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Neurodevelopment of Social / Non-social Functioning Differences in Autism

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Background

Autism is a pervasive developmental disorder that is diagnosed based on behavioural criteria for impairments in social skills, communication and language skills, and restricted interests and repetitive behaviours. Autism is currently considered to be a “spectrum” disorder, with three similar Pervasive Developmental Disorders now being termed Autism Spectrum Disorders (ASDs): *Autistic Disorder*, *Aspergers Disorder*, and *Pervasive Developmental Disorder – Not Otherwise Specified* (PDD-NOS). Individuals with these three different ASDs differ somewhat in regards to the nature and/or severity of their early language and intellectual difficulties, as well as their restricted interests and repetitive behaviours. However, individuals with these different ASDs are similar in that they share impairments in social and communication skills, and that the onset of their difficulties begins by three years of age (American Psychiatric Association, 2004).

Because ASDs are characterised by behavioural impairments in social and communication skills, scientists have very reasonably focused a great deal of attention and research on identifying impairments in social-cognitive brain and behavioural functioning in this population over the past several decades. For example, a great deal of research attention has been focused on both the neural and perceptual bases of the processing of human faces in

individuals on the autism spectrum (Dawson, Webb, & McPartland, 2005; Schultz & Robins, 2005). Much of this work has been motivated by theoretical models positing that previously documented reductions in behavioural orienting to other people's faces and voices in children with autism likely leads to reduced expertise with face stimuli in this population (Carver & Dawson, 2002; Marcus & Nelson, 2001). Others have argued that the face processing and other social-cognitive impairments that have been uncovered may reflect core impairments in specific brain regions or networks, thereby elucidating the potential cause of autism (Schultz, 2005; Schultz, Grelotti, Klin, Kleinman, Van der Gaag, Marois, & Skudlarski, 2003).

Recently, scientists have challenged the proposal that impaired social-cognitive processing is the core characteristic of individuals with autism. For example, Jemel, Mottron, and Dawson (2006) reviewed 10 years of research on face processing in individuals with ASD and came to several conclusions. First, they argue that face processing differences uncovered in individuals with ASD relative to controls are too subtle and inconsistent to warrant the levels of attention they have been given in the literature. Second, they argue that the key difference in face processing in ASD is not an impairment at all and, instead, may be a simple difference in preferred (or "default") perceptual processing strategy. Specifically, they argue that individuals with autism exhibit an increased natural tendency to focus on the local features and details of faces (and other stimuli), as opposed to a perceptual impairment in integrating global or holistic information in faces as had been suggested previously (e.g., McPartland, Dawson, Webb, Panagiotides, & Carver, 2004; Schultz & Robins, 2005). This argument is supported by research showing that individuals with autism are equally as good at using low spatial frequency (i.e., global) information to identify peoples' faces as well-matched controls when they are explicitly asked to do so, and are also better than well-matched controls at using high spatial frequency (i.e., local feature) information under similar conditions (e.g., Deruelle, Rondan, Gepner, & Tardif, 2004; Rondan & Deruelle, 2007). Finally, they argue that this bias in perceptual processing strategy may also be the root cause of both the neural and perceptual differences observed between individuals with ASD and control participants, which have traditionally been interpreted as reflecting core impairments in social brain networks (e.g., McPartland et al., 2004; Schultz & Robins, 2005).

The critique of the face processing literature by Jemel, Mottron, and Dawson (2006) reflects a larger debate in the field, which is related to the roles of impaired versus enhanced abilities in understanding autism. This debate has largely emerged from differences in the types of evidence uncovered by different research groups, as well as differences in the perspectives taken in response to this evidence (Mottron, 2011). Space limitations preclude us from discussing the over-arching theoretical models for cognitive functioning in autism, such as the Theory of Mind (Baron-Cohen, 1995; Baron-Cohen, Leslie, & Frith, 1985), Weak Central Coherence (Happé & Frith, 2006), and Executive Dysfunction (Russell, 1997) theories, in this chapter. We do note, however, that recent debate in this area has resulted in a notable shift in perhaps the most dominant model, the Theory of Mind model. Specifically, a revision of this psychological theory suggests that the cognitive profile of individuals on the autism spectrum is one of impaired Empathising with others and enhanced Systemizing, relative to typical individuals (Baron-Cohen, 2009). Previously, this theory primarily emphasised impairments in the social cognitive ability of understanding what others are thinking, feeling, and intending (Baron-Cohen, Leslie, & Frith, 1985). This recent revision, then, maps onto an increased emphasis on the idea of imbalance between social and non-social processing and abilities in autism.

Importance of Development

Research and debate on the relative roles of social and non-social factors, in terms of both explaining cognition and elucidating causal biological mechanisms for the social difficulties exhibited by those with autism, is important. To date, however, the vast majority of this debate has been had on the basis of experimental assessments of older children and adults. This approach has a high likelihood of continual suffering from the proverbial “chicken and the egg” problem. This is because it is clearly difficult, and often impossible, to determine the direction in which the causal arrow has had its influence. For example, when older children or adults who have been experiencing autism for a number of years exhibit both impairments in social processing and enhancements in non-social processing, it is unclear whether impairments in social cognitive functioning have enhanced development of non-social

abilities, whether enhanced non-social abilities have negatively impacted upon social cognitive development, or whether autism is the direct result of a core imbalance in the functioning of social versus non-social processing mechanisms from very early in life. In order to understand this relationship, it is important to examine social and non-social processing from the earliest onset of the disorder, and even prior to that when possible.

As indicated at the outset of this chapter, at least some of the symptoms of ASDs must onset prior to three years of age (American Psychiatric Association, 2004). Despite extensive research aimed at lowering the age of effective diagnosis, ASDs cannot currently be reliably diagnosed until approximately 36-months of age, with some cases that are associated with notable language and/or cognitive delays presenting clearly and persistently as early as 24 months of age (Chawarska, Klin, Paul, Macari, & Volkmar, 2009; Chawarska, Klin, Paul, & Volkmar, 2007; Rogers, 2009; Zwaigenbaum, Bryson, Lord, Rogers, Carter et al., 2009; see also Klin, Chawarska, Paul, Rubin, Morgan, Wiesner, & Volkmar, 2004). Therefore, the period around this time should be one of the most informative in regards to identifying processing differences that may more accurately reflect the relative roles of social versus non-social mechanisms as core components of autism. We turn to studies of neural processing mechanisms in children in this age range in the next section.

Face and Object Processing in Young Children with Autism

Event-related potentials (ERP) are a technique for the study of human brain functioning. This technique is especially useful in research with infants and children from both typical and clinically disordered populations, including even those who are nonverbal (Nelson & McCleery, 2008). ERPs are non-invasive, pose no known risks to research participants, and do not require an overt behavioural response. This technique capitalises on the fact that, upon stimulus presentation, groups of neurons fire simultaneously and generate electrical activity that can be recorded from electrodes placed over the scalp. ERPs are averages of epoch of this activity that are time-locked to specific stimuli (e.g., a picture or a sound), and appear as a series of positive

and negative deflections. The amplitude, latency, and distribution of these deflections across the scalp provide valuable information about the timing, sequence, amount, and general location of neural activity associated with various sensory, perceptual, and cognitive processes.

Over the last two decades, ERP assessments have provided a wealth of information about the neural processing of social and non-social information in individuals with autism. ERPs have played a particularly critical and dominant role in our understanding of both neural and cognitive/perceptual processing early in life in autism (Dawson, Webb, & McPartland, 2005; Grice, Halit, Farroni, Baron-Cohen, Bolton, & Johnson, 2005; Kuhl, Coffey-Corina, Padden, & Dawson, 2005; McCleery, Ceponiene, Burner, Townsend, Kinnear, & Schreibman, 2010; Nelson & McCleery, 2008; Webb, Jones, Merkle, Venema, Greenson, Murias, & Dawson, 2011). Here, we focus on the literature on visual social and non-social processing; specifically, face and object processing, during early childhood in autism.

A notable advantage of recording brain activity using ERPs is that it allows one to directly examine the processes that may underlie social versus non-social differences observed using traditional behavioural measures. It has long been known that children with autism do not orient to other people as often as do typically developing children (Dawson, Meltzoff, Osterline, & Brown, 1998; Dawson, Toth, Abbott, Osterling, Munson, Estes, & Liaw, 2004; Klin, 1991; Kuhl et al., 2005). More recently, using eye-tracking technology, Klin and colleagues found that, when presented with videos of humans moving and videos of non-human objects moving in a side-by-side comparison, very young children with autism look equally at these two types of videos, whereas typically developing and developmentally delayed children consistently prefer to look at the people over the objects (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; see also Pierce, Conant, Hazin, Stoner, & Desmond, 2011). Klin has also found that children with autism show no preference for listening to their mother's voice relative to the sounds of a noisy café, whereas typically developing children consistently exhibit a preference for their mother's voice (Klin, 1991; see also Kuhl et al., 2005). However, despite the consistency of these results, these findings do not clarify the mechanisms underlying the observed differences in behavioural preference. For example, in the recent study of preference for human motion versus non-human object motion by Klin and colleagues, the authors re-

ported convincing data that the visual preferences of the children with autism were driven by enhanced attention to audio-visual temporal synchrony that cut across the human and non-human motion videos (Klin et al., 2009). Given these results, it is impossible to determine whether the lack of preferential looking for the human versus non-human motion was caused by impaired mechanisms driving preference for human motion, enhanced mechanisms driving preference for non-social auditory-visual temporal synchrony, or a core imbalance between human and non-human processing mechanisms. ERP recordings provide an opportunity for the direct and separate examination of social and non-social processing mechanisms.

Several studies conducted by Dawson and colleagues have utilised ERPs to examine face processing in young children with autism (aged 3- to 4-years). In one study, they examined the processing of familiar and unfamiliar faces and objects. Specifically, they showed children with ASDs and typically developing (TD) children pictures of their mother's face, a stranger's face, their favourite toy, and a toy they had never seen before. In one published report, they compared the early perceptual processing differences for the face versus object stimuli (Webb, Dawson, Bernier, & Panagiotides, 2006), and for the other published report they focused on somewhat later brain activity associated with the discrimination of familiar versus



Figure 1. Young child wearing a high-density (128-channel) electroencephalography (EEG) Sensor Net (Electrical Geodesics, Inc., Eugene, Oregon) for a study of face versus object processing. University of Birmingham, England. Photo Credit: Antonis Christou.

unfamiliar faces and objects (Dawson, Carver, Meltzoff, Panagiotides, McPartland, & Webb, 2002). For the comparison of early perceptual processing of faces versus objects, they found an interaction between stimulus type (face, object) and group (ASD, TD), which was driven by a significant difference in the amount of activity used by the two groups of children during object processing. Specifically, the ASD children exhibited *less* brain activity during object processing compared to the TD children. No differences in face processing were observed between the two groups during this early stage of perceptual processing.

For the comparisons of familiar and unfamiliar face and object processing, the ERPs of the TD children were different for mother's face and stranger's face at both an early cognitive and a late cognitive stage of processing. The same ERP components of these children also differed for their favourite toy versus an unfamiliar toy. On the other hand, the ERP responses of the ASD children differentiated familiar versus unfamiliar toys in the same early and late cognitive components as the typically developing children, but they did not differentiate mother's face from stranger's face at either of these stages of processing (Dawson et al., 2002). These results suggest impaired processing that is specific to social stimuli at both an early cognitive and a late cognitive stage of processing in young children with autism.

Two further studies shed light on social processing mechanisms in young children with autism. The first is a study of emotional face processing in 3- to 4-year old ASD and TD children. In this study, children were presented with pictures of faces posed in fearful and neutral emotional expressions while ERPs were recorded. The results showed that TD children exhibited more brain activity in response to the fearful relative to the neutral face at both an early perceptual stage of processing and a late cognitive stage of processing. The ASD children, however, did not exhibit any differences in terms of amount of brain activity at any stage of processing (Dawson, Webb, Carver, Panagiotides, & McPartland, 2004). These results suggest that the recognition of categories of facial emotion is impaired at both an early perceptual stage and a late cognitive stage in young children with autism.

Another study that sheds light on early social processing mechanisms in young children with autism is a study of eye gaze processing. In this study,

participants were 3- to 7-year old ASD and TD children. Participants were presented with pictures of faces that were either looking directly forward (i.e., gaze directed at the participant) or looking to the side (i.e., averted gaze). This study design was based on a previous study of very young TD infants that had found that gaze directed at the infant participants elicited more brain activity at an early perceptual stage of processing. In this study of children with and without ASDs, the ERPs of the TD children showed no difference in response to direct versus averted eye gaze. However, the ERPs of the children with ASDs differentiated direct and averted gaze at the same early perceptual stage of processing as the infants in the highly similar previous experiment. The authors interpreted these results to reflect delayed development of eye gaze processing mechanisms in the children with autism (Grice et al., 2005).

These studies of the neural correlates of social and non-social processing early in young children diagnosed with autism provide a number of valuable insights into the potential roles of social versus non-social factors in autism. First, in the only published study that has directly compared face and object processing in young children with autism, there was evidence for atypical processing of objects, but not faces, at an early perceptual stage of processing. Specifically, the children with ASDs exhibited less brain activity when processing objects, compared with TD children. This stage of processing is most well-known as the stage at which the structure of face and object stimuli is encoded, suggesting the possibility that there is something unusual about the way in which young children with ASDs initially encode objects as a class of stimuli separate from faces.

The second thing that we can take away from these research studies is that face processing is atypical at several stages in young children with autism, and that the specific stage at which the abnormalities present themselves is at least somewhat dependent upon the specific types of social contrasts presented. For example, while the early perceptual processing of neutral faces appears to be relatively normal in these children, the recognition of fearful faces appears to be atypical at this same stage of processing.

A notable limitation to the ERP literature on young children with autism at the current time is that the majority of studies conducted to date have not included any non-social comparison or control stimuli in their research designs. This makes it impossible to determine whether or not any of the ob-

served differences in brain responses to social stimuli reflect specific impairments in social cognitive processing or, instead, reflect more generic differences in perceptual or cognitive processing.

Face and Object Processing in Infants Siblings of Children with Autism

Autism is believed to be caused by a complex combination of multiple genetic and environmental factors, but twin studies examining the concordance of autism in monozygotic versus dizygotic twins provide evidence that genetics play a key role (Bailey, Braeutigam, Jousmaki, & Swithenby 2005; Folstein & Rutter 1997; Ritvo, Jorde, Mason-Brothers, Freeman, Pingree, Jones et al., 1989; see also Hallmayer, Cleveland, Torres, Phillips, et al., 2011). In addition to high genetic influence on the development of autism itself, milder versions of the social, communication, and other difficulties experienced by individuals with ASD have also been documented in unaffected first-degree relatives (i.e., siblings, parents) of individuals with ASD. A number of studies have documented differences in social and communication skills and preferences (Adolphs, Spezio, Parlier, & Piven, 2008; Bishop, Maybery, Maley, Wong, Hill, & Hallmayer, 2004; Bolton, MacDonald, Pickles, Rios, Goode, Crowson, Bailey, & Rutter, 1994; Dalton, Nacewicz, Alexander, & Davidson, 2007; Murphy, Bolton, Pickles, Fombonne, Piven, & Rutter, 2000; Pickles, Starr, Kazak, Bolton, Papanikolaou, Bailey, Goodman, & Rutter, 2000; Piven, Palmer, Landa, Santangelo, Jacobi, & Childress, 1997; Smith, Lang, Kryzak, Reichenberg, Hollander, & Silverman, 2009), as well as language abilities (Folstein, Santangelo, Gilman, Piven, Landa, Lainhart, Hein, & Wzorek, 1999; Landa, Folstein, & Isaacs, 1991; Piven et al., 1997). Evidence has also been found for subtle impairments in executive functions (Hughes, Leboyer, & Bouvard, 1997; Piven & Palmer, 1997) and for an enhanced locally-oriented processing style in these individuals (Baron-Cohen & Hammer, 1997; Happe, Briskman, & Frith, 2001). These results provide evidence that the complex genetic mechanisms that contribute to the development of autism also affect other members of families affected by autism. This, then, opens up the opportunity to explore the effects of familial/genetic risk factors on brain and behavioural development early in life in

ASD, through the study of infant siblings of children already diagnosed with ASDs (Rogers, 2009; Yirmiya & Charman, 2010).

Extensive research has been conducted on the development of social behaviour in infants who are at high risk for developing autism (i.e., “high risk infants”), with a great deal being learnt about the earliest development of behavioural signs for ASDs (Zwaigenbaum et al., 2009). Despite fairly extensive research in this area, however, a recent review concludes that the evidence suggests that the core social and communication differences that are characteristic of autism later in development do not emerge in early infancy (Rogers, 2009). Instead, social and communication skills often develop on a relatively normal course until at least 9- to 12-months of age in infants who later go on to develop autism, and these social and communication difficulties are not sufficiently clear to warrant diagnosis until after 24, or sometimes 36, months of age. On the other hand, repetitive and unusual sensory behaviours (often with toys) have been found to emerge earlier in development than impairments in social and communications skills in this population (Rogers, 2009).

Over the past few years, a number of ERP studies of infant siblings of children with autism have examined the neural processing of social and non-social information. In fact, the studies conducted to date roughly correspond to those ERP studies of young children diagnosed with autism described above. For example, we recently reported an ERP study of face versus object processing in 10-month-old high-risk infants. In this study, we approximately replicated previous research findings of atypicalities in the perceptual processing of non-social objects in young children with autism. Specifically, we found that the perceptual processing of objects was faster for high-risk infants relative to control infants with no family history of autism. The speed of perceptual processing of faces was the same in these two groups (McCleery, Akshoomoff, Dobkins, & Carver, 2009). Faster object responses of high-risk infants suggests the possibility that familial/genetic risk for autism is associated with either enhanced attention to, or enhanced fluency in, the processing of objects. Interestingly, one year after the publication of our ERP study, Noland and colleagues produced behavioural evidence for enhanced working memory for non-social stimuli in 6- to 9-month old infant siblings of children with autism (Noland, Reznick, Stone, Walden, & Sheridan, 2010). In this study, Noland and colleagues also found

no evidence for impaired memory for faces in these infants.

In 2011, Luyster and colleagues reported an ERP study of the processing of mother's face versus stranger's face in 12-month-old infant siblings of children with autism. The study methods were almost identical to those employed in the previous study of familiar and unfamiliar face and object processing in young children with autism, described earlier, with the exception that only face (and not object) stimuli were used. The results of this study showed that the discrimination of the faces of mother and stranger is highly similar between infant siblings of children with autism and infants without a family history of autism at this age, providing no evidence for an impairment in face recognition (Luyster, Wagner, Vogel-Farley, Tager-Flusberg, & Nelson, 2011).

In another ERP study, Elsabbagh and colleagues utilised ERPs to examine the neural correlates of eye gaze processing in high-risk infant siblings. The study methods were almost identical to those employed in the previous study of direct versus averted gaze processing in young children with autism, described earlier. The results of this study revealed evidence for atypical eye gaze processing in the high-risk infants. Interestingly, however, this atypicality did not reflect an absence of discrimination of direct versus averted gaze in these infants. Instead, the ERPs of both high-risk and low-risk infants reliably discriminated faces presenting direct versus averted gaze, but did so in different ways (Elsabbagh, Volein, Csibra, Holmboe, Garwood, et al., 2009).

These studies of the neural correlates of social and non-social processing in infant siblings of children with autism provide further insights into the potential roles of social versus non-social factors in autism. First, in the only published study that has directly compared face and object processing in infant siblings of children with autism, there was evidence for atypical processing of objects, but not faces, at an early perceptual stage of processing. Second, the evidence for social processing impairments in these infants is less consistent than in young children who have already been diagnosed with autism.

As in the ERP literature on young children diagnosed with autism, a notable limitation to the ERP literature on infant siblings of children with autism is that the majority of studies conducted to date have not included any non-social comparison or control stimuli in their research designs. This

makes it impossible to determine whether or not any of the observed differences in brain responses to social stimuli reflect specific impairments in social cognitive processing or, instead, reflect more generic differences in perceptual or cognitive processing. A number of sensory, perceptual, and cognitive differences that have the potential to account for such atypicalities have already been documented in young infant siblings of children with autism (Elsabbagh, Volein, Holmboe, Tucker, et al., 2009; Holmboe, Elsabbagh, Volein, Tucker, et al., 2010; McCleery, Allman, Carver, & Dobkins, 2007).

Summary and Conclusions

In this chapter, we have reviewed evidence from event-related potentials brain imaging studies of the early development of children with autism spectrum disorders. From the results of these studies, we have argued that autism is best examined in terms of the possibility for atypicalities in both social and non-social functioning. Furthermore, we have argued that the evidence to date suggests the distinct possibility of developmental change, with non-social functioning differences potentially being more prominent early in life in this population. If true, this would suggest different approaches to understanding both the causes and consequences of autism spectrum disorders, as well as how these causes and consequences are addressed in future research and practice.

In terms of causes, the results of the review in this chapter suggest that we must consider the possibility that autism may be caused, in part, by atypicalities in core brain systems involved in sensory, perceptual, and/or cognitive processing that are either specific to non-social (e.g., object) stimuli, or that cut across both social and non-social stimulus processing. In particular, we have raised the possibility that the visual processing of non-social / object stimuli may be somehow enhanced at the perceptual stage of processing, perhaps as a result of increased attention, motivation, or neural processing fluency. This, in turn, may have negative downstream developmental effects on the later development of social interactive and communication skills. This view contrasts sharply with a number of current and previous theories of the causal mechanisms for autism, and most notably those that

have suggested that autism is due, first and foremost, to core impairments in the “social brain network” (Schultz, 2005; Schultz, Grelotti, Klin, Kleinman, Van der Gaag, Marois, & Skudlarski, 2003).

The possibility that autism may be best characterised first by increased motivation toward non-social stimuli early in life also has potential implications for early behavioural intervention. A number of evidence-based behavioural interventions are, in fact, already designed to use existing motivations for engagement with non-social objects in children with autism in an effort to increase engagement with other people (Frost & Bondy, 2002; Ingersoll, 2010; Koegel & Koegel, 1996). Furthermore, recent research has found motivation to engage with objects, as indexed by levels of toy contact, to be a predictor of positive response to naturalistic play-based behavioural intervention in toddlers and young children with autism (Schreibman, Stahmer, Barlett, & Dufek, 2009; Sherer & Schreibman, 2005). These data already provide support for the notion that non-social functioning differences are an important variable to consider in intervention planning. The results of both on-going and future research studies aimed at examining the neural mechanisms associated with improvements in social and communication skills that result from early intensive behavioural intervention will be important for understanding the relationships between social and non-social processing and impaired social and communication behaviours early in life in this population. These findings, in turn, will inform us as to the core causal mechanisms for autism spectrum disorders.

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