Fenske EC, Zalenski S, Krantz PJ, McClannahand LE 1985 Age at intervention and treatment outcome for autistic children in a comprehensive intervention program. Special issue: early intervention. Anal Interv Dev Disabil 5:49–58

Goren CC, Sarty M, Wu PY 1975 Visual following and pattern discrimination of face-like stimuli by newborn infants. Pediatrics 56:544–549

Greenough WT, Black JE, Wallace CS 1987 Experience and brain development. Child Dev 58:539–559

Hobson RP, Ouston J, Lee A 1988a What's in a face? The case of autism. Br J Psychol 79:441–453

Kawashima R, Sugiura M, Kato T et al 1999 The human amygdala plays an important role in gaze monitoring: a PET study. Brain 122:779–783

Klin A, Sparrow SS, de Bildt A, Cicchetti DV, Cohen DJ, Volkmar FR 1999 A normed study of face recognition in autism and related disorders. J Autism Dev Disord 29:499–508

Le Grand R, Mondloch CJ, Maurer D, Brent HP 2001 Neuroperception. Early visual experience and face processing. Nature 410:890

Lovaas OI 1987 Behavioral treatment and normal educational and intellectual functioning in young autistic children. J Consult Clin Psychol 55:3–9

McCarthy G, Puce A, Gore JC, Allison T 1997 Face-specific processing in the human fusiform gyrus. J Cogn Neurosci 8:605–610

McPartland J, Dawson G, Panagiotides H 2001 Neural correlates of face perception in autism. Poster presented at the meeting of the Society for Research in Child Development, April 2001, Minneapolis, Minnesota

Mazur J 1994 Predicting the strength of a conditioned reinforcer: effects of delay and uncertainty. Curr Dir Psychol Sci 2:70–74

Morton J, Johnson MH 1991 CONSPEC and CONLERN: a two-process theory of infant face recognition. Psychol Rev 98:164–181

Nelson CA 2001 The development and neural bases of face recognition. Infant Child Dev 10:3–18

Osterling J, Dawson G 1994 Early recognition of children with autism: a study of first birthday home videotapes. J Autism Dev Disord 24:247–257

Pascalis O, de Haan M, Nelson CA 2002 Is face processing species-specific during the first year of life? Science 296:1321–1323

Rogers S 1998 Empirically supported treatment for young children with autism. In: Special issue on "Empirically supported psychosocial interventions for children". J Clin Child Psychol 27:168–179

Rolls ET 1984 Neurons in the cortex of the temporal lobe and in the amygdala of the monkey with responses selective for faces. Hum Neurobiol 3:209–222

Rolls ET 1992 Neurophysiology and functions of the primate amygdala. In: Aggleton JP (ed) The amygdala. Wiley, New York, p 143–165

Schultz RT, Gauthier I, Klin A et al 2000 Abnormal ventral temporal cortical activity during face discrimination among individuals with autism and Asperger syndrome. Arch Gen Psychiatry 57:331–340

Silverstein A, Lipsitt L 1974 The role of instrumental responding and contiguity of stimuli in the development of infant secondary reinforcement. J Exp Child Psychol 17:322–331

Smith T 1999 Outcome of early intervention for children with autism. Clin Psychol Sci Pract 6:33–49

Smith T, Groen AD, Wynn JW 2000 Randomized trial of intensive early intervention for children with pervasive developmental disorder. Am J Ment Retard 105:269–285

Taylor MJ, McCarthy G, Saliba E, Degiovanni E 1999 ERP evidence of developmental changes in processing of faces. Clin Neurophysiol 110:910–915

Walton GE, Bower TGR 1993 Newborns form 'prototypes' in less than 1 minute. Psychol Sci 4:203–205

Williams B 1996 Conditioned reinforcement: neglected or outmoded explanatory construct? Psychonomic Bull Rev 1:457–475

Williams GV, Rolls ET, Leonard CM, Stern C 1993 Neuronal responses in the ventral striatum of the behaving macaque. Behav Brain Res 55:243–252

DISCUSSION

Skuse: I would like to come back to something Chris Frith mentioned at the end of the last discussion, which was the lack of evidence for sensitive periods during early human development, and tie this in with the results in LeGrand et al (2001). I thought you developed rather beautifully some of the ideas that might be linked to that. Putting these ideas in a slightly different context, we were talking earlier about why the Romanian orphans might have developed autistic features. I suggested that there could be a sensitive period for eye contact which didn't happen, because they didn't have the opportunity to develop eye contact during that time. What I think is happening with some of these autistic infants is we have the same process — lack of eye contact — but for a different reason, because they find eye contact aversive in that early period. You mentioned the fact that at a year eye contact was the best predictor of later autistic behaviours. We propose that it is over-arousal of the threat detection system that lies behind the failure of these infants to make normal eye contact. Effectively, you have two different circumstances: one avoiding eye contact because it is aversive or threatening, the other lack of experience of eye contact, both of which are leading to maldevelopment of the same system. We can easily imagine how to compensate for the lack of experience, but what do you do in order to encourage these infants who may be avoiding eye contact because it is a stressful experience? How are you going to ensure that they have the appropriate experiences so that these neural circuits develop normally and predispose towards better social cognitive skills in later life?

Dawson: The notion that making eye contact is aversive for children with autism is a very attractive one, and it has been around for a long time. But when we try to investigate it, we don't find much evidence for it. Clinically one does not get the experience from the majority of children that they are finding eye contact aversive. I don't think it is a closed question, but the majority of evidence favours the idea that whatever mechanisms drive attention to faces are not working properly, but not necessarily that children find eye contact aversive. There are conditions, such as fragile X syndrome, where that kind of aversive reaction can be demonstrated with physiological measures. It would be nice to do some systematic experiments comparing children with autism and those with fragile X. Marion Sigman's study did this in young children with autism and Down syndrome (Corona et al 1998). They measured autonomic arousal in response to social stimuli, and found that children with autism were hyporesponsive.

C. Frith: The interesting thing about the Romanian orphans is that they recovered to a large extent. But going back to your point about social stimuli not being rewarding for autistic children, it seems to me that there are two aspects to this. In order for social stimuli to be rewarding, the first stage in this process is that the brain has to have a way of distinguishing between social stimuli and non-social stimuli. In the case of faces this may be easier, but there are all sorts of other social stimuli. What I am particularly interested in is how this distinction is made. Perhaps the problem lies in making the distinction rather than with the reward.

Dawson: It could be that the problem is at the encoding level. This would make things somewhat simpler.

Schultz: Yes, but there is also a fast pathway that gets to the amygdala even before it gets to the perceptual areas of the ventral temporal and occipital cortex that can discriminate between faces and objects. This so-called fast pathway may be intimately tied up with the reward system; certainly there are close anatomical connections between the amygdala and the ventral striatum. My point, I guess, is that I don't think we should conceive of perceptual encoding as a singular phenomenon, one that occurs through information processing along just one pathway: there is more than one feed into the fusiform face area, and some feeds may already be contextualized with reward value or information on emotional salience. For the most part, processing of reward value happens before the type of perceptual recognition processing that we are speaking about, but this may well be a reverberating process.

Bailey: There's also a direct fast pathway to the fusiform, as well.

Rutter: As the Romanian adoptees have come up twice, let me outline a few key findings, because they are intriguing in providing partial support and also partial querying of the programming notion. I will focus on two outcomes, cognitive level and attachment dysfunction (meaning mainly disinhibited unselective social interaction). We found remarkable catch-up in cognition, but the effects of duration of institutional care on outcome at age six were enormous (O'Connor et al 2000). There was a 20-point difference between those who had institutional care for more than two years as against those who had it for less than 6 months. Interestingly, the difference was as great at 6 as it was at 4. Cognitive impairment was significantly associated with a smaller head circumference both at the time of UK entry and at follow-up. This is relevant in terms of what was discussed earlier about whether it was possible to make heads grow: it is possible. But what was also striking was that, in the group who had at least two years of institutional care, the range of outcomes was enormous. The IQ as measured at age 6 ranged from the severely retarded level to above 130. The persistence of deficits suggest some type of programming effect in that there was a massive persisting effect of early experience. But what is the cause of the large individual variation in outcome. The attachment results were both similar and different (O'Connor & Rutter 2000). There was the same massive effect of duration of institutional care. It was different, however, in that there was no association, either initially or at outcome, with head circumference. For me, the findings raise distinctions between what two appear to be different types of programming. There is what Bill Greenough talks about as 'experience expectant'. The best model for this is the Hubel & Wiesel findings on vision. Relevant visual experience is necessary for normal development of the visual cortex of the brain. However, the range of visual experiences that provide what is needed is very wide. Variations in experiences within the normal range are not relevant. Experience-adaptive programming, exemplified by the phonological findings of Pat Kuhl and David Barker's work on nutrition, is different in that it concerns variations within the normal range, as well as outside it. But it is not concerned with whether brain growth is normal or abnormal. Rather, it concerns adaptation of neural functioning to the environment that exists during a particular sensitive period in development (Rutter 2002). In relation to autism, which type of programming might be operative? If it is the experience–expectant kind, can one conceptualize that the defects they are born with provide such a restriction on experiences that it is stopping normal development? If it is experience–adaptive programming, what are the implications for intervention? It has been argued in relation to diet that, if in middle childhood extra nutrition is provided to make up for the early lack, it may make things worse (Rutter 2002).

Dawson: Could you expand on that?

Rutter: The empirical evidence is that early subnutrition (prenatal and first year of life) is associated with a marked increase in the liability to coronary artery disease, late onset diabetes and other conditions. In adult life, it is the opposite way round. David Barker argues, plausibly but without a solid physiological basis yet, that the body metabolism is being programmed to deal with subnutrition. If then you overload it you are making things much worse. Whether there is a psychological equivalent of this is unclear. It is an intriguing notion because it would have radical implications for intervention.

Sigman: When I heard about this I went to speak to nutritionists to see whether they thought the evidence is good. Pretty much everyone was sceptical. In our long-term outcomes we will have to look at these kinds of effects.

Lipkin: This is interesting. I heard Barry Levin of the University of Medicine and Dentistry in New Jersey talk about force feeding rats to obesity during pregnancy. He has found that obese mothers give rise to progeny who subsequently become obese (Levin 2000). This becomes a trait that is carried forward for several generations.

Rutter: It is an intriguing set of notions, but this area requires some experimental physiological evidence and testing of whether the mechanism is correct. The empirical findings are indisputable.

Dawson: It would be interesting to find children very young to see what kinds of changes can occur. But when you think about autism and the kinds of things that are disrupted, and the abnormalities that are present in brain function and behaviour quite young, it makes me think we are looking at very early dysfunction in experience–expectant processes. Intervening early on these processes may be our best hope.

Monaco: I was particularly struck by the non-lateralized, non-specific activation you showed with the face processing. How much does this generalize to other things that could be tested as deficits in autism? If this is true, could this gross activation of the brain increase the susceptibility for epilepsy?

Dawson: Pat Kuhl has looked at brain lateralization using ERP for speech sounds. She found abnormal hemispheric specialization. She didn't look at topography in terms of amount of cortex activated, but it is completely measurable. You also could look at this in an fMRI context. In our ERP study comparing three-year olds with autism to those with typical development and that you could use to demonstrate behaviourally that the autistics are not using the fast route.

Schultz: I agree, there are many interesting questions, but unfortunately the studies have not yet been done to provide answers to most of these questions. This subcortical pathway passes information from the retina to the superior colliculus, to the thalamus, and then onto the amygdala. Somehow the superior colliculus and thalamus (primarily the pulvinar) is perceiving something about that stimulus to cause it to be prioritized and fed to the amygdala for rapid analysis. I am not sure about the exact role of each of the three nodes in that pathway in perception. We are very interested in the fast pathway with regards to a possible role in the ontogeny of autism, because it is likely to be the one active in the first months of life, before the cortex comes online. In this regard, it may be the first stumbling block for the person with autism.

Bailey: There is some variability in the face-processing findings between groups, and according to the method used. What strikes me is that it is a good model system because we know a lot about face processing and a fair bit about neuroanatomy very early in life. If we give adults a task in which they simply see a range of objects and faces, we do not currently detect this fast response. It is only evident in a paired task where the subject sees one image after another, and the task is to identify whether the second image is the same as the first. It may be that the difference is simply that there are greater attentional demands, or that working memory is being recruited. But we cannot yet see the fast activity in the single image paradigm. When a first face image is seen by normals in a paired paradigm, there is activity that is either parietal or thalamic, followed by anterior temporal/posterior frontal regions and then fusiform gyrus. In individuals with autism or Asperger syndrome the pattern is completely different in that the activity is elicited by the second image and there is hardly any activity in the fusiform gyrus. They seem to be responding fundamentally differently. What we are having problems with is whether this is a difference in innate wiring, or is it to do with social reward mechanisms which generally lead to faces being processed in the fusiform region? When one examines the current dipoles evoked by faces, they orient in the same direction in normals, who are presumably all activating a similar region in which the neurons are oriented in a similar way. In autistic individuals we find that they are activating a whole host of areas around fusiform and the dipoles are randomly oriented. That is, in each individual it as though face associated activity is colonizing a somewhat different bit of cortex.

Amaral: I wanted to comment on Chris Frith's question about these fast pathways to the amygdala. As far as we know, for the auditory system the subcortical fast pathway that goes directly to the amygdala carries information about the volume of the sound, but not very much about the tones. It is very similar in vision: there are nuclei that have some visual information that project to the amygdala: the peduncular nucleus and the medial nucleus of the pulvinar. As far as I know there are no face neurons in these regions. My presumption has always been that you may be able to get some kind of visual information, but it won't be very discriminative. It would only be by going through the V1 infratemporal cortex pathway that you could get discriminative facial information in the amygdala. This subcortical pathway has not been well studied for the visual system. I presume that there is some kind of visual information getting in.

Bailey: The interesting thing is that we do see some activity with other classes of object, but the pattern is different and the response doesn't seem to be as great (Bräutigam et al 2001). What we are wondering is what are the minimum facial features that are needed to elicit this activity? The experiments we have just done with Anneli Kylliäinen, in Riitta Hari's laboratory, are to show affected children faces in pairs in which either the eyes are open or shut, and with gaze either averted or straight ahead. We suspect that eyes may well be the critical features.

C. Frith: In your experiment, it is interesting that you only found this with the pairs of images. I wonder whether there is some sort of priming effect.

References

Bräutigam S, Bailey AJ, Swithenby SJ 2001 Task-dependent early latency (30–60 ms) visual processing of human faces and other objects. Neuroreport 12:1531–1536

Corona R, Dissanayake C, Arbelle S, Wellington P, Sigman M 1998 Is affect aversive to young children with autism? Behavioral and cardiac responses to experimenter distress. Child Dev 69:1494–1502

Le Grand R, Mondloch CJ, Maurer D, Brent HP 2001 Neuroperception. Early visual experience and face processing. Nature 410:890

Levin BE 2000 Metabolic imprinting on genetically predisposed neural circuits perpetuates obesity. Nutrition 16:909–915

O'Connor TG, Rutter M 2000 Attachment disorder behavior following early severe deprivation: extension and longitudinal follow-up. English and Romanian Adoptees Study Team. J Am Acad Child Adolesc Psychiatry 39:703–712

O'Connor TG, Rutter M, Beckett C, Keaveney L, Kreppner JM 2000 The effects of global severe privation on cognitive competence: extension and longitudinal follow-up. English and Romanian Adoptees Study Team. Child Dev 71:376–390

Rutter M 2002 Nature, nurture, and development: from evangelism through science toward policy and practice. Child Dev 73:1–21