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ORIGINAL PAPER

Perception of Cry Characteristics in 1-Month-Old Infants Later Diagnosed with Autism Spectrum Disorder

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Abstract
This study investigates parental perceptions of cries of 1-month-old infants later diagnosed with autism spectrum disorder (ASD) and non-ASD controls. Parents of children with and without ASD listened to cry recordings of infants later diagnosed with ASD and comparison infants and rated them on cry perception scales. Parents completed the Broad Autism Phenotype Questionnaire (BAPQ) to assess the potential relations between traits associated with autism and cry perception. Across parents, ASD infant cries were rated as more distressed, less typical, and reflecting greater pain, with no significant differences between parent groups. Parents of children with ASD scored higher on the BAPQ compared to parents of children without ASD. Follow up analyses explored the relations between BAPQ score and cry ratings.

Keywords Autism spectrum disorders · Communication & language · Infancy · Cry

Autism spectrum disorders (ASD) are characterized by impairments in social and communicative behaviors, as well as atypical repetitive behaviors. Early screening for and diagnosis of ASD can lead to early treatments and improved developmental outcomes (Vinen et al. 2017; Zwaigenbaum et al. 2015). However, the reliability of screening and diagnosis is challenging in young children, and very limited in infancy (Mandell et al. 2010; Zwaigenbaum et al. 2015). Identifying early indicators of risk would help to improve early screening for ASD. While subtle differences in social attention and social responses may emerge during infancy in children with later autism diagnoses (Jones et al. 2014, 2016; Jones and Klin 2013; McCormick et al. 2018; Ozonoff et al. 2010), alternative neurobehavioral or biological markers may be needed to identify risk for or progression of ASD in early life.

Infant cry can be used as a marker of the neurobehavioral status of newborns and may indicate risk for neurological or developmental disorders (LaGasse et al. 2005). Cry serves as an important distress signal that functions to alert the environment of an infant's needs and mobilizes caregiver responses (Lester 1984; Newman 2007; Pinyerd 1994). This 'protolanguage' is the infant's earliest form of vocal communication and is a physiological response to states of pain, hunger, distress etc. Individual differences in the acoustic quality of cry vocalizations can be used as a potential risk marker for poor developmental outcomes. Acoustic differences can be perceived by listeners and impact caregiver responses, effects that are suggested by animal models (Esposito et al. 2017; Takahashi et al. 2015) and studies of cry perception in humans (Lester et al. 1995; Papousek and von Hofacker 1998).

The effects of crying may be disrupted in at least two ways. The cry signal may be atypical or the caregiver may have an atypical response to the cry, resulting in either a diminished or heightened response to the infant's vocalizations. While cry episodes follow a prototypical pattern, composed of rhythmically organized expiratory utterances

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and inspirations, the parameters and acoustic details may be unique to the specific infant. Since cry is also a communicative signal that involves the infant and the caregiver who responds, cry perception may be influenced by characteristics of the parent. Thus, understanding cry relies not only on the acoustic signal itself, but also on the salience of that signal to any potential caregivers.

Recent studies have shown that vocal characteristics differ between typically developing infants and infants with or at risk for ASD. Atypical vocalizations have been found in infants and toddlers at risk for ASD (Oller et al. 2010; Patten et al. 2014), and atypical vocal quality has been found in young preverbal children with ASD (Sheinkopf et al. 2000). Historical clinical accounts described atypical vocalizations in children with autism diagnoses (Asperger 1991; Kanner 1943; Ornitz and Ritvo 1976) and early research found that children with autism produce vocalizations with more ambiguous emotional signals (Ricks and Wing 1975). Such findings have led to the hypothesis that vocal production in infancy may differentiate those at risk for or later diagnosed with ASD. There is some initial evidence in support of this hypothesis. Esposito and Venuti (2010) reported that 18-month-old infants with ASD produced cries with higher fundamental frequency than healthy controls. Sheinkopf et al. (2012) found higher and more variable fundamental frequency in pain elicited cries in 6-month-old infants at risk for ASD as compared to a low-risk comparison group. Elevated fundamental frequency of distress vocalizations has also been found in infants at high risk for ASD during the separation phase of the Strange Situation procedure in the second year of life (Esposito et al. 2014).

A small body of research has directly addressed the question of whether acoustic differences in cries of infants with ASD as compared with typically developing infants give rise to differences in parent perceptions of cry. Cries of 13 to 20-month old infants with ASD were found to elicit greater negative mental states in both parents and nonparents (Esposito and Venuti 2008), and differences in fundamental frequency and utterance timing appeared to drive these perceptions (Esposito and Venuti 2010). Research has also documented that cries of infants with later diagnoses of ASD elicit differential neural response as measured with fMRI (Venuti et al. 2012) and that the effects on perceptual ratings of cries from ASD infants holds up in cross cultural comparisons (Esposito et al. 2012). Thus, findings on the perceptions of manipulated cry characteristics are consistent with the atypical vocal properties emerging in infants with autism and these vocal atypicalities of infants with ASD may lead to greater experiences of distress in listeners. Overall, these studies reveal initial differences in cry perception and show that cries of infants with ASD, age 13 months and older, elicit stronger negative affect in listeners than cries from infants with typical development. Despite these initial findings, studies have not yet identified ASD-related differences in the perception of cries from infants in the first year of life.

The finding that atypical cry acoustics can be detected in infants at risk for ASD as early as 6 months of age (Sheinkopf et al. 2012) suggests that parents may perceive ASD-related differences in cries in early infancy. Objective acoustic features of cry can be expected to interact with the state and trait of listeners to impact cry perception. According to a "goodness-of-fit" model of cry (Lester et al. 1995), disruptions in early parent-infant interaction could be based on differences in the signaler (the infant) or the perceiver (the parent). Therefore, not just the quality of the signal, but also characteristics of the recipient may influence the interpretation of infant cries. Parents of children with ASD are more likely than parents with no family history of ASD to exhibit a set of sub-threshold social and communication differences that has been referred to as the broader autism phenotype (BAP; Piven et al. 1997). These subclinical differences aggregate in close relatives of children with ASD and may impact social cognition and emotion perception. Alternatively, it can also be hypothesized that the experience of having cared for a child with ASD may impact a parent's perception of affective signals, including cry (Ozturk et al. 2018). It has been shown that parents of children with ASD find their children's cries to be more unexpected and difficult to interpret (Esposito and Venuti 2008), and that cries by older children with ASD appear to elicit different arousal responses in parents of children with ASD versus parents of children with typical development (Ozturk et al. 2018). It is not known whether this would be an indication of differences in the properties of infant cries, or the result of altered perception of cry signals impacted by parental characteristics. It is reasonable then to ask whether these features may impact parental perception and interpretation of infant cries. Thus, another goal of this study is to explore the differences in perceptions of parents of children with ASD and parents of TD children.

Investigating neurobehavioral differences associated with later ASD can be expected to elucidate the early course of ASD symptoms, including an improved understanding of features that can be considered more primary manifestations of underlying etiology, versus those that may be secondary features that emerge with development. Whereas prior studies of infant cry have included infants 6 months of age or older, investigating potential differences in the neonatal period would improve the field's understanding of the early neurobehavioral course of ASD. Thus, in addition to the study of cry in relation to early communication and infant-parent interactions, the timing of developmental divergences will help to specify hypotheses about the underlying neurobiology of ASD, including heterogeneity in the early course and symptom onset (see, for example, Courchesne et al. 2011; Jones and Klin 2009; Miron et al. 2018).

The present study was designed to investigate how listeners perceive cry vocalizations of 1-month-old infants later diagnosed with ASD relative to cries of infants with typical development, and whether parents of children with ASD differ from parents of typically developing children in their perception of these cries. This is an age that precedes the onset of more overt behavioral symptoms, which emerge developmentally over the first 2 years of life. Cry samples were derived from a large library of cry recordings from a previous study. Audio recordings were made during a procedure that elicited cries with a mildly painful standardized stimulus at 1-month of age in infants who were then followed longitudinally to determine later developmental outcomes. Unrelated parents of children with and without ASD recruited for this study were asked to fill out a perception scale following each cry they heard, assessing the level of urgency, distress and typicality each listener perceived.

The aims of this study were as follows: (1) to assess whether the cries of infants with later ASD diagnoses sound different to parents of young children, and (2) to examine whether parents of children with ASD differ from parents of children with TD in how they perceive infant cries. We predicted that parents would rate the ASD cries as more distressing than cries from matched controls. We also hypothesized that parents of children with ASD would rate the cries as less urgent or distressing in comparison to the parents of children with typical development. As a secondary and exploratory aim, we also explored how differences in cry perception relate to individual differences in broader autism phenotypic traits also measured in this study cohort.

Method

Participants

Participants included 42 mothers of typically developing (TD) children or children with ASD. Inclusion criteria for parent participants was having a typically developing child or a child with autism under the age of 10 years. The final sample was comprised of 20 mothers of TD children ($M = 35.80$ years, $SD = 3.49$) and 22 mothers of children with ASD diagnoses ($M = 37.82$ years, $SD = 6.79$). The majority of mothers were married and white. The groups did not differ in parent age, $t(31.99) = -1.23$, $p = 0.23$, or in the age of the youngest child, $t(40) = -1.44$, $p = 0.16$. Additional analyses revealed no significant group differences in race, $\chi^2(2, N = 40) = 1.24$, $p = 0.54$, income, $\chi^2(9, N = 40) = 7.82$, $p = 0.55$, or the number of people in the household, $\chi^2(5, N = 40) = 6.12$, $p = 0.30$. However, there were differences between groups in the highest school grade completed, $\chi^2(5, N = 42) = 12.70$, $p = 0.03$. More parents of TD children had college or higher education. Parent demographic data are summarized in Table 1.

The parents of children with ASD were recruited from an autism diagnostic clinic, through community organizations for families of children with ASD, and from the Rhode Island Consortium for Autism Research and Treatment (RI-CART; Gerber et al. 2014) patient registry. Of the 22 parents in the ASD group (i.e., having a child with autism), all reported that there was a clinical diagnosis of autism made for their child with autism. The Autism Diagnostic Observation Schedule, 2nd Edition (ADOS-2; Lord et al. 2012) was completed for 15 of these children as part of the patient registry study. Of these ADOS-exams, all exceeded cut-off for elevated autism symptoms, with 12 of 15 exceeding cut-off for Autism and 3 exceeding cut-off for autism spectrum. The parents of children with typical development were recruited from local childcare facilities and by word-of-mouth. All parents gave written informed consent for participation and the research received approval from the Institutional Review Board at Women and Infants Hospital of Rhode Island.

Stimuli

Cry samples were selected from the existing libraries of cry recordings from a longitudinal investigation of the outcomes of children who were prenatally exposed to cocaine and other substances (the Maternal Lifestyle Study; Lester et al.

Table 1 Demographics by parent group

	Parent grouping	
	TD (n = 20)	ASD (n = 22)
Race/ethnicity (%)		
White	94.3	85.7
Hispanic	5.3	9.5
African American	0	4.8
Highest grade completed (%)		
Some high school	0	9.1
High school/GED	0	4.5
Some college	0	27.3
College degree	100.0	59.1
Household income (%)		
< $25,000	0	9.5
$25,000–50,000	26.3	14.3
$50,000–100,000	36.8	42.9
> $100,000	36.8	33.3
Parent age: mean (SD)	35.8 (3.5)	37.8 (6.8)
Number of children in household: mean (SD)	1.9 (1.1)	2.2 (0.8)
Age (years) of youngest child: mean (SD)	3.5 (2.6)	4.6 (2.3)

2002). This multi-site study occurred at Brown University/Women and Infants Hospital of RI, University of Miami, University of Memphis, and Wayne State University, and methods related to perinatal and early infant assessment have been previously published (Bauer et al. 2002; Lester et al. 2002). From an initial sample of 1388 infants, children with possible autism diagnoses were identified using information from medical history forms and from reports by each of the study sites. There were 19 children with potential diagnoses of autism. Diagnostic confirmation was performed at ages 8–16 years of age (see Table 2). These diagnoses were confirmed by the presence of a community diagnosis of an ASD, an above threshold score on the Autism Diagnostic Observation Schedule (Lord et al. 1989) and/or the Autism Diagnostic Interview, Revised (Lord et al. 1994), and consensus clinical judgment by experienced clinicians (authors 3 and 5) using DSM-IV-TR criteria (APA 2000). Diagnosis was confirmed for 13 of 19 children. One of these individuals had a below threshold score on the ADOS, but had a community diagnosis of autism, and had elevated scores on both the Social Communication Questionnaire (SCQ; Rutter et al. 2003; total score = 16) and the Social Responsiveness Scales (SRS; Constantino 2005; T = 77). Based on this information, clinical observations and developmental history, a diagnosis of Autistic Disorder was made using DSM-IV-TR criteria and consensus clinical judgment by a child psychiatrist and clinical psychologist with expertise in autism. Of the children with unconfirmed diagnoses, 4 could not be contacted and 2 had below threshold scores on the ADOS as well as clinician impressions that autism was not present.

Not all children with later ASD diagnoses had a cry recorded at 1 month. Four cry samples were selected from the infants with later ASD diagnoses on the criteria of no prenatal exposure to cocaine or opitates, and having an existing cry recording with sufficient sound quality (having no background noise or static). These four infants with ASD (all male) were then matched to infants without ASD based on sex, absence of prenatal cocaine/opiate exposure, full term birth status, and later estimates of cognitive ability based on last available score results from the Bayley Scales of Infant & Toddler Development, 2nd Edition (Bayley 1993) or the Wechsler Preschool and Primary Scales of Intelligence, revised (WPPSI-R; Wechsler 1989). Because families did not attend every visit of the longitudinal MLS study, there was inconsistency in the availability of cognitive scores. The individual characteristics of the infants whose cries were used as stimuli are presented in Table 2. As can be seen, 2 of 4 exhibited cognitive and developmental delays, 1 of 4 was in the borderline range based on last available developmental score, and 1 of 4 was in the average range of cognitive functioning.

Four cry recordings were randomly selected from the available matched controls with cry recordings of acceptable quality. This method allowed for a reasonable number of cries from children with ASD for adult participants to listen and rate and an unbiased matched selection of cries from non-ASD children. The individual characteristics of these infants are also presented in Table 2. A total of eight cry episodes were chosen for this study, four from infants with later ASD diagnoses and four from infants without ASD matched on the above criteria. As can be seen in Table 2, presence of global developmental delays was balanced across groups, as was the presence/absence of prenatal exposure to alcohol, marijuana, and tobacco.

Recordings contained only the infant cry and were stripped of any identifiable information. All cries were recorded at 1-month postnatal age. Cries were elicited after completion of a standardized infant neurobehavioral exam, the NICU Network Neurobehavioral Scales (NNNS; Lester and Tronick 2004). After the NNNS, the infant was placed in an isolette and maintained in an awake, non-crying state for 30 s before the cry was elicited. Cries were recorded with a Marantz PMD201 cassette recorder and Radio Shack Dynamic Unidirectional Microphone. The infant was supine with the microphone suspended 5 in. above the infant's mouth. Cries were elicited by stimulation to the sole of the infant's right foot. If the infant did not cry, then a second stimulus was applied. A specially designed stimulator and tone box automatically placed a tone on the recording to coincide with the time of the cry stimulus. Cries selected for this analysis were excerpted and digitized (16 bit, 48 kHz) from audio recordings, clipped to the appropriate length and saved as a standard .wav audio file that could be played on a PC or digital audio recorder. Cries were initially recorded for 30 s. For this cry perception study, recordings were clipped to a length of 15 s from the onset of the cry episode. This method resulted in a set of cry stimuli that was standardized in the following ways: infants' pre-cry state and position, strength of eliciting stimulus, recording method, and length of stimuli.

Description of Cry Samples Used

In order to describe the characteristics of the cry samples, each cry was analyzed using a previously validated automated cry analysis method (Reggiannini et al. 2013). In brief, cry analyses applied a cepstral-based analysis to extract a range of acoustic features. The analysis used a frame rate of 25 ms with a frame advance of 12.5 ms. An initial analysis phase produced frame-level data and a second analysis phase organized the frame level data so as to yield acoustic descriptors of cry utterances. Cry episodes (samples) consisted of a varied number of utterances, with a cry utterance defined as being ≥ 500 ms. A description of the acoustic characteristics of the first 3 utterances from each of the 8 cry samples is presented in the supplemental materials.

Table 2 Characteristics of individual infants with ASD (a) and non-ASD infants (b) contributing cry stimuli

	Sex	Age at diagnosis[a]	ADOS information				Cognitive ability[c] (most recently available study visit)	Standard score	Prenatal exposures[d]			
			Module	Age	Result	Verbal ability[b]	Test (age)		Alcohol	Tobacco	Marijuana	Any
(a) ASD cases												
1	M	6	1	9	+	Min	BSID (24 m)	50	No	Yes	Yes	Yes
2	M	9	4	16	+	Fluent	WPPSI (36 m)	61	No	No	No	No
3	M	8	3	8	+	Fluent	BSID (12 m)	80	Yes	Yes	No	Yes
4	M	9	4	16	–	Fluent	WPPSI (36 m)	109	Yes	Yes	No	Yes
								M = 75.0	2/4	3/4	1/4	3/4
(b) Control cases												
1	M	n/a	n/a	n/a	n/a	n/a	WPPSI (36 m)	69	No	No	No	No
2	M	n/a	n/a	n/a	n/a	n/a	WPPSI (36 m)	70	Yes	No	No	Yes
3	M	n/a	n/a	n/a	n/a	n/a	WPPSI (36 m)	85	Yes	Yes	No	Yes
4	M	n/a	n/a	n/a	n/a	n/a	WPPSI (36 m)	94	Yes	Yes	No	Yes
								M = 74.7	3/4	2/4	0/4	3/4

[a]Age at diagnosis refers to the age that parents/caregivers reported that a community diagnosis was made

[b]Verbal ability derived from item A1 of the ADOS exam (observed language use). Min.= minimally verbal, with some single word speech

[c]Cognitive ability scores from latest cognitive assessment available from the Maternal Lifestyle Study dataset for these individuals

[d]Prenatal exposure history obtained from maternal interview for Alcohol, Tobacco, and Marijuana, as described in Lester et al. (2002). None of the eight children contributing cry stimuli had prenatal exposures to cocaine or opiates

These characteristics include fundamental frequency, which is heard as pitch, the energy or loudness of the cry, the length of the utterance, and the space between utterances. Spectrograms of each cry sample are also included in the Supplemental Materials.

An examination of these cry samples indicated that fundamental frequency, although somewhat higher across all utterances for the Typical cries than for the ASD cries, were within what would be considered a normal range for both groups (LaGasse et al. 2005). The most notable differences between the Typical and ASD cries were related to the timing and duration of utterances and inter-utterance intervals, differences in the intensity or energy of utterances (loudness in dB's) and degree to which utterances reflected increased tension in the vocal tract (frication). Specifically, the ASD cries contained fewer utterances, had utterances and inter-utterance intervals that were longer and more variable, had greater energy (mean dB), and had a greater percentage of analysis frames with frication. Detailed tables about these summary characteristics and individual values for utterances 1 to 3 can be found in the supplemental materials.

Procedure

Administration of Forms and Questionnaires

Following the informed consent process, parents completed a demographic questionnaire and the Broad Autism Phenotype Questionnaire (BAPQ; Hurley et al. 2007). The BAPQ is a brief questionnaire that measures personality and language characteristics that have been shown to correlate with having a close relative with autism. Scores on the BAPQ have been demonstrated to predict genetic liability for autism in a family. This 36-item self-report questionnaire contains three subscales corresponding to the major domains of autism as depicted in the DSM-IV-TR (APA 2000): social deficits, stereotyped-repetitive behaviors and language deficits. Internal consistency of this measure is excellent ($\alpha = 0.95$ overall; 0.85–0.94 across its three subscales). Validity as reported by Hurley et al. (2007) was evidenced by comparisons to other measures of the BAP construct, with good sensitivity and specificity (both ~ 0.80 for the total score) as compared to clinician ratings.

Administration of Cry Rating Scale

A 13-item scale was developed for the purposes of this study to measure the listeners' perceptions of the infant cries. The cry descriptors chosen were based on adjectives from frequently used scales developed to measure cry perception (Zeskind and Lester 1978). Listeners were asked to rate each cry on a seven-point Likert scale for each descriptor. There were seven items that described the perceived quality of the cry and included level of urgency, healthiness, arousal, distress, typicality, readability, and pain (the cry perception scale is presented in supplemental materials).

The order of cry presentation was counterbalanced across four versions of the experiment. Each participant heard the same eight cry recordings in one of four orders of presentation. Stimuli were presented on over-the-ear noise attenuating headphones in a quiet room. All participants used the same headphones. After each cry sample, participants were instructed to complete the corresponding cry perception scale for that cry. Each cry was played only once and participants were instructed to respond based on their initial impression.

Scale Development

Bivariate correlations between all cry perception variables revealed inter-item relationships and suggested an internal structure to the items. Four items on the scale: urgency, distress, healthiness, and arousal were all highly correlated with one another. These items were found to be highly reliable using Cronbach's alpha across ASD and non-ASD cries (4 items; overall $\alpha = 0.88$). These four items were subsequently averaged to create an aggregate measure that was termed the Distress Scale and used for subsequent analyses.

The correlation analyses also revealed a relationship between typicality and readability items (2 items; $r = 0.62$). Based on this relationship, we computed an additional aggregate variable by averaging the ratings of these two items for each cry sample. This is referred to as the Atypicality Scale.

There were no significant relations between the pain item and the remaining items on the scale. The pain-rating item was retained as an independent measure for the remaining analyses. Thus, for analyses comparing the effects of infant diagnosis and parent characteristics on cry ratings we utilized 3 scales as dependent measures: Distress, Atypicality, and Pain.

Results

Parental Perceptions of Cry

A 2×2 multivariate analysis of variance (MANOVA) with a between subject factor of parent type and a within subject factor of cry type was used to determine whether the cries of 1-month olds who did and did not go on to receive diagnoses of ASD were rated differently by listeners and whether parents of children with ASD differ from parents of TD children in how they perceive infant cries. Mean ratings for the three scales by cry type and parent group are shown in Table 3.

Table 3 Mean ratings (standard deviation) by cry and parent group

Scale	Cry group	Parent group	
		TD parents	ASD parents
Distress	ASD infants	4.74 (0.86)	5.01 (0.79)
	Non-ASD infants	3.73 (1.07)	3.81 (0.81)
Atypicality	ASD infants	3.87 (0.84)	3.88 (1.02)
	Non-ASD infants	3.18 (0.83)	2.94 (0.68)
Pain	ASD infants	4.15 (1.02)	3.80 (1.18)
	Non-ASD infants	2.99 (1.17)	2.83 (0.98)

Cries from infants with ASD were rated as more distressing, $F(1, 36) = 45.62$, $p < 0.01$, less typical, $F(1, 37) = 18.57$, $p < 0.01$, and more likely to be reflective of pain, $F(1, 39) = 32.20$, $p < 0.01$, than cries from non-ASD infants across parent groups. There was no effect of parent group nor any interactions between parent group and cry type

On the Distress Scale, results revealed a significant main effect for diagnosis, $F(1, 36) = 45.62$, $p < 0.01$. Cries of infants with ASD were rated significantly higher on the Distress Scale than cries of non-ASD infants. There was not a significant main effect of parent group, $F(1, 36) = 0.55$, $p = 0.46$. There was no significant interaction between parent group and cry type, $F(1, 36) = 0.24$, $p = 0.63$.

On the Atypicality Scale, results revealed a significant main effect of cry type, $F(1, 37) = 18.57$, $p < 0.01$. Cries of infants with ASD were rated as significantly less typical than cries of non-ASD infants. There was no main effect of parent group, $F(1, 37) = 0.31$, $p = 0.58$. There was no significant interaction between parent group and cry type, $F(1, 37) = 0.67$, $p = 0.42$.

On the pain item, results revealed a significant main effect of cry type, with ASD cries rated as more reflective of pain than the non-ASD cries, $F(1, 39) = 32.20$, $p < 0.01$. There was not a significant main effect of parent group, $F(1, 39) = 0.80$, $p = 0.38$. There was not a significant interaction between parent group and cry type, $F(1, 39) = 0.32$, $p = 0.58$.

These results indicated on average parents rated the cries produced by infants with later ASD as more atypical, more distressing, and reflecting greater pain than infants without ASD. Visual examination of these results indicated that there was minimal overlap between the average parent ratings for each of the four ASD cries as compared to the non-ASD cries (see Fig. 1). Thus, the results indicating mean differences between ASD and non-ASD cries did not appear to be influenced by outlier values or by any one case.

Broad Autism Phenotype Questionnaire

Descriptive data for the BAPQ summary scores as well as the individual subscale scores among parent groups are presented in Table 4. Parents of children with ASD had significantly higher BAPQ total scores than parents of TD children ($M_{ASD} = 2.75$, $SD_{ASD} = 0.61$; $M_{TD} = 2.38$, $SD_{TD} = 0.48$;

Table 4 Parent Broad Autism Phenotype Questionnaire (BAPQ) scores: mean (SD)

Parent group	BAPQ subscales			Total score*
	Aloof	Pragmatic language	Rigidity	
TD	2.13 (0.66)	2.27 (0.60)	2.73 (0.71)	2.38 (0.48)
ASD	2.55 (0.75)	2.46 (0.61)	3.23 (0.81)	2.75 (0.61)

These scores are out of a maximum of 6. Groups were significantly different on the sum scores, with a trend towards significance on Bonferroni corrected alpha of 0.016 for the Rigid Subscale

*$p < 0.05$

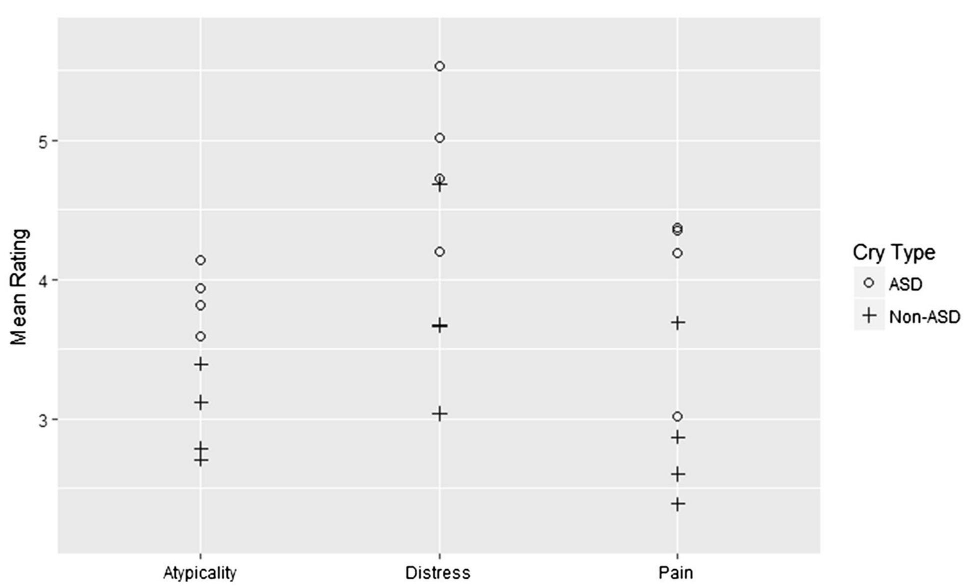

Fig. 1 Average parental ratings of each cry sample from infants with later ASD and non-ASD infants

$t(40) = -2.16$, $p = 0.04$). Independent samples t tests were conducted to compare the subscale scores on the BAPQ between parents of children with ASD and parents of TD children (Bonferroni corrected; alpha of 0.016). Differences between parents of children with ASD and parents of TD children on the Rigid Subscale score trended towards significance ($t(40) = -2.11$, $p = 0.04$). Parent groups did not differ significantly on either the Pragmatic Language Subscale ($t(40) = -1.00$, $p = 0.33$) or the Aloof Subscale ($t(40) = -1.90$, $p = 0.07$). Bivariate correlations were run to determine whether there was a relationship between the BAPQ sum score and parent perceptions on the distress, atypicality, and pain scales. No correlations were statistically significant.

Discussion

In the present study, we investigated how parents of children with ASD and parents of TD children perceive cries produced by 1-month-old infants later diagnosed with ASD as compared to cries of non-ASD infants. Consistent with a priori hypotheses, parents rated the cries of infants with ASD differently than the cries of non-ASD matched-controls. In particular, parents rated the cries of ASD infants as reflecting a greater degree of distress, as being less typical, and as reflecting a higher level of pain. These findings are consistent with prior research reporting acoustic differences between the cries of infants with later ASD diagnoses and non-ASD infants, with ASD cries showing both higher fundamental frequencies and atypical vocal quality (Esposito and Venuti 2010; Sheinkopf et al. 2012). The differences in parent ratings of ASD versus non-ASD cries are also consistent with previous literature showing different parental perceptions of ASD and non-ASD infants' cries (Esposito et al. 2012; Esposito and Venuti 2008). For the most part, these prior studies have examined acoustic characteristics and perceptual ratings of ASD cries in the second year of life, with one study reporting acoustic differences associated with later ASD in 6 month old infants (Sheinkopf et al. 2012). The current study reports differences in adult perceptions of cries produced by infants in very early infancy, specifically at 1-month of age, thereby extending the previous research to a much earlier point in development than previously studied. These results are based on a small sample of infants with later ASD diagnoses and do not indicate which acoustic features account for the differences in parent perception. Thus, follow up work is needed to describe which acoustic features differentiate diagnostic groups and impact cry perception. However, these results strengthen the rationale for hypothesizing that neurobehavioral features associated with later ASD may be present in very early infancy, and that differences in vocal production may be a useful method for investigating these differences.

Cry samples were collected during a standardized cry elicitation method that has been used in investigations of other pediatric populations (LaGasse et al. 2005). Prior research on infants with later ASD diagnoses has used cries recorded from parent-generated home videos (Esposito and Venuti 2009) or experimenter generated video recordings (Esposito et al. 2014; Sheinkopf et al. 2012). These methods have the advantage of ecological validity that comes with sampling behavior in children's natural settings and activities. In contrast, methods that utilize cry elicitation protocols such as those used in the current study offer the strength of experimental control that helps to reduce the impact of extraneous and difficult to control influences on neurobehavioral responses. Here we report cries that were elicited with a procedure that was standardized in several ways, including the force of the stimulus, the location of the stimulus on the infant's foot, the positioning of the infant, the age of the infant, and the state of the infant when the cry was elicited. Moreover, the recording apparatus and the distance between the infant's mouth and the microphone were consistent across infants. These methods can be expected to increase the signal-to-noise ratio and thereby increase the likelihood of detecting subtle differences in neurobehavioral status in early infancy.

This study also explored the relation between parental characteristics and cry perception. Comparing parents of children with ASD to parents of children with typical development provided an initial test of the potential impact of the caregiving experience on later cry perception. We did not find significant differences in the cry ratings of parents of children with ASD as compared to parents of children with typical development. Thus, these analyses do not support a hypothesis that caregiving experiences with infants later diagnosed with ASD will impact later perception of infant cries. However, a strong interpretation of this finding is tempered because the parents who completed these ratings were not caring for infants at the time of their participation. It is conceivable that such relations would be localized to the period of time that a parent is caring for their infant.

Exploratory analyses were conducted to examine parents' scores on a measure of broader autism phenotypic characteristics and to test whether cry perception ratings would be related to mild traits that have been found to be elevated in relatives of those individuals with ASD. In this study, parents of children with ASD had higher scores than TD parents on the BAPQ, indicating an elevated level of subclinical autism related characteristics in this group. However, parents' scores on the BAPQ did not significantly correlate with cry ratings. While a study with larger sample sizes could conceivably have more power to detect such relationships, the current results are not consistent with such parental characteristics being associated with parents' perceptions of infant crying.

While this study has a number of strengths, these findings should be considered within the context of certain limitations. Most importantly, this study was limited to only a small number of cries that were rated by parents. We were able to guard against systematic selection bias between cries of the ASD and comparison infants by randomly selecting controls from a large library of available cry recordings. However, the small number of cries used in the current study may not be representative of the range of cry features in the ASD population. In addition, there will likely be variation in neurobehavioral features of ASD in early infancy that will require large samples to describe. One potential source of variation is gender. All cries were recorded from male infants, due in part to the known overrepresentation of males in the ASD population. Further, all ratings were completed by mothers who may be less likely than fathers to evidence characteristics of the BAP. Future research should assess for gender differences in cries of later diagnosed infants. However, it is noted that prior research does not support gender differences in acoustic cry characteristics in early infancy (Murry et al. 1977). Of additional importance for research on infant cry characteristics, as well as for research on autism in infancy more generally, is to account for potential differences in etiology. A substantial minority of individuals with ASD are affected by what are individually rare genetic abnormalities (Iossifov et al. 2014), and at later ages these genotypes impact developmental outcomes (Bishop et al. 2017). Larger samples of infants with later ASD diagnosis will allow for tests of the potential impact of genetic etiologies on early neurobehavioral characteristics (including but not limited to cry production) and developmental trajectories.

Finally, this study was not designed to determine which acoustic features or timing characteristics may have been most salient to the parent raters and which may have accounted for the differences in parental ratings of the ASD versus typical cries. Interestingly, the average pitch (fundamental frequency) of the cries was in a range that would be considered normative for both cry types. This contrasts prior research with somewhat older infants with or at risk for ASD (Esposito and Venuti 2010; Sheinkopf et al. 2012). Timing characteristics of the cries differed between groups. The utterance duration and inter-utterance intervals were longer and more variable, and there was an elevated degree of tension in the vocal tract of the infants contributing the ASD cry samples (see Supplemental Materials). Follow up studies will be needed to determine whether these or other acoustic features differentiate cries of infants in the neonatal period who go on to have a diagnosis of ASD, and alternative methodology and experimental design is needed to determine which features drive differences in perceptual ratings of the cries. Prior studies of older infants with ASD implicate differences in pitch and utterance timing as factors in cry perception (Esposito and Venuti 2010).

This study investigated the differences in parental perception of cries elicited from infants later diagnosed with ASD as compared to non-ASD infants. Overall, the results demonstrated that parents rated cries of 1-month-old infants with later ASD as reflecting greater levels of distress, as being less typical, and as reflecting higher levels of pain when compared to matched controls. Future research should work to describe the acoustic features that may more objectively differentiate cries of infants at risk for autism. While preliminary in nature, the results reported here strengthen the hypothesis that individuals or subgroups of individuals with ASD may be characterized by subtle differences in neurobehavioral responses in very early infancy.

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Author contributions MSE, TPL, BML, and SJS contributed to the study design and conceptualization. MSE was responsible for study execution and drafted the manuscript. TPL and SJS conducted diagnostic assessments. MSE, EJT, and SJS were responsible for data analysis. MSE, EJT, and SJS edited the draft and refined the conceptualization. All authors read, edited, and approved the final manuscript.

Compliance with Ethical Standards

Conflict of interest M. Samantha English declares that she has no conflict of interest. Elena J. Tenenbaum declares that she has no conflict of interest. Todd P. Levine declares that he has no conflict of interest. Barry M. Lester declares that he has no conflict of interest. Stephen J. Sheinkopf declares that he has no conflict of interest.

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