Published in final edited form as:

J Autism Dev Disord. 2017 September ; 47(9): 2690–2702. doi:10.1007/s10803-017-3192-3.

Developmental Changes in Empathic Concern and Self-Understanding in Toddlers at Genetic Risk for Autism Spectrum Disorder

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Abstract

Toddlers with an older sibling with autism spectrum disorder (ASD) and low risk (LR) toddlers were observed at 22, 28, and 34 months during two empathy probes: concern for a crying baby and an adult who pretended to hurt her finger. Toddlers with a later ASD diagnosis showed less empathic concern and self-distress at each age on both empathy probes than LR toddlers. HR toddlers with no diagnosis showed growth in empathic concern between 22 and 34 months in response to the adult's pain, differing from the children with ASD, but not the LR children, by 34 months. Developmental changes in parent-rated self-understanding showed a similar pattern. Results highlight individual differences in the social development of HR toddlers.

Keywords

High-risk siblings; empathic concern; self-understanding; self-distress; Autism Spectrum Disorder

Empathy is an affective response to the emotional displays of others that develops over infancy and toddlerhood along with other important aspects of social engagement and social understanding, including social referencing, awareness of the perspectives and intentions of social partners, and prosocial behavior (e.g., Brownell and Kopp 2007; Hobson 2007; Moore 2007; Zahn-Waxler et al. 1992). Emotional contagion is considered an early precursor of empathy in infancy (Hoffman 1981), but by the second year of life, empathy is evident when toddlers show concern in response to another person's distress (Roth-Hanania et al. 2011; Zahn-Waxler et al. 1992). Children with autism spectrum disorder (ASD), however, show only limited social engagement and awareness of other people's feelings, and thus are less likely to respond to another person's distress with concern than typically developing children (Bacon et al. 1998; Hobson 2007; Sigman et al. 1992). Delays or deficits in emerging empathy, therefore, may be one early sign of ASD. In the current study, we assess changes in social and emotional reactions to the distress of a crying infant and the distress of

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Compliance with Ethical Standards

Conflict of Interest: The authors have no conflicts of interest.

Ethical Approval: This study was approved by the Internal Review Board. Informed consent was obtained from all parents who participated in this study.

an adult social partner in toddlers at high and low genetic risk for ASD, followed longitudinally from 22 months to 34 months and assessed for ASD at 36 months.

Empathy Development

Empathy has its roots in both neurobiological processes and early experiences with caregivers (Hoffman 2007; Zahn-Waxler et al.1992). In the second year of life emerging empathy is closely tied to the development of self-awareness and self-other differentiation, as toddlers express both self-distress and other-directed concern when witnessing another person's pain and negative affect (Zahn-Waxler et al.1992). Self-distress appears to be a more basic response to another's negative affect, reflecting both awareness of the other's discomfort and emotional contagion, whereas the ability to express concern directed to another person seems to require some degree of perspective-taking ability and awareness of inner states, including the ability to read facial and vocal cues of emotion and understand something about what the other person is feeling (Brownell and Kopp 2007; Hoffman 2007; Moore 2007; Nichols et al. 2009). Developmental studies of typically developing infants and toddlers indicate that empathic concern is evident in rudimentary form prior to 12 months and consolidates over the second and third years of life (Knafo et al. 2008; Nichols et al. 2009; Roth-Hanania et al 2011; Zahn-Waxler et al. 1992).

Most experimental studies of emerging empathy in toddlers have relied on simulated distress situations during which the parent or an examiner feigns pain or distress, for example by banging their knee or hitting their finger with a hammer (Knafo et al. 2008; Spinrad & Stifter 2006; Zahn-Waxler et al.1992). A few studies have also assessed empathic concern for a crying infant or toddler, on the assumption that young children may express stronger reactions when witnessing the distress of someone more like themselves. Spinrad and Stifter (2006) presented 18-month-old typically developing toddlers with a realistic-looking doll swaddled in a blanket who then began to cry. The toddlers showed more concern for the crying "baby" than for the examiner or their mother both of whom feigned distress in other probes, suggesting that another child's distress may be especially salient to young children. Nichols et al. (2009, 2015) also examined the responses of 18 and 24 month old toddlers to the cries of a realistic doll and reported that, even with age controlled, children who were higher in social understanding showed more concern for the crying baby, highlighting associations between emerging empathy and other aspects of social cognitive development, including self-awareness.

Empathy and ASD

In contrast to typically developing children, children with ASD are less socially connected to others (American Psychiatric Association 2000; Dawson 2008) and evidence limited responsiveness to the affective displays of social partners. Sigman et al. (1992) compared the responses of preschool children with ASD, developmental delays, and typical development to feigned pain and fear expressed by their mothers and a female experimenter. Children with ASD showed less concern for and awareness of either adult's negative affective state than did comparison children. Other studies have also reported that preschool-age children with ASD show less attention to and concern for the distress of others than typically-

developing children or children with language or developmental delays (Bacon et al. 1998; Charman et al. 1997), reflecting the lower level of social awareness and social motivation that characterizes children with autism (Dawson 2008).

To understand the early emergence of ASD, including early signs of low social engagement and social interest, recent research has focused on infants who are at genetic risk for ASD because they have an older sibling with the disorder. One large-scale study found that nearly 20% of high risk (HR) infant siblings received a diagnosis of ASD by 36 months (Ozonoff et al. 2011). Thus, the prospective study of HR siblings can track the similarities and differences in early development in toddlers who do and do not receive a diagnosis of ASD. Studies that examine aspects of social development that have been described in typically developing toddlers and that map onto known social deficits in children with ASD can provide new information about the early developmental course of social difficulties in children who receive a diagnosis of ASD by 36 months.

HR toddlers who do not receive a later diagnosis of ASD are also important to study, as some may show subtle subclinical difficulties including atypical social behavior, reflecting the broader autism phenotype (e.g., Brian et al. 2008; Ozonoff et al. 2014; Szatmari et al. 2016), whereas others may not differ from low risk (LR) children (Hutman et al. 2010; Malesa et al. 2012) on early measures of social and language development. Examining early developmental changes in key aspects of social functioning in HR toddlers without a diagnosis, therefore, may identify characteristics that are unique to the emergence of autism as well as behaviors suggesting uneven development.

Studies of empathic responding in toddlers at risk for ASD are especially relevant to understanding the development of social functioning in this population. Hutman et al. (2010) rated attention and affective responses of high and low risk children at 12, 18, 24, and 36 months to the distress of an examiner who pretended to hit her finger with a toy mallet. Significant differences were obtained between the 14 children who received a diagnosis of ASD at 36 months and the LR and HR children without a diagnosis on ratings of both attention and affect, with group differences becoming more pronounced across age. The HR children without a diagnosis did not differ from the LR children at any age. McDonald and Messinger (2012) also reported that HR toddlers with an ASD diagnosis ($n=13$) were less responsive to their parent's distress at 24 and 36 months than HR toddlers without a diagnosis ($n=25$). Thus, these two studies suggest that in the second year of life, when empathic responsiveness first appears, HR toddlers who later receive a diagnosis of ASD are less responsive to distress expressed by either a parent or an unfamiliar examiner than toddlers who do not evidence symptoms of ASD by 36 months. This is consistent with a general deficit in affective responsiveness to others that extends to empathic concern, a fundamental component of developing prosocial and moral behavior.

In a preliminary report on a smaller sample of high and low risk 22-month olds (Campbell et al. 2015a), we examined the generality of this deficit further by comparing HR and LR toddlers' responses on two distinct measures of empathic concern, one using the standard feigned pain of an examiner and the second in response to a crying "baby." Results indicated that toddlers with a later diagnosis of autism evidenced less empathic concern than LR

toddlers on both probes. Following Zahn-Waxler et al. (1992), we also rated children's own personal distress, distinct from empathic concern, and during the crying baby probe, we added a measure of children's attempts to engage their parents. Toddlers with a later diagnosis of ASD were not only less empathic, but also less likely than LR toddlers to engage their parents when the baby cried. Although the HR toddlers who did not receive a diagnosis of ASD were more likely than the children with a diagnosis to engage their parents when the baby cried, they engaged their parents less and demonstrated less empathic concern than the LR toddlers. However, when the examiner pretended to hurt her finger both the HR toddlers without a diagnosis (HR-noASD) and the LR toddlers evidenced more empathic concern and self-distress than did the children with a diagnosis. Empathic concern was also related to parent reports of children's level of self-understanding, which was lower in both the HR-noASD children and children with ASD. Thus, the HR-noASD toddlers were similar to the LR toddlers in being responsive to an adult's distress, but they were apparently unsure about how to interpret a baby's distress; thus, they engaged their parents about the baby, consistent with their lower self-other understanding.

The Current Study

In the current study, we build on these preliminary findings by examining the empathic responses of LR toddlers and HR toddlers with and without a diagnosis of ASD longitudinally and in a larger sample ($n=168$; 20 with ASD). We adopt a growth modeling analytic approach to better characterize patterns of development across the second and third years of life at 22, 28, and 34 months, utilizing these two different empathy probes, the simulated distress of a crying infant and of an adult social partner. We expected the children with a diagnosis of ASD to differ from the LR toddlers on measures of empathic concern and self-distress at each time point. We also expected both the LR toddlers and the HR-noASD toddlers to show increases in empathic concern from 22 to 34 months, but we did not have specific hypotheses about whether the increases would be similar in these two groups or follow different growth trajectories. Finally, although we expected group differences between the LR children and children with ASD to be maintained over time, we were uncertain about the magnitude of differences or the degree of developmental change to be observed in the ASD group.

Because some degree of self-understanding appears to be necessary for empathic concern (Hoffman 2007; Nichols et al. 2009; Zahn-Waxler et al. 1992), parental reports of children's self-understanding were also obtained. We expected that trajectories of self-understanding would be similar to trajectories of observed empathic concern over this period. We also expected that toddlers with ASD would differ from LR toddlers on self-understanding, with LR children showing the steepest increases in self-understanding across the second and third years and children with ASD showing both the lowest level and the least developmental change. Based on our preliminary findings on a smaller subsample of 22 month olds, we expected the HR-noASD toddlers to differ from both the LR toddlers and the toddlers with ASD at the initial assessment, but we also expected the HR-noASD toddlers to show significant developmental change in self-understanding between 22 and 34 months.

Method

Participants

The 168 children included in this report are participants in a prospective study of children at risk for ASD. Infants with an older sibling with ASD and comparison infants with a typically developing older sibling were seen at 22, 28, and 34 months for a play-based assessment of social behavior that included the empathy probes described below. Most were seen at 36 months for a follow-up diagnostic assessment (details below). Groups did not differ in age at any assessment (See Table 1). Parents signed informed consents prior to participation; the research protocol was approved by the University Institutional Review Board.

HR toddlers (78, 46 males) were recruited between 6 and 16 months for a study of cognitive and social development, through the Autism Center at the University of Pittsburgh, with the exception of four HR children who joined the study between 18 and 22 months. To be eligible for inclusion in the HR group, children had to be born full-term after an uncomplicated pregnancy and delivery, and have an older sibling diagnosed with autism spectrum disorder according to research criteria. The older sibling's diagnosis was confirmed by research reliable staff at the Autism Center who administered the Autism Diagnostic Observation Schedule (ADOS; Lord et al. 2000) under the supervision of a licensed psychologist, prior to the younger sibling's enrollment in the study. Infants whose older siblings had known genetic or other anomalies, such as Fragile X, were excluded. Four HR toddlers were half-siblings of the child with ASD.

LR control participants (90, 51 males) were recruited from the local obstetrics hospital, community groups, pediatric offices, and word of mouth. Full-term healthy children with a typically developing older sibling and negative family history of ASD in first and second degree relatives comprised the LR group, most of whom were also recruited in infancy. Parents of LR children completed the Social Communication Questionnaire (Rutter et al., 2003) on the older sibling prior to study enrollment; all scored well below the ASD cut-off of 15.

Participant characteristics are summarized in Table 1, including comparisons between the LR toddlers, the HR toddlers without a diagnosis, and the toddlers with a later ASD diagnosis (see below). Participating children are predominantly Caucasian and non-Hispanic (87%); all but six lived in two-parent families. Parent education was scored according to the Hollingshead Scale and averaged when data for both parents were available. Although the majority of parents in both groups had at least a college degree, there was a main effect of parent education, $F_{(2, 161)} = 4.44$, $p = .013$; follow-up tests indicated that the LR parents were more highly educated than the parents of the toddlers with ASD, $p = .012$. The sample included in this report overlaps with participants in three prior publications (Campbell et al. 2015a, 2015b, 2016) including an earlier paper on empathic concern at 22 months in a smaller subsample.

Data were available for 145 toddlers at 22 months, 157 at 28 months, and 159 at 34 months; 136 children were seen for all three visits. Data at 22 and 28 months were missing for some

children because most HR and many LR toddlers were recruited in infancy for a separate study of attention and cognitive functioning; the current toddler study did not begin until some of these children were already two years old. Scheduling difficulties, experimenter error, child noncompliance, and equipment problems accounted for the remainder. In addition, although we began conducting assessments only in our playroom, in order to minimize data loss, we also collected some data during home visits. This is discussed further under preliminary analyses.

Procedure

Toddlers' Responses to Another's Distress.—As part of a longer assessment of social engagement and behavior in toddlerhood, two empathy probes were administered. The first focused on the child's responses to the distress of a crying infant ("crying baby") and the second involved the feigned distress of the examiner with whom the child had been playing ("hurt finger"). A parent, usually the mother, remained with the child for the entire visit. At 22 and 28 months, 14 fathers participated and at 34 months, 21 fathers participated. During the empathy probes parents were seated in a corner of the room within view of the child. Prior to the start of the session, parents were told about the probes and asked not to prompt their child or make suggestions, but to respond neutrally to their child's questions.

Crying Baby. About half-way through the play session, while the child was engaged with an interesting toy, the examiner entered the room with a realistic looking baby doll swaddled in a blanket and secured in an infant seat on a rolling cart, above the toddler's reach and eye level (Nichols et al., 2009; 2015). A tape-recorder was hidden beneath the blanket and a baby bottle, second blanket, and small stuffed animal were on the cart's bottom shelf. The examiner explained that she needed to leave her baby there to take a nap. Twenty seconds after the examiner left the room, the recording of an actual baby crying played for 20 seconds. The crying subsided for 20 seconds and then resumed for another 20 seconds. After the second cry, the examiner returned, removed the cart and doll, and left the child and parent together for the next activity. The entire episode lasted 80 seconds, with the first 20 seconds prior to the first cry not coded

Hurt Finger. The second empathy probe occurred toward the end of the roughly 45-minute play visit. The examiner, with whom the child had previously been playing, returned with questionnaires for the parent to complete and a toy pounding bench with colored blocks and a mallet. As the examiner demonstrated the toy by pounding the blocks, she hit her finger with the mallet, and said "ouch, I hurt my finger with the hammer." She then rubbed her finger with a pained expression on her face, repeating "ouch, it hurts" while continuing to rub her finger for about 20 seconds. Before leaving the room, the examiner said: "my finger feels better now."

Coding and Reliability. Toddlers' responses to the two distress situations were coded from videotapes by trained coders who were blind to group designation (HR or LR) and diagnostic outcome. Both probes were rated on 4-point (0–3) scales of empathic concern and self-distress, derived from the work of Zahn-Waxler et al. (1992). Ratings of 0 were given when the child showed no concern; ratings of 1 indicated slight concern, if the child showed

a brief sobering of expression that lasted at least 3 seconds; a rating of 2 indicated moderate concern including sobering or a concerned/worried facial expression lasting about 8 seconds; ratings of 3 reflected substantial concern that included sustained sadness, a sympathetic facial expression, and looks to the baby (or to the examiner). Self-distress was also rated on a 0–3 scale, with negative arousal and fussing, seeking comfort from the parent, and self-comforting behavior (e.g., looking away, fiddling with hair or clothing, sucking thumb) contributing to higher ratings.

During the crying baby episode, specific behaviors were also coded as present or absent during each of three 20-second intervals: baby's first cry; the interval between cries; and the baby's second cry. Behaviors that reflected interest in the baby while also engaging the parent were summed over the three intervals into an "engage parent" variable. This composite included three social communicative behaviors: referencing the parent (looking between parent and baby), pointing to the baby, and talking to the parent about the baby (e.g., "she's crying") (possible range 0–9). A second "interest" composite that did not involve the parent included two behaviors: looking at and/or approaching the crying baby (possible range 0–6).

Inter-observer reliability on the composited behavioral codes making up the "engage parent" and "interest" measures in response to the crying baby and on the ratings of empathic concern and self-distress was calculated on 20% of the video records. The average intraclass correlations across the three behaviors making up the engage parent composite were .89 at 22 months, .91 at 28 months, and .91 at 34 months. The average intraclass correlations for the two behaviors making up the interest composite were .96 at 22 months, .85 at 28 months, and .93 at 34 months. Intraclass correlations for the empathic concern and self-distress ratings during the crying baby probe were .82 and .90 at 22 months, .73 and .75 at 28 months, and .93 and .89 at 34 months. Reliability on the ratings for the hurt finger probes were as follows: empathic concern .90, .84, and .97; self-distress .75, .91, and .83 at 22, 28, and 34 months respectively.

Toddlers' Self-Understanding.—At each assessment, parents completed the UCLA Self-Understanding Questionnaire (Stipek et al. 1990), a 24-item scale tapping children's self-recognition and self-awareness. For example, items assess mirror self-recognition, use of the word "mine", and awareness of being a girl or boy. Parents rated each item on a 3-point scale from 0 = definitely not, 1 = sometimes, and 2 = definitely yes. In the current sample, Cronbach's alpha for the total scale was .89 at 22 months, .92 at 28 months, and .93 at 34 months.

Developmental and Autism Assessments

Mullen Scales of Early Learning.: The Mullen Scales of Early Learning (MSEL; Mullen, 1995), a standardized measure of cognitive development, was administered at 24 months. T-scores on the Receptive Language and Expressive Language scales were averaged to provide a language development score. Similarly, the Visual Reception and Fine Motor scores were averaged to provide a measure of non-verbal development. Six children were missing Mullen scores at 24 months, so their 36 month score was substituted. Another four children

(2 HR-noASD, 2 ASD) are missing Mullen scores at both ages because of missed appointments ($n=3$) or lack of cooperation ($n=1$).

Evaluations for Autism.: Both HR and LR toddlers were evaluated for an ASD diagnosis at follow-up, using the Autism Diagnostic Observation Schedule (ADOS, Lord et al., 2000). The ADOS, a semi-structured observational assessment, includes play-based activities that are meant to elicit reciprocal social interaction, communication, and stereotyped behaviors and provides scoring rules for a diagnosis of ASD. All children received either Module 1 or 2. Evaluations were conducted by a research-reliable tester under the supervision of a licensed clinical psychologist from the Autism Center with extensive experience assessing children with ASD; no one involved in the diagnostic assessments conducted the laboratory visits. Diagnostic decisions were based on the 36-month assessment or later for all HR-noASD children. Two children with a diagnosis were seen at 24, but not 36 months, so their 24-month ADOS scores were used. Finally, one HR child with a diagnosis of ASD was seen at a local developmental clinic specializing in autism, but the ADOS score was not available. Most LR children were assessed at 36 months, but three missed the 36-month visit and their 24-month ADOS scores were substituted.

Children were classified as ASD if they met cut-off scores on the ADOS (Lord et al., 2000) and also met DSM-IV criteria for an autism spectrum disorder (American Psychiatric Association, 2000), as determined by interview and observation. Parents of children with elevated ADOS scores and/or serious clinical concerns were interviewed using the Autism Diagnostic Interview-Revised (ADI-R, Lord et al. 1994) to provide further information. Final diagnoses were based on a combination of structured diagnostic measures, DSM-IV criteria, and clinical judgment and made by a licensed clinical psychologist; 19 HR toddlers (13 boys) received a diagnosis of ASD. One LR boy with an earlier language delay and some social concerns received a diagnosis of ASD and is included in the ASD group in the analyses.

In addition, ADOS scores were converted to severity scores using the algorithm provided by Gotham et al. (2009) to allow for comparability across age; scores are summarized in Table 1. As expected, there was a main effect of group status, $F_{(2,165)} = 155.15, p < .001$. The children with a diagnosis (ASD) had substantially higher severity scores than the LR children ($p < .001$) and the HR-noASD children ($p < .001$). LR and HR-noASD children did not differ from one another.

Data Analysis Plan.—Because there were questions about the validity of the crying baby probe at 34 months (see below), two by three repeated measures analyses of variance/covariance were used to examine age (22, 28 months), group (LR, HR-noASD, ASD), and age by group interactions for the four variables coded during the crying baby probe. Child sex, visit location, and accompanying parent were controlled when indicated. Analyses were conducted with and without controls for Mullen Verbal Scores.

Empathic concern and self-distress from the hurt finger probe and scores on the UCLA Self-Understanding Questionnaire were available at three time points (22, 28, and 34 months); thus, we utilized Hierarchical Linear Modeling (HLM, Bryk & Raudenbush, 1992) to

describe differences between groups in growth trajectories from 22 to 34 months on these measures. HLM is an appropriate analytic tool for data consisting of multiple time points nested within individuals and assesses the data at two levels. First, HLM assesses variation *within individuals* over time (i.e. growth trajectories; level 1), and second, it assesses variation *between individuals* in growth trajectories (level 2). HLM can also accommodate missing data (Willett et al. 1998), thereby allowing for the inclusion of all participants with at least one visit.

For all three models, we set 22 months as the intercept and used the LR group as the reference group. Thus, at level 1 of each of our three models, HLM estimated individual linear growth trajectories in each variable as a function of VISIT (coded 0, 1, 2, to represent the three visits at 22, 28, and 34 months). The coefficients on the intercept and growth terms were modeled as random effects in all models. In cases where a variable differed based on visit location, this variable was included as a fixed-effect time-varying covariate at level-1 (see Preliminary Analyses below).

At Level 2 (between individuals) we included the two HR Groups as person-level predictors: HR-noASD and ASD. The LR group served as our reference group; thus analyses at Level 2 examined differences in growth trajectories between LR toddlers and the two HR toddler groups. Therefore, the coefficients (β) represent deviations from the LR group on each of these terms. Where significant intercept differences occur between groups, we have included Cohen's d as a measure of effect size. In cases where a variable differed based on sex, this variable was included at Level 2 (see Preliminary Analyses below). In addition, all models were run with and without Mullen Verbal Scores included at Level 2.

All analyses were rerun after rotating the reference group in order to examine potential differences between the ASD and HR-noASD groups. When appropriate, follow up analyses were conducted to examine intercept differences over time by systematically re-centering the VISIT variable. This allowed us to determine the point at which developmental trajectories of the different groups diverged or came together. All three models met assumptions of normality and homoscedasticity.

Results

Preliminary Analyses.

Preliminary analyses were conducted to examine whether empathy measures varied systematically as a function of child sex, participating parent (mother vs. father), or visit location (lab vs. home), using one-way ANOVAs separately by age to avoid listwise deletion. To examine sex differences, only boys and girls in the LR and HR groups were compared, because sex and diagnosis are confounded. There were only two significant sex differences: at 22 months, girls showed more self-distress than boys when the examiner hurt her finger with the toy mallet, $F_{(1,122)} = 5.07$, $p = .026$, and at 34 months, girls were rated higher than boys in empathic concern during the hurt finger probe, $F_{(1,133)} = 8.55$, $p = .004$. Thus, child sex was controlled in the analyses of these two variables. At 28 months, children expressed more self-distress, $F_{(1,139)} = 6.63$, $p = .01$, but less interest in the crying baby, $F_{(1,139)} = 4.09$, $p = .045$ when observed with their fathers than mothers; parent was

controlled in the analyses of these two variables. There were no differences on the empathy measures as a function of visit location at either 22 or 28 months, but visit location did matter at 34 months. At 34 months, children showed less self-distress during the hurt finger probe at home visits, $F_{(1,149)} = 4.95$, $p = .028$, so visit location was also controlled in the analysis of this variable. Children were also less interested in, concerned about, or distressed by the crying baby when the probe was conducted at home at 34 months.

There were two additional concerns about the crying baby probe at 34 months, over and above visit location. First, a number of children realized that the “crying baby” was really a doll. Second, we introduced a new more age-appropriate toy at 34 months, different from the toy used at 22 and 28 months. Many children were so engrossed with the toy that they paid much less attention to the crying doll than they had at earlier ages. Given these issues, the responses to the crying baby did not appear to be valid at 34 months and are not considered further.

There were significant group differences on both the Verbal, $F_{(2,163)} = 29.19$, $p < .001$, and Non-Verbal $F_{(2,162)} = 11.24$, $p < .001$, portions of the Mullen Scales (See Table 1). Both LR and HR-noASD children scored significantly higher than the children with a diagnosis of ASD, $p < .001$, but they did not differ from each other. On the measure of non-verbal skills, each group differed from the others (LR vs. HR-noASD, $p = .021$; LR vs. ASD, $p < .001$; HR-noASD vs. ASD, $p = .03$). Analyses were conducted with and without controls for Mullen Verbal Scores.

Outcome Group and Age Differences in Responses to the Crying Baby.

A series of two by three repeated measures ANOVAs was conducted on the 130 children with complete data on the crying baby probe at 22 and 28 months (75 LR, 39 HR-noASD, 16 ASD). Descriptive statistics on the entire sample with data at either age are summarized in Table 2. First, almost all children showed some interest in the crying baby and there were no effects of either age or group on this measure, indicating some awareness that the baby was crying. Ratings of empathic concern, however, showed main effects of both age and group, but no group by age interaction. Children received higher ratings of empathic concern at 28 months than 22 months, $F_{(1,127)} = 4.63$, $p = .033$, $\eta^2 = .035$. Group differences were also in evidence, $F_{(2,127)} = 6.95$, $p = .001$, $\eta^2 = .099$. Follow-up tests with a Bonferroni correction indicated that the LR toddlers were rated higher on empathic concern than the toddlers with ASD ($p = .003$) and they were marginally higher than the HR-noASD toddlers ($p = .056$). The HR-noASD and ASD toddlers did not differ from one another. Self-distress and engage parent showed group main effects, but no age or age by group interactions. For self-distress, the group main effect, after controlling for participating parent, was significant, $F_{(2,126)} = 4.96$, $p = .008$, $\eta^2 = .073$ and post hoc tests indicated that the only significant contrast was between the LR children and those with ASD ($p = .009$). The group main effect for engage parent was also significant, $F_{(2,127)} = 7.67$, $p = .001$, $\eta^2 = .108$; the children with ASD were less likely to engage their parent when the “baby” cried than either HR-noASD toddlers ($p = .025$) or LR toddlers ($p = .001$). The HR-noASD and LR toddlers did not differ from each other on the engage parent composite at either 22 or 28 months.

When the analyses for empathic concern were rerun controlling for Mullen Verbal Scores, both the main effect of age, $F_{(1,124)} = 8.30, p = .005, \eta^2 = .063$, and the main effect of group, $F_{(2,124)} = 3.66, p = .029, \eta^2 = .056$, remained significant. However, group differences on ratings of self-distress, $F_{(2,123)} = 2.39, p = .096, \eta^2 = .037$, and the engage parent composite score, $F_{(2,124)} = 2.48, p = .088, \eta^2 = .039$, were attenuated to non-significance with verbal scores included in the model.

Outcome Group and Age Differences in Response to the Examiner's Hurt Finger.

Descriptive statistics are summarized in Table 3 and results from the HLM analyses are summarized in Table 4. Child sex and visit location were controlled when indicated (see Preliminary Analyses). Figure 1 displays the mean empathic concern ratings for each of the three outcome groups at 22, 28, and 34 months. Results of the conditional HLM model indicated that, at 22 months, LR children were rated as showing more empathic concern than children in the HR-noASD group, $\beta_{0HR-NoASD} = -0.49, SE = 0.13, t = -3.75, p < .001, d = 0.58$, and children in the ASD group, $\beta_{0ASD} = -1.06, SE = 0.19, t = -5.62, p < .001, d = 1.26$. The children in the ASD group were also rated as less empathic than the HR-noASD group at this time point $\beta_{0ASD} = -0.57, SE = 0.20, t = -2.87, p = .005, d = .68$. With regard to developmental change, the HR-noASD group showed significantly faster growth in ratings of empathic concern than the LR group, $\beta_{1HR-NoASD} = 0.25, SE = 0.09, t = 2.88, p = .005$, and the ASD group, $\beta_{1ASD} = -0.28, SE = 0.14, t = -2.03, p = .044$.

Given differences in rate of change in empathic concern between the HR-noASD group and the two other groups, we conducted follow-up analyses to examine differences between groups in empathic concern at 28 and 34 months. Results indicated that the ASD group continued to be rated as significantly less empathic than the other two groups at both subsequent time points, all p 's $< .001$. The HR-noASD group, on the other hand, continued to differ from the LR group at 28 months ($p = .007$), but was no longer significantly different from the LR group at 34 months ($p = .988$).

Results remained largely unchanged with 24-month Mullen Verbal Scores included in the model, with the exception that the ASD group's 22-month empathic concern ratings were no longer significantly different from the HR-noASD group's ratings, $p = .239$. However, the difference between the ASD and HR-noASD groups remained significant at both 28 ($p < .001$) and 34 months ($p < .001$).

Mean self-distress ratings for the three groups at 22, 28, and 34 months are presented in Figure 2. Results of the conditional HLM model indicated that, at 22 months, the ASD group showed significantly lower self-distress than children in the LR group, $\beta_{0ASD} = -0.60, SE = 0.20, t = -2.95, p = .004, d = 0.68$, and the HR-noASD group, $\beta_{0ASD} = -0.64, SE = 0.22, t = -2.96, p = .004, d = 0.73$. The LR and HR-noASD groups did not differ from each other. There were no significant differences in slope between groups, although the slope for the ASD group was marginally lower than the slope for LR group, $\beta_{1ASD} = -0.26, SE = 0.15, t = -1.79, p = .075$. As is evident from the Figure, the ASD group differed from both the LR and HR-noASD groups at 28 (p 's $< .001$) and 34 (p 's $< .001$) months.

With Mullen Verbal Scores included in the model, the ASD group was no longer significantly lower in self-distress than the LR ($p = .185$) or HR-noASD ($p = .116$) groups at 22 months. However significant differences were still evident at 28 and 34 months, with both the LR (28 months: $p = .002$; 34 months: $p = .001$) and HR-noASD (28 months: $p = .011$; 34 months: $p = .018$) children expressing more self-distress than the children with a diagnosis of ASD.

Outcome Group and Age Differences in Parent Reports of Self-Understanding.

Figure 3 shows mean scores from the UCLA Self-Understanding Questionnaire for the three groups at 22, 28, and 34 months. The final conditional HLM model revealed significant group differences in self-understanding at 22 months. Specifically, the HR-noASD group scored significantly lower than the LR group, $\beta_{0HR-NoASD} = -4.68$, $SE = 1.38$, $t = -3.38$, $p < .001$, $d = 0.52$, and the ASD group scored significantly lower than both the LR, $\beta_{0ASD} = -14.71$, $SE = 2.02$, $t = -7.32$, $p < .001$, $d = 1.65$, and the HR-noASD group, $\beta_{0ASD} = -10.11$, $SE = 2.13$, $t = -4.75$, $p < .001$, $d = 1.13$. The HR-noASD group also displayed significantly faster linear growth than both the LR group, $\beta_{1HR-NoASD} = 1.55$, $SE = 0.64$, $t = 2.44$, $p = .016$ and ASD group, $\beta_{1ASD} = -3.01$, $SE = 1.01$, $t = -2.97$, $p = .003$. Given the faster growth in the HR-noASD group as compared to the LR and ASD groups, we examined group differences at 28 and 34 months. The ASD group remained significantly different from the LR and HR-noASD groups at both subsequent time points, all p 's $< .001$. The HR-noASD group differed from the LR ($p = .005$) group at 28 months, but was no longer significantly different from the LR group by 34 months ($p = .168$). The difference between the HR-noASD and the ASD groups at 22 months became non-significant with Mullen Verbal Scores included in the model ($p = .159$), but these group differences remained significant at 28 ($p < .001$) and 34 months ($p < .001$).

Discussion

We examined developmental changes in the responses of HR toddlers with an older sibling with ASD and LR toddlers with typically-developing older siblings to two probes meant to elicit concern for the distress of another: a crying “baby” and an adult social partner with whom the child had been playing. Children were studied at 22, 28, and 34 months and most children were assessed for ASD at 36 months. Comparisons among children with a diagnosis of ASD, HR children without a diagnosis of ASD, and LR children revealed different patterns of developmental change and stable group differences, many of which were maintained even with controls for verbal abilities.

In an earlier paper from this data set (Campbell et al. 2015a), on a smaller subsample of 22-month-old HR and LR toddlers, we found that the children later diagnosed with ASD were less empathic in response to both the crying baby and their adult playmate, less likely to engage their parent when the baby cried, and less distressed when the examiner hurt her finger than LR toddlers. The HR toddlers without a diagnosis differed from the LR toddlers during the crying baby probe, showing less empathic concern, but not during the hurt finger probe where they, like the LR children, showed both more concern and self-distress than the

children with ASD. In the current follow-up through 34 months, many of these group differences were maintained with some noteworthy variations in developmental patterns.

During the crying baby probe, all three groups showed a small, but significant increase in empathic concern between 22 and 28 months. Unfortunately, because of validity issues with the 34 month crying baby probe, we could not determine whether empathic concern would continue to increase with age on this measure. However, at both 22 and 28 months, the children with ASD showed less empathic concern and self-distress than children in the LR group; they also made fewer attempts to engage their parents when the baby cried than either LR or HR-noASD toddlers who did not differ from each other. It is important to note that almost all children showed awareness when the baby cried; at both ages children in all three groups showed interest in the doll by looking at it and/or approaching it. These group differences in overt responses are therefore not because the children with ASD failed to notice the crying baby; rather, they indicate lack of affective responsiveness to the baby's distress.

Whereas the children with ASD consistently differed from the LR children by showing only limited responsiveness when left with the crying baby, the HR-noASD children fell between the LR and ASD children in both empathic concern and self-distress. However, in contrast to the children with a diagnosis, the HR-noASD children attempted to engage their parents by referencing, pointing or talking about the baby, suggesting that their discomfort in response to the infant's cries was reflected in their attempts to elicit parental intervention. Although most of these group differences were attenuated when the analyses were rerun controlling for Mullen Verbal Scores, children with ASD continued to show lower empathic concern than LR children. This points to the co-development of skills across multiple domains in young children, including cognitive, communicative, and social development.

During the hurt finger probe with the adult playmate, the children with ASD showed the least empathic concern, differing from both the HR-noASD and LR groups. At 22 months, the HR-noASD children were also less empathic than the LR children. However, the HR-noASD children showed a sharp increase in empathic responses to the examiner's pained expressions between 22 and 28 months, an increase that continued through 34 months when their scores reached the same level as the LR children. In contrast, from 22 to 34 months, the children with ASD showed only minimal growth in empathic concern from their quite low initial level. Thus, the magnitude of differences between the HR children with and without a diagnosis increased over time from 22 to 34 months, with the HR-noASD children showing significant growth in empathy and the children with ASD exhibiting little developmental change. Although there was no significant change in levels of self-distress when the examiner hurt her finger across the three assessments, the children with ASD were least likely to respond with either signs of negative arousal or discomfort and they received lower ratings of concern or distress than either the LR or HR-noASD children. It appears, then, that during the second and third years of life limited affective responsiveness to another's distress, perhaps especially empathic concern, is an important indicator of emerging ASD among those who are at genetic risk for the disorder.

Importantly, these group differences were not accounted for by verbal development, as controls for Mullen scores did not eliminate group differences. Indeed, it was noteworthy that a high proportion of children in the ASD group did not react at all when the examiner hit her finger with the mallet and then clearly expressed pain by saying “ouch, it hurts” and rubbing her hurt finger; this lack of responsiveness was evident at each assessment age. At both 22 and 28 months, over 50% of the children with a diagnosis of ASD showed no affective response whatsoever, receiving ratings of “0” on measures of both empathic concern and self-distress; most of these children continued to play with the toy or quickly lost interest altogether; at 34 months, 44% showed no response. In contrast, only 14% of HR-noASD and 7% of LR children showed no response at 22 months; fewer than 6% showed no response at later ages, underscoring how salient this situation was to the children without an ASD diagnosis, regardless of risk status. Both the HR-noASD and LR children clearly reacted to the feigned pain of the examiner, with concern for her and some degree of discomfort themselves, while many of the children with ASD seemed either unconcerned or unaware of her distress.

In summary, across two different empathy probes administered during the second and third years of life, the toddlers who received a diagnosis of ASD by preschool age showed limited concern for the distress of others, as reflected in either their own discomfort or more subtle expressions of empathy. They were also less likely to elicit parental support at either 22 or 28 months when the hypothetical baby cried. The HR toddlers who did not receive a diagnosis, on the other hand, were indistinguishable from the LR toddlers by 34 months. Although there were some subtle differences in their reactions at 22 months, these disappeared by 34 months, suggesting that any mild social impairments shown by some of the HR-noASD toddlers were time-limited and no longer evident by 34 months.

There were several noteworthy findings in these data. First, the use of growth modeling techniques showed minimal change in either empathic concern or self-distress among the children with ASD. Although it is well-documented that children with a diagnosis of ASD show only limited concern for another’s distress, only one other study has examined developmental change in HR siblings with and without a diagnosis of ASD. Hutman et al. (2010) found that children with an ASD diagnosis by 36 months showed less attention to an examiner who hurt her finger and also less change in affect, a pattern that was evident from 12 to 36 months. Our results are therefore consistent with Hutman et al., although we used different rating scales during the hurt finger probe, distinguishing between empathic concern and self-distress, and we included responses to a novel and especially salient empathy probe, a crying baby. In addition to measures of empathy and distress, we examined whether toddlers tried to engage their parents when the baby cried. This measure, too, distinguished toddlers later diagnosed with ASD from HR-noASD toddlers. Thus, it is not only toddlers’ affective responses to others’ distress that may be an early marker of developing ASD, but also their appeals to or sharing of their affect about the other with their parent.

In addition to observations of responses to distress, we examined parental reports of children’s self-understanding on the assumption that self-awareness would be related to self-other understanding and awareness of the feelings of another (Brownell and Kopp, 2007). On this measure, the children with an ASD diagnosis again had significantly lower scores

than the other two groups at all three assessment points. The HR-noASD children, however, scored lower than the LR group at 22 and 28 months, but again showed significant improvements in self-understanding, paralleling their faster growth in empathic concern relative to the other two groups. By 34 months, the HR-noASD children no longer differed from the LR children on parent reports of self-understanding.

Limitations of the study include the somewhat small sample of toddlers with a later diagnosis, and the relatively educated and racially homogeneous sample overall. It will be important to determine whether the group differences, especially the rapid growth in empathic concern among the HR-noASD group, are true of children growing up in more diverse circumstances. Questions about the validity of the crying baby probe at 34 months and the inability to examine growth over three time points on this measure constitute an additional limitation. Finally, although the rating scales assessing empathic concern and self-distress are well-anchored in specific behaviors that define each point on the scales, the possibility remains that toddlers' distress responses show some developmental variation between 22 and 34 months that is not captured in the ratings.

Taken together, these results indicate that in this sample of HR infant siblings, the children with a diagnosis by 36 months show stable social deficits across the second and third years of life on measures of empathy, engagement with parents, and self-understanding. Although some of these were confounded with developmental level, the HR children who did not receive a diagnosis look remarkably similar to LR peers on these measures by 34 months, despite some subtle differences at 22 and 28 months, suggesting delayed, but not disrupted development on these important measures of early social functioning.

Although we had initially expected to identify a subgroup of HR-noASD children showing subclinical social and/or cognitive difficulties, using criteria similar to Ozonoff et al. (2014), very few HR-noASD children had scores that were either slightly elevated on the ADOS and/or more than 1–1/2 standard deviations below average on the verbal or nonverbal scales of the Mullen. Moreover, several LR children showed similar patterns suggesting that these variations merely reflect uneven development in early language and social skills, rather than the broader autism phenotype. The current results are also consistent with two other recent studies that found no differences between their LR and HR-noASD children at follow-up (Hutman et al. 2010; Malesa et al. 2012).

From a clinical perspective, young HR toddlers who show developmental delays in attending to and responding to the emotions of social partners, engaging parents when distressed, and developing self-awareness are more likely to receive a diagnosis of ASD by 36 months than HR siblings who show some degree of concern when confronted with another's distress and enlist their parents' help. Longitudinal follow-up also suggests that some HR children overcome early deficits; they show not only higher levels of empathic concern at 22 months than those who receive a diagnosis, but also are more engaged with their parents and rated as showing more self-awareness. Thus, within the HR sibling group, variability in functioning was evident by 22 months on these measures, and the ASD and HR-noASD groups showed different growth trajectories, with implications for early identification.

Future research that examines HR siblings' responses to a wider range of others' emotions, including sadness, anger, and guilt as well as positive emotions, would clarify how specific this deficit or delay is, with implications for intervention. Studies examining the emotional responsiveness and emotion understanding of HR siblings in the natural environment via observations in preschool and home settings, and by maternal diaries would be especially informative.

Acknowledgments

Susan B. Campbell, University of Pittsburgh, Pittsburgh, PA, USA, Elizabeth L. Moore, University of Pittsburgh, Pittsburgh, PA, USA, Jessie Northrup, University of Pittsburgh, Pittsburgh, PA, USA, Celia A. Brownell, University of Pittsburgh, Pittsburgh, PA, USA.

This study was supported by the National Institute of Mental Health R01 MH091036 to Dr. Campbell. We thank Dr. Nancy Minshew, Dr. Mark Strauss, Dr. Carla Mazefsky, Dr. Holly Gastgeb, Ms. Stacey Becker, and the staff at Autism Center of Excellence, University of Pittsburgh for overseeing initial recruitment and assessment of participating families. The Autism Center of Excellence was supported by award number HD055748 (PI Minshew) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Recruitment was also facilitated by the Clinical and Translational Science Institute, supported by the National Institutes of Health through Grant Numbers UL1 RR024153 and UL1TR000005. Thanks are due to Taylor Day, Kristen Decker, Stephanie Fox, Phebe Lockyer, Amanda Mahoney, and Emily Schmidt for overseeing data collection, and to Ari Fish, Rachel Fleming, Kendra Guinness, Megan Messmer, Michelle Meyer, Jenna Obitko, and Amy Tavares for assistance with data collection and coding. Special thanks go to the parents and children who participated in this study.

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Figure 1.
Mean Empathic Concern Ratings during the Hurt Finger protocol

Figure 2.
Mean Self- Distress Ratings during the Hurt Finger protocol

Figure 3.
Mean UCLA Self-Understanding Ratings

Table 1

Sample characteristics

	ASD (n=20)	HR-noASD (n=59)	LR (n=89)
Gender, male	70%	55.9%	56.2%
Ethnicity, Caucasian	80%	86.4%	88.8%
	M (SD)	M (SD)	M (SD)
Parent education	5.61 (0.98)	6.01 (0.79)	6.18 (0.72)
Age at 22 mo assessment	22.82 (0.68)	22.70 (0.73)	22.78 (0.71)
Age at 28 mo assessment	28.69 (0.63)	28.68 (0.51)	28.52 (0.42)
Age at 34 mo assessment	34.88 (0.88)	34.69 (0.84)	34.62 (0.61)
Mullen Verbal Score	35.78 (12.95)	51.09 (8.32)	53.56 (8.50)
Mullen Non-Verbal Score	43.68 (9.08)	49.68 (7.45)	53.57 (8.87)
ADOS severity score	5.79 (1.55)	1.53 (0.90)	1.42 (0.85)

Table 2

Means and standard deviations: Crying Baby Probe

	ASD 22m (n=17) 28m (n=18)		HR-noASD 22m (n=44) 28m (n=43)		LR 22m (n=77) 28m (n=80)	
	M (SD)		M (SD)		M (SD)	
Empathic Concern ¹						
22 months	1.24	(1.09)	1.66	(0.94)	1.97	(0.78)
28 months	1.61	(0.98)	1.84	(0.92)	2.06	(0.77)
Self-Distress ¹						
22 months	1.00	(1.12)	1.59	(0.84)	1.79	(0.77)
28 months	1.50	(0.86)	1.53	(0.83)	1.79	(0.76)
Engage parent ²						
22 months	1.65	(2.64)	3.13	(2.24)	3.73	(2.49)
28 months	2.11	(2.37)	3.67	(2.43)	4.24	(2.22)
Interest ³						
22 months	3.18	(1.78)	3.14	(1.44)	3.21	(1.06)
28 months	3.22	(1.40)	3.16	(1.23)	3.11	(1.09)

¹ 0–3 Ratings: 0 = no concern or distress; 1 = slight concern or distress; 2 = moderate concern or distress; 3 = substantial concern or distress

² Engage represents the sum of pointing, referencing, or talking about the crying baby (possible range 0–9)

³ Interest represents the sum of approaching or looking at the crying baby (possible range 0–6)

Table 3

Means and standard deviations: Hurt Finger and Self-Understanding

	ASD 22m (n=17) 28m (n=20) 34m (n=16)	HR-noASD 22m (n=46) 28m (n=51) 34m (n=55)	LR 22m (n=78) 28m (n=81) 34m (n=80)
	M (SD)	M (SD)	M (SD)
Hurt Finger			
Empathic Concern [/]			
22 months	0.47 (0.62)	1.00 (0.82)	1.50 (0.77)
28 months	0.50 (0.76)	1.45 (0.73)	1.72 (0.62)
34 months	0.63 (0.62)	1.71 (0.74)	(0.74)
Self-Distress [/]			
22 months	0.35 (0.61)	1.07 (0.98)	1.00 (0.82)
28 months	0.45 (0.89)	1.18 (0.93)	1.43 (0.81)
34 months	0.44 (1.03)	1.27 (0.99)	1.54 (0.91)
UCLA Self-Understanding Questionnaire			
22 months	15.88 (9.12)	24.42 (8.34)	29.38 (7.27)
28 months	21.33 (11.66)	35.60 (8.46)	38.41 (6.72)
34 months	25.65 (14.09)	41.47 (5.53)	43.17 (4.31)

[/] 0–3 Ratings: 0 = no concern or distress; 1 = slight concern or distress; 2 = moderate concern or distress; 3 = substantial concern or distress

Table 4

Results from the HLM Analyses

	Hurt Finger				UCLA	
	Empathic Concern		Self-Distress			
	β	SE	β	SE	β	SE
Intercept						
Intercept, β_{OLR}	1.45 ***	0.10	0.91 ***	0.11	30.09 ***	0.85
HR-NoASD, $\beta_{0HR-NoASD}$	-0.49 ***	0.13	0.04	0.14	-4.68 ***	1.38
R-ASD, β_{0ASD}	-1.06 ***	0.19	-0.60 **	0.20	-14.79 ***	2.02
Sex, β_{0SEX}	0.15	0.12	0.35 **	0.13		
Linear Growth						
Intercept, β_{ILR}	0.09	0.06	0.32 ***	0.07	6.86 ***	0.39
HR-NoASD, $\beta_{1HR-NoASD}$	0.25 **	0.09	-0.15	0.10	1.55 *	0.64
HR-ASD, β_{1ASD}	-0.03	0.13	-0.26	0.15	-1.47	0.97
Sex, β_{1SEX}	0.05	0.08	-0.08	0.09		
Visit Location, β_2			-0.16	0.10		

Note.

*
p < .05,**
p < .01,***
p < .001