Infants at-Risk for Autism Spectrum Disorder: Patterns of Vocalizations at 14 Months

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Lay abstract

Differences in early development are crucial for early detection of autism spectrum disorder (ASD). Previous studies have shown large differences between children later diagnosed with ASD and their typically developing peers in the early use of canonical vocalizations (i.e., vocalizations that include well-formed consonant-vowel syllables, like *ba*) and the use of vocalizations for communicative purposes. These findings suggest that the structure (i.e., canonical versus non-canonical) and communicative use (i.e., directed toward others versus non-directed) of early vocalizations may be useful indicators of later ASD outcomes. Early detection of ASD, however, requires the accurate prediction of clinical outcomes for infants and toddlers who show developmental differences that evoke concerns in parents and/or professionals. In this study, we examined the extent to which infant vocalizations at 14 months would later predict ASD symptom groups (Autism, Spectrum, and Non-ASD) based on Autism Diagnostic Observation Schedule (ADOS) algorithm scores at 23 months. Participants in this study were 82 infants identified at 12 months of age through a community screening as at-risk for later diagnosis of ASD. Thirty minute video samples were coded to categorize and quantify both speech (canonical/non-canonical and directed/non-directed) and non-speech (atypical, distress, and pleasure) vocalizations. Results revealed that fewer canonical directed vocalizations and more non-directed vocalizations (both canonical and non-canonical) at 14 months were associated with a greater likelihood of being in the Autism versus Non-ASD group at 23 months. Despite these statistically significant findings, the clinical utility of infant vocalizations alone for accurately predicting later ASD-related outcomes among at-risk infants was limited.

Abstract

Differences in the early development of children are crucial for early detection of autism spectrum disorder (ASD). Previous studies have shown large differences between children later diagnosed with ASD and their typically developing peers in the early use of canonical vocalizations (i.e., vocalizations that include well-formed consonant-vowel syllables) and the use of vocalizations for communicative purposes. In this prospective study, we examined the extent to which infant vocalizations at 14 months would predict Autism Diagnostic Observation Schedule (ADOS) diagnostic symptom groups, i.e., Autism, Spectrum, and Non-ASD, for 82 community-identified at-risk infants at 23 months. Thirty minute video samples were coded with the intention to categorize and quantify speech (canonical/non-canonical and directed/non-directed) and non-speech vocalizations (atypical, distress, and pleasure vocalizations). Our results revealed that more canonical directed (OR=1.039, p=.036), and fewer non-canonical directed (OR=.607, p=.002) and non-canonical non-directed (OR=1.200, p=.049) vocalizations were associated with a greater likelihood of being in the Non-ASD group versus the Autism group, with no variables significantly predicting Autism versus Spectrum group membership. Despite some statistically significant findings, models performed poorly in classifying children into correct ASD symptom group at age 23 months based on vocalizations at 14 months. Thus, the utility of infant vocalizations alone for predicting toddler clinical outcomes among infants initially identified at an elevated risk for ASD appears limited; however, considering the structure and function of early vocalizations combined with other early developmental and behavioral features may improve the confidence for clinicians in making an early diagnosis of ASD.

Infants at-Risk for Autism Spectrum Disorder: Patterns of Vocalizations at 14 Months

Understanding the early behavioral symptoms of autism spectrum disorder (ASD) not only can elucidate the developmental course of infants later diagnosed with this disorder, but also contribute to early identification and intervention planning. Compared to their peers, infants who go on to be diagnosed with ASD show significant group differences related to a wide range of behavioral risk markers, including eye contact, imitation, shared affect, orienting to name, response to caregiver language input, joint attention, gestures, and sensory modulation difficulties (Baranek, 1999; Cohen et al., 2013; Luyster, Seery, Talbott, & Tager-Flusberg, 2011; Mulligan & White, 2012; Ozonoff et al., 2010; Watson, Crais, Baranek, Dykstra & Wilson, 2013; Zwaigenbaum, Bryson, Rogers, Roberts, Brian & Szatmari, 2005). However, it is important to note that individual behavioral risk markers for ASD are rarely specific to categorical differences in clinical outcomes, but instead reflect different distributions in the frequency or intensity of behaviors for groups of infants later diagnosed with ASD versus those who are not. Thus, early ASD symptoms are generally manifested as more subtle differences across multiple behaviors rather than a clear presence or absence of one or two behaviors. This is consistent with the wide heterogeneity in the specific behavioral symptoms and severity of the impact of these symptoms among older children diagnosed with ASD (e.g., Johnson, Myers, & American Academy of Pediatrics Council on Children With Disabilities, 2007).

Both to advance understanding the early development of children prior to an ASD diagnosis and to contribute to the applicability of research findings to the clinical goals of early identification and intervention planning, it is important to know about the broad range of early behaviors that show different distributions among infants later diagnosed with ASD and those who are not. For the purposes of this paper, we define infants as children under the age of 24 months. Findings from several studies address the use of speech-like vocalizations (i.e., vocalizations with vowels or consonant-vowel combinations recognizable by adults as similar to sounds used by mature speakers) in infants with ASD. Retrospectively, parents of children with ASD indicate that their children's use of speech-like vocalizations at around 12 months of age differed significantly from what is reported by parents of typically developing children; however, parents' recall of their infants' vocalizations at 12 months does not consistently discriminate children with ASD from those with other developmental disabilities (DD) (Watson et al., 2007; Werner, Dawson, Munson, & Osterling, 2005).

Findings using other methods have been fairly consistent with the findings from retrospective parent reports related to the use of speech-like vocalizations. For example, through a retrospective analysis of early home videos made by parents of children with later diagnoses of ASD versus children later confirmed to be typically developing, Patten et al. (2014) reported large differences at both 9-12 months and 15-18 months. Infants with ASD produced fewer speech-like vocalizations (i.e., lower volubility) and less canonical babbling (syllables including well-formed consonants and vowels) than typically developing infants. Typically developing infants were 17 times more likely to meet an established criterion for being in the canonical stage (i.e., >.15 ratio of canonical syllables to all syllables; Oller, 2000) than infants with ASD at 9-12 months, and still 6 times more likely to meet this criterion level at the relatively late age of 15-18 months. Although Patten et al. did not include a comparison group of children with other DD, other studies have looked at this comparison. An earlier retrospective video analysis of first birthday parties yielded no between group differences in vocalizations among infants later diagnosed with ASD only, ASD plus intellectual deficits, intellectual deficits only, or with typical development

(Osterling, Dawson & Munson, 2002); however, it is not clear whether vocalizations in this study were confined to speech-like vocalizations or included both speech-like and non-speech-like vocalizations. In a later study, researchers analyzed home videos of first and second birthdays for three groups of infants: (a) infants with ASD with reported early onset of symptoms; (b) infants with ASD whose parents reported regression after 12 months of age; and (c) typically developing infants (Werner & Dawson, 2005). In this study, infants with ASD with regression showed higher rates of "complex babbling" (which was undefined in the study) at 12 months than infants with early onset ASD and used complex babbling *twice as frequently* as typically developing infants. By 24 months, however, typically developing infants used twice as much complex babbling as either subgroup of infants with ASD, who by this age were very similar to one another.

In a prospective study of toddlers identified through a community screening as being at heightened risk for communication disorders, including ASD, Plumb and Wetherby (2013) observed that of the vocalizations produced by 18- to 24-month-old infants later diagnosed with ASD, a lower proportion contained speech-like sounds compared to their typically developing peers, with a similar but nonsignificant trend in comparison to infants later diagnosed with other DD. Additional evidence from a study of infants at elevated risk for ASD due to having an older sibling diagnosed with ASD indicated these infants produced fewer total speech-like vocalizations at 6, 9 and 12 months, as well as a lower proportion of vocalizations with canonical syllables at 9 months, compared to low-risk infants (i.e., those who had an older sibling without ASD (Paul, Fuerst, Ramsay, Chawarska, & Klin, 2011). In this study, however, it is not clear whether group differences were driven largely by the high-risk infants who went on to be diagnosed with ASD, or instead represented a more generalized reduction in speech-like vocalizations and canonical syllables among high-risk infants.

Taken together, the existing studies lead to an expectation of generally fewer speech-like vocalizations and canonical syllables among infants later diagnosed with ASD compared to their typically developing peers. What is less clear is the extent to which specific patterns in early speech-like vocalizations may predict clinical outcomes among high-risk infants, either those who are at familial risk for ASD or those who screen as at-risk for ASD based on early behavioral symptoms related to ASD.

In addition to studying speech-like vocalizations, some researchers have also examined whether the production of non-speech vocalizations is different for infants with ASD compared to other infants. Evidence suggests that a larger proportion of vocalizations of infants with ASD are non-speech vocalizations than for typically developing infants (Plumb & Wetherby, 2013). Toddlers with ASD (16 to 36 months old) have been found to produce speech-like vocalizations at similar rates to 12-month-old typically developing peers matched for language level, but to produce more atypical non-speech vocalizations than either language level-matched or chronological age-matched typically developing peers (Schoen, Paul & Chawarska, 2011). Atypical vocalizations included squeals, growls, and yells. Infants at heightened risk for ASD based on having an older sibling with ASD showed a similar pattern of producing more non-speech vocalizations than low-risk infants across the ages of 6, 9 and 12 months (Paul et al., 2011).

A final question of particular relevance to the current study is whether infants later diagnosed with ASD are different from other infants in their use of vocalizations for communicative purposes. A lower frequency of vocalizations directed to others has been observed in infant siblings of children with ASD who themselves were later diagnosed with

ASD compared with infants with typical development at 12 months but not at 6 months of age (Ozonoff et al., 2010). In addition, another study found that infants with an older sibling with ASD (compared with low-risk infants) used fewer non-word speech-like vocalizations for communicative purposes at both 13 and 18 months (Winder, Wozniak, Parladé & Iverson, 2013).

Thus, the available evidence suggests that low volubility of speech-like vocalizations, delayed onset or restricted use of canonical babbling, a greater use of non-speech vocalizations (including unusual vocalizations), and fewer speech-like vocalizations directed to others are potential markers of emergent ASD. However, relatively few studies have compared vocalizations of infants later diagnosed with ASD to infants diagnosed with other DDs. Also, in the few available studies, much more consistent differences have emerged between infants with ASD outcomes when compared to typically developing infants than to infants with other DD. In addition, studies of infant siblings of children with ASD have not clarified how specific the differences in any of these vocalization features are to infant siblings who go on to be diagnosed with ASD versus those who exhibit broader autism phenotype characteristics and/or those who do not show elevated ASD symptoms. In general, very limited prospective research is available on infants identified as at-risk for ASD through community screenings. Specific to the focus of the current study, we only identified one such study providing data on infant vocalizations, with data collected when infants were 18 to 24 months of age (Plumb & Wetherby, 2013).

In the current study, we extend the available evidence related to vocalizations among infants at-risk for ASD by analyzing data from a sample identified by a community screening with the First Year Inventory, version 2.0 (FYIv2.0; Baranek Watson, Crais & Reznick, 2003; Reznick, Baranek, Reavis, Watson, & Crais, 2007). Our aim was to examine the extent to which infant vocalizations would be related to later ASD outcomes within this at-risk sample. Vocalizations were recorded during an assessment of the infants when they were between the ages of 13 and 15 months (mean of 13.74). Coded vocalizations were then used to predict ASD symptom group membership for the infants at 20 to 25 months of age (mean of 22.57). These symptom groups were based on Autism Diagnostic Observation Schedule Module 1 algorithm scores at the second assessment, using the cutoff criteria for “Autism,” “Spectrum,” and “Non-ASD.”

Our research question was as follows: To what extent is ASD symptom group membership at 23 months predicted by infant vocalizations at 14 months, including their (a) speech-like vocalizations – canonical/non-canonical and directed/non-directed, (b) non-speech vocalizations – atypical, distress and pleasure, and (c) volubility?

Method

The current study was a secondary analysis of data collected as part of an efficacy study of a parent-mediated early intervention for infants at-risk for ASD, led by the second and last authors (Watson et al., under review), which we will refer to as the parent study. The parent study was designed as a pretest-posttest randomized controlled trial. The vocalization data coded for the current study were drawn from the pretest assessment.

Participants

A total of 82 participants (55 male, 27 female) between 13 and 15 months at entry into the parent study were included in the present analyses. These infants all met criteria for being at-risk for ASD based on a parent report screening tool (see below). As part of participant recruitment, infants with identified genetic conditions associated with developmental disorders (e.g., Down syndrome), severe physical or sensory impairments, or in families speaking English less than 50% of the time in the home were excluded from the study.

Measures

The First Year Inventory version 2.0 (FYIv2.0; Baranek et al., 2003) is a 63-item parent questionnaire, normed for 12-month-old infants and designed to screen for risk of ASD. The FYIv2.0 items assess infant behaviors in two broad domains: social-communication and sensory-regulation. Using state birth records, the FYIv2.0 was distributed to families in the catchment area for the parent study approximately a week prior to each infant's first birthday. To be eligible for the parent study, infants had to meet pre-established criteria for being at-risk for later diagnosis of ASD on this questionnaire (i.e., (≥ 94%ile for risk in the social-communication domain and ≥ 88%ile in the sensory-regulatory domain).

The Mullen Scales of Early Learning (Mullen, 1995) is an examiner-administered developmental assessment standardized for children from birth to 48 months. It has four scales: Visual Reception, Receptive Language, Expressive Language, and Fine Motor. We used the Visual Reception T-score (a standard score with a mean of 50 and a standard deviation of 10) to characterize the infants' nonverbal cognitive functioning.

The Communication and Symbolic Behavior Scales-Developmental Profile (Wetherby & Prizant, 2002) is an examiner administered assessment of social, communication and symbolic skills standardized for infants from 9 to 24 months of age. We used the total standard score for this tool, with a mean of 100 and a standard deviation of 15, to characterize the infants' general communication functioning.

The Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, DiLavore, & Risi, 1999) is a semi-structured observational measure to evaluate symptoms of ASD in children and adults. At the initiation of the parent study, a validated version of the Toddler Module, currently recommended for assessing infants and toddlers, was not yet available; thus, all infants were assessed at 23 months using the ADOS Module 1, scored using the revised algorithms (Gotham, Risi, Pickles & Lord, 2007). To examine the association of vocalizations with later outcomes, we subgrouped the infants into one of three symptom categories, based on their ADOS algorithm scores: (a) Autism, (b) Spectrum, or (c) Non-ASD. Although the Diagnostic and Statistical Manual of the American Psychiatric Association – 5^{th} edition (American Psychiatric Association, 2013) does not recognize diagnostic subcategories within ASD, we maintained the divisions between Autism, Spectrum and Non-ASD as a broad indicator of ASD symptom severity at 23 months. It is important to recognize that these categories did not represent definitive clinical diagnoses for these infants, due to an a priori decision in the parent study not to give clinical diagnoses at posttest due to the young age of the children. We will refer to these groups as “ASD symptom groups” to reinforce the point that they are based on the quantitative outcomes of the ADOS algorithm scoring. Although it is reasonable to question whether the infants' ASD symptom groups at 23 months may have been affected by exposure to the experimental parent-mediated intervention tested in the efficacy study, the parent study documented no statistically significant differences between the experimental and control groups for ADOS algorithm total scores at 23 months (Watson et al., under review). As further confirmation of the lack of a clinically important impact on autism symptoms, the effect size for the comparison of ADOS algorithm scores was small, $d = .18$. Thus, for the purposes of the current study, we did not include treatment group in our models.

Procedures

As part of the parent study, participants were evaluated with the Mullen Scales of Early Learning (MSEL; Mullen, 1995) and the Communication and Symbolic Behavior Scales-Developmental Profile (CSBS-DP; Wetherby & Prizant, 2003) at 14 and 23 months. Parents and infants also were videotaped during a 10-minute free-play interaction with access to a standard set of toys at both assessment time points. At 23 months, participants were evaluated with the Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999) by trained, experienced examiners who met established research standards for reliability of scoring.

Coding procedure and observer agreement

Samples were coded from audiovisual recordings of the evaluation in a clinical context, so the audio-video quality was appropriate and all videos were recorded in similar rooms, with the same situational context and toy set. All participants included in this study except two had 30 minutes of video recording. The first ten minutes of video coded for vocalizations were from the parent-infant free play session. The next twenty minutes of coded video were recorded while an examiner assessed the infant with the CSBS-DP. We chose these two contexts in an effort to get a more representative sample of the infants' vocalizations. That is, the parent-infant free play was more naturalistic, with parents only being asked to, "Play with your child as you would if you were at home," whereas the CSBS-DP involves a protocol through which an examiner attempts to elicit social, communication, and play behaviors from the infant via direct cues (e.g., questions and directions) and indirect strategies (e.g., showing toys to the infant and waiting to see how s/he will respond). Per standard administration procedures, the parent sits beside the infant during the CSBS-DP assessment and is encouraged to respond to the infant if s/he tries to engage with the parent.

Based on previous literature (Oller, Eilers, Neal, & Schwartz, 1999; Oller, Eilers, Steffens, Lynch, & Urbano, 1994; Patten et al, 2014; Paul et al., 2011; Scherer, Boyce & Martin, 2013; Sheinkopf et al., 2000), we coded two types of speech vocalizations (canonical and non-canonical) and three types of non-speech vocalizations (atypical, distress, and pleasure vocalizations). Vocalizations were coded as discrete events. The onset of a vocalization occurred when the infant initiated the sound. A vocalization ended if there was at least one second break in the infant's vocalizing. Furthermore, we coded whether the infant directed the vocalization to another person, as evidence of intentionality. Vocalizations were considered to be "directed" if the infant accompanied the vocalization with gestures (e.g. touching a person, pointing to an object, shaking head "no") and/or eye contact, if the vocalization occurred within an interactive context involving reciprocal vocalizations/ verbalizations of the parent and infant (e.g., while both were looking at a book, or both were engaged in a game), or if the vocalization was an imitation of an adult's preceding vocalization (Colgan et al., 2006; Sheinkopf et al., 2000; Watson et al., 2013; Wetherby, Cain, Yonclas, & Walker, 1988). In the absence of these indicators of intentionality (e.g. not sharing interest with another person, not looking at another person's face/eyes, not touching person, no imitation), speech vocalizations were coded as non-directed. Each vocalization was coded, and frequencies of occurrence were calculated for each vocalization type. The decision making process is shown in Figure 1 and operational definitions of vocalizations are provided in Table 1. Three coders who were blind to infant outcome (i.e., ADOS results at 23 months of age) completed the coding for this study. The three coders first completed a training program on identifying different kinds of vocalizations. They achieved 90% agreement on event-by-event coding during training. The samples used during training were not included in the analysis. All videos were randomized and distributed among the three coders. To assess interrater reliability, two coders independently coded 20% of the videotapes, selected at random. They were unaware of which videos would be coded for the evaluation of interrater reliability. Following independent coding of a video (these data were used to compute interrater reliability), disagreements were resolved through discussion, to help prevent coder drift across the data coding period. Reliability was estimated from intraclass correlation coefficients (ICCs), using SPSS statistics version 22.0, using a two-way random effects model for absolute agreement.

INSERT TABLE 1 & FIGURE 1 ABOUT HERE

The results indicated that interrater agreement was excellent, with ICCs (single measures) as follows: speech vocalizations, $r = .990$, 95% CI [.970, .996]; non-speech vocalizations, $r = .986$, 95% CI [.961, .995]; canonical directed vocalizations (CD), $r = .995$, 95% CI 95 [.985, .998]; canonical non-directed vocalizations (CND), $r = .987$, 95% CI [.965, .995]; non-canonical directed vocalizations (NCD), $r = .958$, 95% CI [.820, .987]; non-canonical non-directed vocalizations (NCND), $r = .964$, 95% CI [.903, .987]; pleasure vocalizations (P), $r = .942$, 95% CI [.851. .979]; distress vocalizations (D), $r = .992$, 95% CI [.979, .997]; and atypical vocalizations (A), $r = .907$, 95% CI [.764, .965].

Our initially planned metric for volubility was the rate of speech-like vocalizations during the full 30 minutes (i.e., speech-like vocalizations per minute). During the coding process, however, coders noted salient differences across the two contexts, with generally lower volubility during the parent-infant interaction sessions. This led to a post-hoc decision to explore volubility separately in each context (parent-infant interaction and CSBS-DP).

Results

We used SPSS statistics version 22.0 to carry out the analyses. First, we compared demographic variables for the three groups and documented no significant differences on chronological age, $p = 0.71$, gender, $p = 0.97$, or race, $p = 0.98$ (see Table 2). In addition, there were no significant differences in MSEL VR T-scores, $p = 0.15$, or CSBS-DP total SS, $p = 0.08$, at 14 months. At 23 months, the comparison of MSEL VR T-scores remained nonsignificant, $p = 0.35$, but the model for the CSBS-DP total SS indicated significant differences, $p = .009$. Post-hoc tests indicated that infants in the Autism group had significantly lower scores than both the Spectrum group and the Non-ASD group, whereas the latter two groups were not statistically different from one another.

INSERT TABLE 2 ABOUT HERE

For descriptive purposes, Figure 2 shows the mean frequency data for each vocalization type by ASD symptom group. The means for total vocalizations per group were very similar: Autism = 115.3 (55.2), Spectrum = 107.0 (56.5), non-ASD = 121.5 (46.8), F = .45, p = .64. The standard deviations reflect the large variability within each group.

INSERT FIGURE 2 ABOUT HERE

Descriptive statistics for the mean frequency and range of each vocalization type,by group are provided in Table 3. The number of vocalizations was used in the regression analyses to examine the extent to which group membership could be predicted by vocalization type. Prior to the regression analyses, we conducted descriptive statistics in order to find statistical outliers, and detected three outliers who produced very high numbers of canonical directed vocalizations, exceeding the mean in all groups by more than 3 SDs. Coincidentally, one outlier was detected in each group. In order to minimize the potential impact of bias, we winsorized the data. Comparing results from the winsorized data to results without any transformation, we determined that the outcomes were relatively unaffected by irksome data. Thus, the final analyses included untransformed data from all participants.

INSERT TABLE 3 ABOUT HERE

We addressed the components of our research question using multinomial logistic regression analysis (an extension of regression that allowed us to predict from our vocalization variables to our categorical outcome –Autism, Spectrum, and Non-ASD). We tested models for speech and non-speech vocalizations separately, followed by a set of models examining whether volubility discriminated between the groups. The Autism group was used as the referent group in each model. Results are presented in Table 4. Odds ratios (ORs) from these models reflect the increase (or decrease) in the odds of a child being in the contrast group relative to the Autism group, based on a one-unit increase in the predictor variable – in this case, an increase of one vocalization. Thus, although these ORs may seem small as presented, they should be considered with respect to the range of vocalizations of each type. To facilitate interpretation of the ORs for each predictor variable, we include the range of vocalizations of each type seen in the full sample.

The first multinomial logistic regression model tested whether there were group differences in different types of speech vocalizations (CD, CND, NCD, NCND). Results revealed there were significant differences between infants in the Autism vs. Non-ASD groups on CD, CND and NCND (CD= OR: 1.039, p = .036; CND = OR: .607, p = .002, and NCND= OR = 1.200, p = .049). This model did not find any significant difference between infants in the Autism vs. Spectrum groups. We will use the finding for the CD vocalizations in the comparison of the Autism group to the Non-ASD group to illustrate the interpretation of the ORs in these analyses. The OR of 1.039 indicates the increased odds of being in the Non-ASD group rather than the Autism group associated with producing one additional CD vocalization in the 30-minute sample. Producing 20 additional CD vocalizations would increase the odds of being in the Non-ASD group rather than the Autism group to 2.149. Given the range of CD vocalizations from 0 to 107, infants at the extremes of this range of CD vocalizations clearly have much different likelihoods of ending up in the Autism versus Non-ASD group. The second model revealed a significant difference on A (OR: .915, p= .024) between infants in the Autism vs. Spectrum groups, indicating each additional A vocalization is associated with a decrease in the likelihood of being in the Spectrum group rather than the Autism group. This model did not find any significant difference between infants in the Autism vs. Non-ASD groups.

INSERT TABLE 4 ABOUT HERE

The Nagelkerke coefficient exhibited evidence that our model including the four subtypes of speech-like vocalizations explained 28% of the variance among groups, and demonstrated significant differences on chi-squared distribution $\chi^2 = 23.55$, $p = .003$. However, the model showed a weak performance in classifying children accurately into the correct ASD symptom group with only 48.8% of the children correctly classified overall. As shown in Table 5, although 76.5% of children were correctly predicted to be in the Autism group, the model over-assigned Non-ASD children to the Autism group and over-assigned Spectrum children to the Non-ASD group.

INSERT TABLE 5 ABOUT HERE

In contrast to the results reported in speech vocalizations, we did not observe any difference between Autism vs Non-ASD groups on any of the non-speech vocalization types of distress, pleasure or atypical vocalizations (see Table 4). This model found a significant difference on A (OR: .915, p= .024) between infants in the Autism vs Spectrum groups.

Finally, we evaluated the volubility of vocalizations, or the mean rate of speech-like vocalizations per minute (see the lower portion of Table 4). A series of three models indicated that volubility across the entire 30-minute video samples did not make a significant contribution to predicting group membership, nor did volubility during the 20 minutes coded from the CSBS-DP. However, during the 10-minute parent-infant interaction sessions, the model reported statistically significant differences between the Autism vs Non-ASD groups (OR: 1.570, p=.015). Infants in the Autism group showed lower volubility than infants in either of the other groups. The Nagelkerke coefficient exhibited evidence that the 10-minute model explained 9% of the variance among groups, and demonstrated significant differences on chi-squared distribution $\chi^2 = 6.99$, $p = .03$.

Discussion

In this study, we examined the extent to which characteristics of vocalizations at 14 months served to discriminate between infants falling into one of three ASD symptom groups at 23 months of age. The symptom groups, Autism, Spectrum, and Non-ASD are based on ADOS Module 1 algorithm score criteria. It is important to remember that these groups are based only on the algorithm scores and do not reflect clinical diagnoses for the infants. Also impacting the interpretation of our study results is the fact that all of the infants in this study were identified as being at-risk for later diagnosis of ASD with the FYIv2.0. Based on estimates from a prior study (Turner-Brown, Baranek, Reznick, Watson, & Crais, 2013) approximately one-third of 12-month-old infants who meet the FYIv2.0 criteria for being considered at-risk for ASD will show symptoms warranting an ASD diagnosis at age 3, and approximately 85% of these infants will have developmental concerns of some type (ASD or other) at age 3. Thus, none of the three symptom groups can be considered a “typically developing” or “low risk” comparison group. The nature of this sample is congruent with our study aim. That is, previous research has yielded replicated findings of differences in vocalizations between infants and toddlers with ASD and their peers who are typically developing (Patten et al., 2014; Plumb & Wetherby, 2013). In order to extend the existing literature, our primary aim was to examine the utility of vocalizations for predicting ASD-related outcomes among a group of infants at-risk for ASD.

To first consider canonical vocalization types (directed or non-directed), infants in the Autism group in the current study used fewer CD vocalizations and more CND vocalizations than infants in the Non-ASD group, and showed nonsignificant trends in the same directions when compared to the Spectrum group. Then turning to non-canonical vocalizations, the tendency of infants in the Autism group to use more non-directed vocalizations was seen again in their higher use of NCND vocalizations than the Non-ASD group. Thus, the differences seen among the groups in their use of speech-like vocalizations seem to be related more to the communicative use of vocalizations (i.e., directing them to other people or not) than to canonical versus non-canonical syllable shapes. This is consistent with the findings reported by Ozonoff et al. (2010) and Winder et al. (2013), as well as being congruent with the later deficits in social-communication that are part of the diagnostic criteria for ASD.

Our findings run counter to the implications of findings of Patten et al. (2014) that syllable structure early in the second year of life might be a powerful risk marker for autism specifically. While acknowledging methodological differences between Patten et al. (2014) and the current study, infants in the Autism group in our study appeared to be producing canonical vocalizations much more consistently at 14 months than those studied by Patten et al. at either 9-12 months or 15-18 months, and the syllable structure of speech-like vocalizations per se was not significantly predictive of ASD symptom group at 23 months. Possibly syllable structure is more closely related to global developmental delays and/or delays in general communication development than to autism specifically. The credibility of this explanation could be explored more fully in future prospective studies of infants at-risk for ASD, particularly if children are followed sufficiently long to make definitive clinical diagnoses. Comparing groups that are predefined in ways that create non-continuous distributions of relevant variables (e.g., ASD versus typical, as in Patten et al.) is likely to over-estimate the extent to which early markers predict ASD-related clinical outcomes.

We observed differences in the use of atypical non-speech vocalizations among these high-risk infants based on their ASD symptom group at 23 months of age. Although Plumb &

Wetherby (2013) documented that infants later diagnosed with ASD used proportionately more non-speech vocalizations than typically developing children, they did not find a difference on this variable between the ASD group and the group of infants later diagnosed with other DD. Thus, our results support previous findings that infants' use of speech versus non-speech vocalizations may not be helpful in predicting which infants will later be diagnosed with ASD (or present more symptoms consistent with an ASD diagnosis) among infants who are demonstrating some signs of ASD and developmental risk.

Our findings related to volubility extend the previous literature by suggesting that low volubility within relatively unstructured, more naturalistic contexts (such at the parent-infant interactions sessions in our study or the home videos used by Patten et al., 2014) may indicate risk for a later autism diagnosis, whereas volubility in a context specifically designed to elicit communicative behaviors from infants may not. This finding has a parallel in a study of pretend play in preschoolers, where children with ASD produced significantly fewer spontaneous than scaffolded pretend play acts, whereas children with other developmental disorders and children with typical development did not show these discrepancies (Rutherford, Young Hepburn & Rogers, 2007). This finding highlights the importance of eliciting information from parents regarding a child's characteristic behaviors at home as well as observing children under unstructured conditions during clinical assessments related to ASD diagnosis, rather than relying solely on observations during structured assessments.

Despite the emergence of this and other significant differences related to vocalizations among the subgroups of at-risk infants in our cohort, the heterogeneity within the groups and considerable overlap between them is perhaps more striking than the between-group differences. Evidence of the heterogeneity and overlap is supported both by the group means and standard deviations shown in Table 3 as well as by the low overall accuracy of our models in classifying children into ASD symptom groups, as illustrated in Table 5. Certainly, vocalizations could be salient risk markers for ASD in an infant who shows extreme patterns of limited rate of speech-like vocalizations, few canonical syllables, and few speech-like vocalizations directed to others. Such a risk profile might be quite specific to ASD. In addition, this symptom profile would suggest a critical need for early intervention is to address both the form and function of the infant's emerging speech, even if a definitive diagnosis of ASD is not yet possible. Our data suggest, however, that none of the vocalization variables we examined in this study is likely to be a very sensitive marker, in isolation, for later ASD symptom outcomes among at-risk infants. However, examining the quantity and quality of vocalizations may be clinically useful in predicting later ASD diagnosis when considered along with other behavioral risk markers.

Another possibility is that the dimensions of vocalizations examined in this study may be more useful in predicting later language outcomes than later ASD outcomes among these at-risk infants. As shown by the MSEL Receptive and Expressive Language scores in Table 2, the infants in all three groups were 1.5 to 2.0 standard deviations below the mean at 13-15 months. On average, language scores improved by 20-25 months, especially for the Spectrum and Non-ASD groups, and the variability generally increased as well. In a young sample of initially preverbal children diagnosed with ASD, Yoder, Watson and Lambert (2015) found that consonant diversity in the vocalizations of the children at study entry predicted later expressive language outcomes. Thus, the dimensions of vocalizations we examined in this study may have utility for predicting language outcomes among at-risk infants, or perhaps would help to identify infants who will later have both poorer language outcomes and ASD, but may be insensitive to ASD-related diagnoses among infants with a better trajectory of language development.

Limitations

The current study has several limitations, primarily related to our use of data collected for other purposes as a mechanism for looking at vocalizations in infants at-risk for ASD. Interpretation of the consistency of our results with prior research would have been enhanced by the inclusion of a comparison group drawn from among infants whose parents returned the FYIv2.0 for the same parent study, but whose infants scored at low-risk for ASD. Second, although the data from the parent study indicated that the intervention tested did not have a main effect on ADOS results for these infants, there may be some unidentified moderators of the effect of the treatment on ASD symptoms that changed the association between vocalizations at 14 months and ASD symptoms at 23 months. Third, our reliability for coding atypical vocalizations was lower than for other vocalization categories, and thus measurement error may have masked between-group differences in atypical vocalizations in this study. Finally, grouping infants based on later definitive diagnostic outcomes may have yielded different findings and implications than our use of groups based on ADOS algorithm scores at 23 months; unfortunately, we did not have access to definitive diagnostic outcomes. Previous studies suggest that toddlers whose ADOS scores place them in the Autism or Non-ASD groups are likely to be given corresponding clinical diagnoses of ASD or non-ASD, respectively; however, for toddlers whose algorithm scores place them in the Spectrum group (or mild-to-moderate range of concerns on the ADOS-Toddler module), clinical diagnosis is more likely to diverge from the ADOS results (Chawarska, Klin, Paul, & Volkmar, 2007; Kim & Lord, 2009). False positives appear to be more likely among toddlers who are young in comparison to true positives, and, like true positives, show relatively low performance on nonverbal cognitive and adaptive measures, whereas false negatives appear to be more likely among toddlers who are young in comparison to true positives and have relatively higher scores on nonverbal cognitive and adaptive measures (Kim & Lord). As shown by the MSEL VR scores (Table 2), our participants had mean nonverbal cognitive scores in the average to low average range across all three ASD symptom groups. Due to both their young age and their relatively good nonverbal cognitive skills, clinical diagnoses, if available, may not have shown a high agreement with the ASD symptom groups.

Conclusions and Future Directions

Despite its limitations, our study extends previous research on vocalizations of infants at-risk for ASD by examining these behaviors in a community-identified at-risk cohort shortly after their first birthdays. Previous studies of at-risk infants this age or younger largely have been confined to studies of infant siblings of children with ASD. Given that our entire cohort was at high risk for a later diagnosis of ASD and/or other DD, the significant association of some features of their vocalizations with ASD symptom group outcomes is a notable finding. Given the findings of Paul et al. (2011) that the inventory of consonants in infant siblings of children with ASD distinguished between the infants who went on to be diagnosed with ASD and those who did not, examining the predictive value of the consonant inventory in community screened infants at-risk for ASD would be a worthwhile future direction. In addition, research with this population offers exciting opportunities to understand the roles that vocalizations of infants at-risk for ASD may play in eliciting different input from caregivers of these infants (cf., Warlaumont, Richards, Gilkerson & Oller, 2014), that could in turn impact opportunities for social engagement and language learning for the infants (cf., Woynaroski, Watson, Gardner, Newsom, Keceli-Kaysili & Yoder, 2016).

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Table 1. Definitions of vocalizations used in the coding procedure

Vocalization	Definition
Speech	The production of consonants and/or vowels that have a speech-like vocal quality (Ozonoff et al., 2010; Paul et al., 2011).
Canonical vocalizations	Vocalizations that include at least one well-formed syllable (syllables containing the basic consonant-vowel (CV) structure, including single CV syllables such as [da], reduplicated sequences such as [bababa] and sequences with variable consonants such as [dʌgʌ]). Each canonical vocalization must have at least one full vowel-like element and at least one consonant-like element, and must have a rapid formant transition between consonant and vowel (examples, [ba][ata][nunu][di][dada] (Oller, Eilers, Neal, & Schwartz, 1999; Paul et al., 2011;
Non-canonical vocalizations	Speech-like vocalizations that do not include any well-formed syllables with C-V structure; these vocalizations include those with marginal syllables (i.e., having a C-V structure but with a long C-V transition rather than a rapid formant transition), isolated consonants (mmmmmmm), speech-like full vowels, isolated vowels, and quasivowels. (Oller, Eilers, Steffens, Lynch, & Urbano, 1994; Scherer,
Non-speech	Vocalizations characterized by the production of non-speech resonance and vocal quality (e.g., squeals, growls) without recognizable consonants (Paul et al., 2011).
Atypical	Squealing (vocalizations at high pitch), growling (vocalizations at low pitch, often in squeaky voice), glottal fricative and glottal stop sequences (vowels or quasivowels occurring in syllable-like sequences with glottal consonants, which require no supraglottal articulation), raspberries (labial trills or vibrates) (Oller et al., 1994).
Pleasure	Laughing or giggling, an audible vocalization that is usually associated with pleasure (Paul et al., 2011).
Distress	A vocalization associated with a negative emotional state like crying, whining, screaming or fussing (Paul et al., 2011).

Table 2. Participant demographics and developmental test performance

ADOS classification	AUTISM	SPECTRUM	NON-ASD
N	34	25	23
Mean age (*sd*) at 13-15 m	13.79 (.77)	13.64 (.76)	13.78 (.74)
Mean age (*sd*) at 20-25 m	22.79 (.91)	22.48 (.65)	22.35 (1.03)
Child's gender (M:F)	23:11	17:8	15:8
Child's race (White:African-American:Other)	24:7:3	18:4:3	16:5:2
Mean (*sd*) MSEL VR T-score, 13-15 m	43.00 (12.49)	48.36 (9.89)	40.06 (8.71)
Mean (*sd*) MSEL RL T-score, 13-15 m	33.21 (12.34)	34.88 (12.58)	31.00 (6.16)
Mean (*sd*) MSEL EL T-score, 13-15 m	34.26 (11.71)	35.64 (12.06)	32.91 (9.53)
Mean (*sd*) CSBS-DP Total SS, 13-15 m	84.29 (11.39)	86.29 (13.45)	89.87 (15.31)
Mean (*sd*) MSEL VR T-score 20-25 m	43.88 (15.13)	48.92 (10.28)	46.26 (12.49)
Mean (*sd*) MSEL RL T-score, 20-25 m	38.26 (17.99)	48.16 (14.29)	48.65 (13.86)
Mean (*sd*) MSEL RL T-score, 20-25 m	38.85 (14.63)	45.32 (12.10)	40.17 (8.95)
Mean (*sd*) CSBS-DP Total SS, 20-25 m	83.64 (16.53)	96.12 (16.24)	92.87 (13.29)

Table 3. Descriptive statistics for vocalization types and volubility

		Group								
		AUTISM			SPECTRUM			NON-ASD		
		M	SEM	Range	M	SEM	Range	M	SEM	Range
Speech	CD	24.94	3.19	0-65	31.32	5.42	2-107	27.74	5.11	0-97
	CND	5.76	1.23	0-38	2.56	1.17	0-29	1.57	.387	0-6
	NCD	44.97	4.93	6-124	43.80	6.15	9-99	53.87	5.64	4-116
	NCND	5.85	.993	0-21	3.44	1.00	0-20	4.57	.873	0-13
	Total Directed	69.91	7.01	12-161	75.12	.9.99	12-188	81.61	7.77	7-155
	Total Non-directed	11.62	2.04	0-57	6.00	2.06	0-49	6.13	1.04	0-16
Non-speech	A	13.24	1.96	0-50	8.04	1.04	0-19	12.78	2.04	1-36
	D	18.03	3.01	0-59	13.60	2.35	0-38	15.39	3.38	2-76
	P	2.50	.516	0-10	3.80	1.01	0-17	2.57	.482	0-8
Total	Speech	81.53	7.83	15-194	81.48	10.99	13-237	87.74	8.01	7-167
Total	Non-speech	33.76	3.86	0-98	25.52	2.63	9-55	30.74	3.71	8-83
Volubility	10MIN	1.92	1.28	0-6.4	2.73	1.76	.3-6.2	3.03	1.85	.6-7.0
	20MIN	3.12	2.23	0-8.40	2.50	2.03	0-11.7	2.94	1.92	0-5.8
	30MIN	2.72	1.52	.5-6.5	2.50	1.51	.5-7.9	2.92	1.28	.2-5.6

Note: CD: canonical directed, CND: canonical non-directed, NCD: non-canonical directed, NCND: non-canonical non-directed, A: atypical, D: distress, P: pleasure. 10MIN: parent-infant context, 20MIN: CSBS-DP context, 30MIN: parent-infant + CSBS-DP contexts. Vocalization types are represented as number of vocalizations. Volubility is represented as the rate of speech-like vocalizations per minute.

Table 4. Multinomial logistic regression, based on autism group as reference group

	Range		AUTISM vs. SPECTRUM			AUTISM vs. NON-ASD		
			OR	95% CI	*p*	OR	95% CI	*p*
Speech model	0 - 107	CD	1.03	.998 -	.062	1.039	1.003 -	.036
	0 - 38	CND	.830	.674 -	.079	.607	.445 - .827	.002
	4 - 124	NCD	.994	.972 -	.624	1.008	.985 -	.501
	0 - 21	NCN	1.02	.866 -	.753	1.200	1.001 -	.049
Non-speech	0 - 50	A	.915	.848 - .989	.024[a]	.995	.943 -	.857
	0 - 76	D	.985	.950 -	.414	.989	.956 -	.545
	0 - 17	P	1.14	.972 -	.107	1.008	.845 -	.928
Volubility	.00 - 7.70	10MI	1.12	.772- 1.630	.546	1.570	1.090 -	.015
	.00 -	20MI	.988	.780 -	.919	.981	.769 -	.876
	.23 - 7.90	30MI	1.01	.718 -	.930	1.141	.806 -	.456

Note: Range: the range of vocalizations of each type seen in the full sample, CD: canonical directed, CND: canonical non-directed, NCD: non-canonical directed, NCND: non-canonical non-directed, A: atypical, D:

distress, P: pleasure, 10MIN: parent-infant context, 20MIN:CSBS-DP, 30MIN:parent-infant context + CSBS-DP. OR: Odds ratio

[a] $p < 0.05$

Table 5. Classification table for vocalization model

	Predicted			
Observed	Autism	Spectrum	Non-ASD	Percentage correct
Autism	26	4	4	76.5%
Spectrum	12	4	9	16.0%
Non-ASD	10	3	10	43.5%
Overall Percentage	58.5%	13.4%	28.0%	48.8%

Figure 1. Coding tree for infant vocalizations

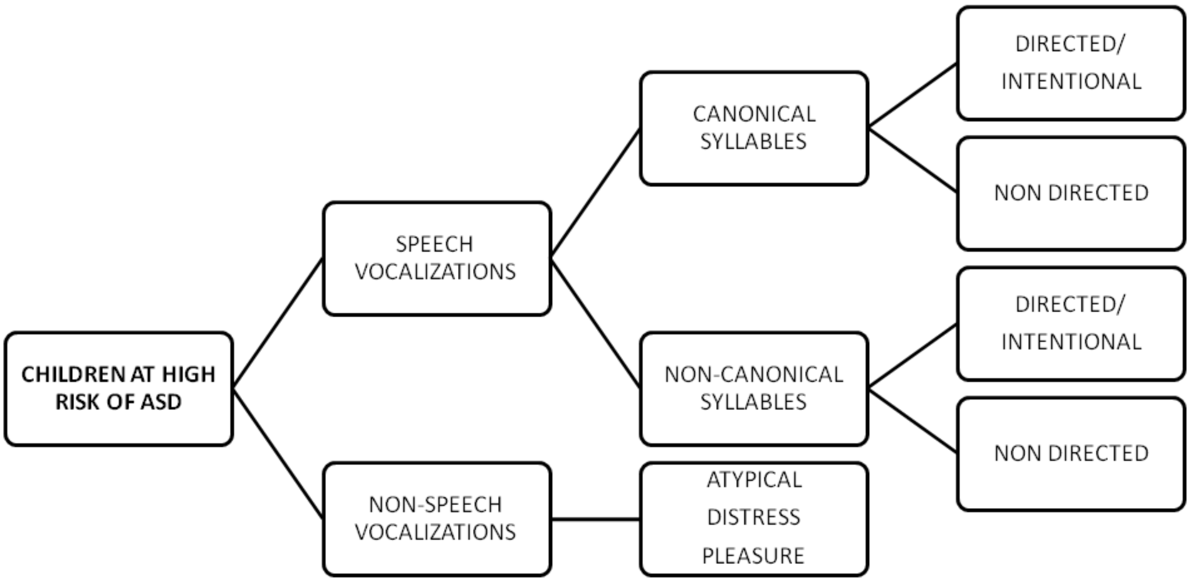

Figure 2. Mean frequency of each type of vocalization for infants in ADOS algorithm groups (Autism, Spectrum and Non-ASD) during a 30-minute sample