Disengagement of Visual Attention in Infancy is Associated with Emerging Autism in Toddlerhood

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Background: Early emerging characteristics of visual orienting have been associated with a wide range of typical and atypical developmental outcomes. In the current study, we examined the development of visual disengagement in infants at risk for autism.

Methods: We measured the efficiency of disengaging from a central visual stimulus to orient to a peripheral one in a cohort of 104 infants with and without familial risk for autism by virtue of having an older sibling with autism.

Results: At 7 months of age, disengagement was not robustly associated with later diagnostic outcomes. However, by 14 months, longer latencies to disengage in the subset of the risk group later diagnosed with autism was observed relative to other infants at risk and the low-risk control group. Moreover, between 7 months and 14 months, infants who were later diagnosed with autism at 36 months showed no consistent increases in the speed and flexibility of visual orienting. However, the latter developmental effect also characterized those infants who exhibited some form of developmental concerns (but not meeting criteria for autism) at 36 months.

Conclusions: Infants who develop autism or other developmental concerns show atypicality in the development of visual attention skills from the first year of life.

Key Words: Autism, disengagement, familial risk, infant, prospective study, visual attention

Autism spectrum disorders (ASD) (henceforth autism) are primarily defined on the basis of social and communication impairment in childhood. Recent lessons from genetic studies have highlighted substantial overlap between autism and related conditions (1). Strictly defined, clinical categories do not capture our current understanding of the increasingly multidimensional and complex clinical, cognitive, and behavioral phenotypes associated with the condition (2). There is increasing interest in understanding neurodevelopmental pathways, potentially overlapping across multiple clinically defined childhood disorders.

Central to the phenotype of autism are patterns of focal and narrowed attention focus (3,4). Individuals with autism are often described as having a narrow focus of attention and interest, as well as acute perception for details. For example, unlike typically developing individuals, the cognitive processing style in autism appears to be biased toward local rather than global or configural information (3,5). This sometimes results in superior performance on tasks that benefit from these abilities (4). In brain imaging studies of adults with autism, increased activation of sensory ventral-occipitotemporal areas and decreased activation in prefrontal areas have been described as reflective of these processing differences in local versus global information (6).

A specific developmental account of the origins of the narrow processing style observed in autism relates to early emerging difficulties in visual attention (7). According to this view, the infant's inability to flexibly switch the locus of attention leads to problems in self-regulation, as well as a decrease in orienting to socially relevant stimuli. Reduced orienting to social stimuli has been documented in preschool age children with autism (8,9). Moreover, in research on typical infants, individual differences in attention skills relate to differences in local versus global processing styles, and this association may have implications for the emergence of autism. As typically developing children begin to flexibly scan their environment and switch their attention between different objects, global forms become processed more rapidly and efficiently. Individual infants who exhibit a pattern of prolonged look durations on a single feature or object tend to rely more on local elements when processing visual stimuli (10,11).

Supporting evidence for the proposal that the development of visual attention plays a critical role in autism comes from studies using the gap-overlap task with children and adults. This task measures flexibility in attention switching in response to the presentation of a peripheral target in the presence or absence of a central fixation stimulus. A disengagement index is typically derived from this task measuring the cost of disengaging from a central stimulus to orient to a peripheral one. Thus, the gap task is also thought to reflect top-down control of attention (12). A number of studies using this task have demonstrated impairments in children and adults with autism both behaviorally as well as neurophysiologically (13,14).

Little is known about the early development of visual attention in autism because the condition is rarely diagnosed before 2 years of age. Converging lines of evidence indicate that general deficits, as well as specific precursors to some symptoms, are present early on in autism [reviewed in (15)]. By the age of diagnosis, several co-occurring impairments are clear and encompass both social and nonsocial domains. After the onset of these

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symptoms in the early years, different sets of abilities show varying trajectories of development. Some abilities, such as face processing, begin as seriously impaired, but over time, compensatory strategies and atypical neural systems may restore behavioral performance to within the typical range (7). Other deficits, such as executive dysfunction, may not be evident at younger ages but become clearer over development (7). In all cases, apart from aspects of behavior that define the disorder itself, substantial variability is seen in the resulting phenotype.

Recent studies focusing on infants at risk for autism by virtue of having an older diagnosed sibling have highlighted a range of atypical brain and behavioral functions not only in those infants who receive a diagnosis but also in the at-risk group as a whole (15). Atypical visual orienting has been reported by a number of studies. In our previous studies with a group of infants at risk at 9 to 10 months of age, we reported that relative to the control group, infants at risk were slower to disengage their fixation from a central stimulus to orient toward a peripheral distractor (16). In a second task, the same group required peripheral targets to remain on the screen for longer durations before infants reliably oriented to them (17).

Preliminary evidence from several longitudinal studies suggests that characteristics of visual attention are associated with autism symptoms emerging in toddlerhood. In one study, an increase, rather than the expected decrease, in latencies to disengage from a central fixation to a peripheral object between 6 and 12 months characterized those infants who went on to a provisional autism diagnosis at 2 years (18). Using a dimensional approach in quantifying the degree of emerging symptoms in the at-risk group as a whole, another study suggested that preference for a repetitive boring fixation stimulus was associated with more impairment in social and communication skills at 3 years of age (19).

In the current study, we tested the hypothesis that atypical visual disengagement during infancy is associated with autism-related outcomes in a new cohort of infants at risk for autism due to having an older sibling with the disorder [different from the group reported in our previously published work (16,17)]. Given the mixed evidence regarding the specificity of disengagement difficulties to autism, we also assessed if the same developmental pattern would be observed in infants who go on to exhibit some forms of developmental concerns without meeting criteria for a diagnosis.

Methods and Materials

Participants

One hundred four infants from the British Autism Study of Infant Siblings (www.basisnetwork.org) took part in the current study (54 at-risk, 21 male infants and 50 low-risk, 21 male infants). Along with several other measures, the infants were seen for the visual attention task when they were 6 to 10 months and again when they were 12 to 15 months. Subsequently, 52 (from 54) of those at risk for autism were seen for assessment around their second birthday and 53 were seen around their third birthday by an independent team. During the 36-month visit, a battery of clinical research measures was administered including the Autism Diagnostic Observation Schedule and the Autism Diagnostic Interview. Consensus ICD-10 criteria were used to ascertain diagnosis in a subgroup of infants at risk using all available information from all visits by experienced researchers (T.C., K.H., S.C., G.P.). Supplement 1 presents detailed participant characteristics including ascertainment of risk status, background measures at each visit, and outcome characterization including clinical classification. The at-risk groups were classified as having ASD (at-risk-ASD), other developmental concerns (at-risk-other), or typically developing (at-risk-typical). More specifically, infants were classified as at risk-other either because they did not meet criteria for a diagnostic classification for autism but scored above cutoff on the Autism Diagnostic Observation Schedule or Autism Diagnostic Interview or they had low IQ scores ($<$1.5 SD). Detailed characteristics of each group are presented in Supplement 1.

It is worth noting that the recurrence rate reported in the current study (32.1%) is higher than that reported in the large consortium paper recently published by Ozonoff *et al.* (20) (18.7%) and above the higher 95% confidence interval reported in that study (20). This is likely to reflect the modest size at-risk sample in the current study ($n = 53$). While recurrence rates approaching 30% have been found in other moderate size samples (21,22), these rates are sample specific and will likely not be generalizable, as findings from larger samples show autism recurrence rates converge between 10% and 20% (20,23). Similar procedures combining all information from standard diagnostic measures and clinical observation and arriving at a clinical best estimate ICD-10 diagnosis were used in the present study in line with other familial at-risk studies and were conducted by an experienced group of clinical researchers.

Gap-Overlap Study at 6 to 10 Months and 12 to 15 Months

During their first and second visits, infants were administered a battery of tasks containing stimuli that varied across different tasks and with short breaks in between. The stimuli and procedure for the gap task were adapted from those reported in our previous study (16). Infants were presented with the stimuli on a 46-inch liquid crystal display monitor, while seated on their parent's lap at 60 cm distance. Looking behavior was monitored and recorded through video from an adjacent room. All trials in this task began with a centrally presented animation. The animations, subtending around $13.8^\circ \times 18^\circ$, expanded and contracted to attract the infant to the center before the onset of the trial. The peripheral target was presented randomly either to the right or the left of the central fixation stimulus at the eccentricity of 15°. Peripheral targets were always the same (a dynamic green balloon) subtending $6.3^\circ \times 6.3^\circ$. The purpose of freezing the motion of the central stimulus during the overlap period was to better match the relative attractiveness of the two competing stimuli. Without this feature, the central and peripheral stimuli would have been unbalanced, leading to artificially lengthened disengagement values. The peripheral target remained displayed until the infant looked at it or until 2.5 seconds elapsed. Once the infant looked to the target or if the maximum duration was reached, an attractive animation of an animal with sound replaced the peripheral target and the next trial was presented. The rate of trial presentation was controlled by the experimenter.

In the baseline condition, the central fixation stimulus was extinguished and the peripheral target appeared simultaneously; in the overlap condition, the animated peripheral target appeared while the central fixation stimulus remained displayed (but not animated) so that the two stimuli overlapped. More overlap trials were presented because these trials are less likely to yield valid reaction times (infants may look away or become stuck on the central fixation), especially in atypical infants. The two conditions were presented pseudorandomly across two blocks that were identical except for the central fixation stimulus, to maintain the infant's interest in the task. Trial presentation