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Newborn Auditory Brainstem Responses in Children with Developmental Disabilities

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Abstract

We integrated data from a newborn hearing screening database and a preschool disability database to examine the relationship between newborn click evoked auditory brainstem responses (ABRs) and developmental disabilities. This sample included children with developmental delay ($n = 2992$), speech impairment (SI, $n = 905$), language impairment ($n = 566$), autism spectrum disorder (ASD, $n = 370$), and comparison children ($n = 128{,}181$). We compared the phase of the ABR waveform, a measure of sound processing latency, across groups. Children with SI and children with ASD had greater newborn ABR phase values than both the comparison group and the developmental delay group. Newborns later diagnosed with SI or ASD have slower neurological responses to auditory stimuli, suggesting sensory differences at birth.

Keywords Auditory brainstem response · Autism spectrum disorder · Speech impairment · Developmental disabilities · Early identification

Introduction

Fifteen percent of children (ages 3–17) have a developmental disability (Boyle et al., 2011). The underlying deficits associated with developmental disabilities can result from aberrant prenatal developmental processes (Huang et al., 2016) and, as such, newborns can be screened for some of these deficits. For example, newborn screening for hearing impairment is common in developed countries around the world (Morton & Nance, 2006). This screening has led to earlier identification and, through early intervention, has improved children's language, academic, and social outcomes (Joint Committee on Infant Hearing, 2019; Korver et al., 2010; McCann et al., 2009; Patel & Feldman, 2011).

Auditory brainstem response (ABR), a noninvasive method that measures the response of the auditory nerve and brainstem to sound (Brama & Sohmer, 1977), yields information about brainstem and inner ear function and the circuits connecting these structures (Fig. 1; Hall, 2006). ABR is used to evaluate hearing loss, including both conductive and sensorineural components (Mason & Herrmann, 1998; Morton & Nance, 2006), but also shows promise as a sensory screening tool for other disabilities (Geva & Feldman, 2008). Using ABR, neurological differences in response to sound have been identified in children and adults with autism spectrum disorder (ASD) (Cohen et al., 2013; Dabbous, 2012; Fujikawa-Brooks et al., 2010; Kwon et al., 2007; Maziade et al., 2000; Miron et al., 2016; Miron et al., 2018; Rosenhall et al., 2003; Roth et al., 2012; Santos et al., 2017; Talge et al., 2018; Tas et al., 2007; Thivierge et al., 1990; Wong & Wong, 1991),

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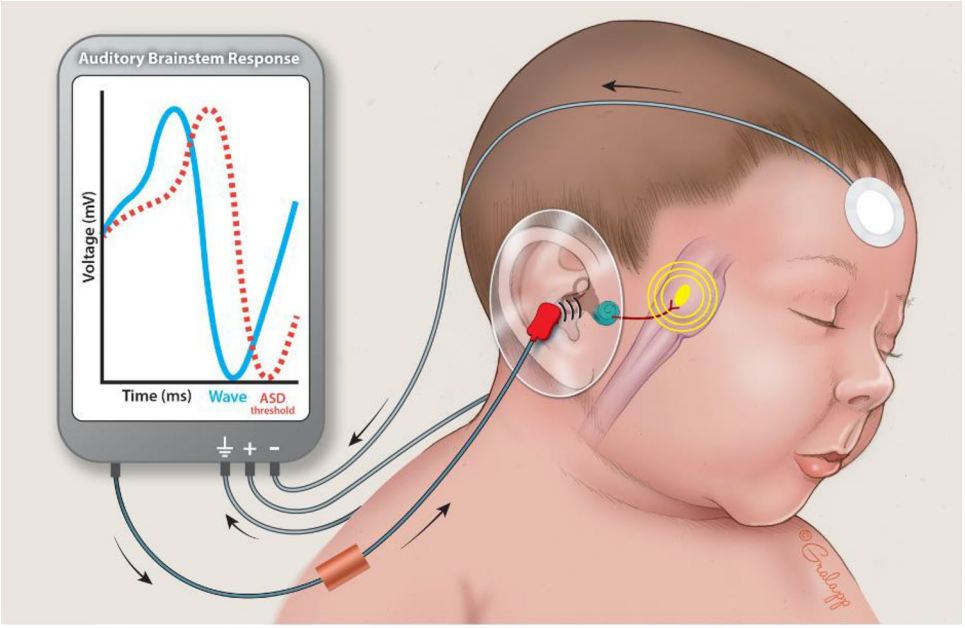

Fig. 1 Illustration of ABR latency delay in wave V in ASD that demonstrates the concept of classifying ASD based on a latency delay. Wave differences simulated to represent an ideal screening situation

intellectual disabilities (Ferri et al., 1986; Mochizuki et al., 1986), speech and/or language impairments (Abadi et al., 2016; Gabr & Darwish, 2016; Gonçalves et al., 2011; Mason & Mellor, 1984; Roth et al., 2012), learning impairments (King et al., 2002), and dyslexia (Hornickel & Kraus, 2013). Much of this research on developmental disabilities used suprathreshold ABR which provides more salient responses with better defined peaks compared to screening ABR. Although ABR data collected through newborn hearing screening is acquired at lower stimulation levels that result in smaller and broader responses, it still provides consistent data of known latency characteristics. The ability of newborn hearing screening ABR to detect risk for disability therefore merits investigation because it is currently conducted on approximately 2 million children per year through universal hearing screening in the US alone.

Newborn hearing screening data can also provide ABRs that were acquired years before children's developmental disability diagnosis. With few exceptions (Cohen et al., 2013; Miron et al., 2016, 2021), most research on ABRs and developmental disabilities has been on older children and adults, often well after developmental disabilities are diagnosed. Further, research on newborns has focused on those in the neonatal intensive care unit (NICU; Cohen et al., 2013; Miron et al., 2016) or on only a single developmental disability (e.g., ASD; Miron et al., 2021). Therefore, additional research on newborns is needed to determine the nature of deficits present at birth, as well as the potential of ABR as a newborn screening tool for a wider range of developmental disabilities within the broader population beyond the NICU (Miron et al., 2021).

To address this need, we used large secondary data sources to examine ABR patterns of children with developmental disabilities. This approach allowed us to obtain a larger sample than previous studies, to examine the general population of newborns (including healthy and typically developing newborns, not just those in the NICU), and to examine a wider variety of developmental disability outcomes, beyond just ASD. We hypothesized that newborns who were later diagnosed with developmental disabilities as preschoolers would, like older children and adults with developmental disabilities, have longer ABR latencies than newborns who were not later diagnosed with developmental disabilities.

Identification of ABR differences among children with developmental disabilities has the potential to not only inform our understanding of the biological bases of these disabilities, but also may lead to the development of newborn screening tools for developmental disabilities. Indeed, the early postnatal period is a vastly understudied time in development, particularly for developmental disabilities that lack overt symptoms until later in development (Marschik et al., 2017). Identification of newborns at increased risk for future developmental disabilities allows for the provision of early intervention services, which may lead to greater gains and ultimately improve children's outcomes (Barger et al., 2018; Committee on Children with Disabilities, 2001; Dawson et al., 2010; Dubois et al., 2014; Guralnick, 1997; Hebbeler et al., 2007; Huang et al., 2006; McLean & Cripe, 1997; Nagy, 2011; National Research Council 2001; Ward, 1999; Webb et al., 2014). Newborn screening for developmental disabilities also has the potential to substantially reduce racial and ethnic disparities (Delgado & Scott, 2006;

Magaña et al., 2012; Wiggins et al., 2020) by providing early screening and risk identification to all children.

Methods

We integrated two secondary datasets to examine the newborn ABRs of children born between 2009 and 2015 who were later diagnosed with a developmental disability. This study was approved by the University of Miami Institutional Review Board.

Newborn Hearing Screening (Auditory Brainstem Response)

ABR data, acquired using the Smart Screener-Plus2 (Intelligent Hearing Systems Corp.) from infants ($N = 144{,}993$) born in Florida, were obtained from the Pediatrix Medical Group (a MEDNAX® company) Soundata database. Pediatrix Medical Group is the United States' largest provider of newborn hearing screening. Newborns were screened for hearing loss before leaving the hospital (typically within 2 days after birth). Newborn hearing screening records contained raw ABR recordings, acquisition parameters, and recording system automated responses.

The ABRs were elicited using 100 µs clicks at 35 dB normal hearing level (nHL) and a simultaneous stimulation rate of 77 and 79 Hz for the right and left ears, respectively. The testing device used different stimulation rates for each ear to differentiate the responses originating from each ear (Delgado & Lim, 2010). The analyses for the left and right ears were conducted separately to account for any potential stimulation rate effect due to the use of slightly different stimulation rates for each ear.

A typical suprathreshold ABR consists of three major peaks marked using Roman Numerals I, III, and V. At the lower testing intensities (35 dB nHL) used to screen newborns, only peak V may be present, and this peak may be difficult to visually pinpoint accurately and/or consistently across recordings. Therefore, we utilized an automated phase measurement method to determine latency. Phase represents the phase angle of the response group delay, which indicates the latency of the peak components. We determined phase using an objective spectral Fast Fourier Transform (FFT) technique (Hall, 2006). As a measure of latency, phase is analogous to wave V latency (Miron et al., 2021).

Infants often receive more than one hearing test due to various factors including infant state (crying), vernix in the ear canal, fluid in the middle ear, or noisy recording conditions. We used the ABR data from the first hearing test in which the newborn passed both ears in the same recording. In cases where the newborn did not pass both ears simultaneously, we used the ABR data from the last test resulting in a pass for each ear individually.

Preschool Disability

We obtained preschool developmental disability data from the Florida Department of Education, Bureau of Exceptional Education and Student Services, Children's Registry and Information System (CHRIS) database. The CHRIS database contains referral, screening, evaluation, and eligibility information for preschool-aged children (3–5 years) throughout Florida who were referred to the Florida Diagnostic and Learning Resources System. We focused on the most commonly reported developmental disorders, including children identified with a primary exceptionality of developmental delay (DD), speech impairment (SI), language impairment (LI), or autism spectrum disorder (ASD). Children with other primary exceptionalities, including hearing impairment which affects ABR, were excluded from this study. Children can only have one specified primary exceptionality, which resulted in groups that were mutually exclusive. Developmental disability diagnoses were based on the diagnostic criteria specified in the Florida Statutes and State Board of Education Rules (Florida Department of Education, 2014). A summary of each developmental disability is provided below. More detailed descriptions and criteria for eligibility are provided in the Supplementary Materials.

ASD refers to a broad range of conditions, often characterized by impairments in social interaction, communication, and the presence of restricted repetitive, and/or stereotyped patterns of behavior, interests, or activities (American Psychiatric Association, 2013). ASD represents a spectrum of disorders that includes Autistic Disorder, Pervasive Developmental Disorder Not Otherwise Specified, Asperger's Disorder, or other related pervasive developmental disorders.

SI refers to an impairment in speech sound production (atypical production of speech sounds characterized by substitutions, distortions, additions, or omissions that interfere with intelligibility), fluency (deviations in continuity, smoothness, rhythm, or effort in spoken communication), and/or voice (atypical production or absence of vocal quality, pitch, loudness, resonance, or duration of phonation). Speech impairments are not primarily the result of factors related to chronological age, gender, culture, ethnicity, or limited English proficiency. In contrast, LI refers to a disorder in one or more of the basic learning processes involved in understanding or in using spoken or written language, including phonology, morphology, syntax, semantics, or pragmatics.

Unlike ASD, SI, and LI, which refer to specific developmental disabilities, DD is a less specific eligibility category that is only applicable to children younger than 3–9 years of age, depending on the state (6 years is the age limit for

Florida). Past this age, children must be identified with a more traditional disability to remain eligible for special education services. In Florida, the most common disabilities that children with DD will ultimately be identified with are specific learning disability or intellectual disability (Delgado, 2009). The DD eligibility category allows children with significant delays in adaptive or self-help, cognitive, communication, social/emotional, and/or physical development to receive needed services without being assigned to a specific disability label, as assigning such labels can be difficult in young children (Bernheimer et al., 1993; Gallmore et al., 1999). Children identified with DD did not meet diagnostic criteria for the other disability categories.

Data Linkage

We linked the databases using Microsoft SQL Server Integrated Services. We matched records with the child's first name, last name, date of birth, and sex using a probabilistic algorithm (Fuzzy Lookup Add-In for Excel, miscrosoft.com). In this method, each record was assigned a similarity score for each matching variable (first name, last name, date of birth, and sex) based on the commonality between the input record and the possible match records. Similarity values ranged from 0 to 1, with 1 representing a perfect match. Records were considered a match if date of birth and sex were a perfect match (similarity = 1) and either (a) both first name and last names had similarity scores > 0.9 or (b) records were determined to match after individual review (e.g., comparing parents' names to make a match determination).

The disability groups (ASD, DD, LI, and SI) were determined using the primary exceptionality code in the CHRIS database. The comparison group consisted of all children with ABR data who were a non-match with the CHRIS database. After the data linkage, we de-identified the integrated dataset to maintain confidentiality.

Participants

ABR records were available for 144,993 children. Records were excluded ($n = 11{,}979$) if sex was not indicated, the child was > 28 days at the time of the ABR test, age at ABR was not indicated, ABR phase value was not indicated, or the record linked with the CHRIS records but the child did not have a developmental disability diagnosis of interest. Age was limited to the newborn period because ABR rapidly develops after birth (Moore et al., 1996; Skoe et al., 2013).

The final integrated dataset included 133,014 children (Table 1). The higher rates of males in the disability groups is consistent with previous reports in Florida (U.S. Department of Education, 2014). The average age at the time of ABR testing was 1.81 days after birth ($SD = 3.00$; range: 0–28 days) with 93% of children tested within 3 days of birth and 96% tested within 1 week of birth. There was a difference in ABR testing age among our groups, $F(4, 133{,}004) = 9.48$, $p < 0.001$, $\eta^2 < 0.001$. Tukey's Honestly Significant Difference (HSD) test revealed that children with DD were older at the time of the ABR test, compared to children in the comparison group ($p < 0.001$, 95% CI [0.17, 0.47]) and SI group ($p < 0.001$, 95% CI [0.19, 0.81]). The age at ABR test also differed by sex, $F(1, 133{,}004) = 52.43$, $p < 0.001$, $\eta^2 < 0.001$, as males ($M_{age} = 1.87$ days, $SD = 3.08$) were older than females ($M_{age} = 1.74$ days, $SD = 2.91$). There were 12,792 infants from the neonatal intensive care unit (NICU; 9.62%; see Table 1 for NICU percentages in each developmental disability group). A chi-squared test of independence revealed differences in the proportion of NICU infants across disability groups, $\chi^2(4) = 12.11$, $p = 0.017$. Post Hoc comparisons showed that newborns who were in the NICU, compared to those not in the NICU, were more likely to be diagnosed as DD than the comparison group, $\chi^2(1) = 8.40$, $p = 0.004$. We detected no other differences in the proportion of NICU newborns between the comparison group any any other disability groups (ASD: $\chi^2(1) = 1.12$, $p = 0.289$; SI: $\chi^2(1) = 1.11$, $p = 0.292$; $\chi^2(1) = 0.69$,

Table 1 Demographic information by group

Group	*N*	Male percentage (%)	Male *N*	NICU percentage (%)	NICU N	Mean age	Age *SD*
Comparison	128,181	49.84	63,882	9.60	12,303	1.80	2.98
DD	2992	71.76	2147	11.20	335	2.12	3.64
SI	905	68.40	619	8.51	77	1.62	2.28
LI	566	68.55	388	8.48	48	1.93	3.34
ASD	370	77.30	286	7.84	29	1.74	2.93
Total	133,014	50.61	67,322	9.62	12,792	1.81	3.00

Age at time of ABR is reported in days

DD developmental delay, *SI* speech impairment, *LI* language impairment, *ASD* autism spectrum disorder, *NICU* Neonatal Intensive Care Unit, *SD* standard deviation

$p = 0.407$). We therefore controlled for newborns' age and included sex and NICU status in our analysis.

We built upon a prior study, which used a subset of these data (Miron et al., 2021). The current study expands on the previous study by utilizing a larger dataset as well as by examining the ABR recordings for a wider range of developmental disabilities, including children with DD, SI, LI, and ASD (while the previous study only examined ASD).

Analyses

Our primary dependent variable was ABR phase, which we explored with two 2 × 5 analyses of covariance (ANCOVAs), one for each ear, with the between subjects independent variables of sex (male, female) and group (comparison, ASD, DD, SI, LI). We included the covariates of ABR testing age (in days) and NICU status. Following up statistically significant main effects, we used Tukey's HSD tests to explore differences ($M_{difference}$) between each group. An advantage of this test is that it controls for the elevated Type 1 error rate due to multiple pairwise comparisons (Tukey, 1949). Finally, we analyzed whether ABR phase values predict disability diagnoses with a tenfold cross-validation logistic regression classification. We also conducted the ANCOVA analyses excluding the newborns in the NICU and the effects were the same (see Supplementary Materials); we therefore retained all newborns in the primary analysis.

Results

Controlling for the age, there was a main effect of sex, in which ABR phase was greater for males than females in both ears, $ps < 0.001$ (Tables 2, 3, 4). There was also a main effect of groups, in which ASD and SI groups had greater ABR phase values compared to the comparison group in both ears, $ps < 0.001$ (Fig. 2). More specifically, for the right ear, children with ASD ($M_{difference} = 7.48$, $p < 0.001$, 95% CI [2.73, 12.24]) and SI ($M_{difference} = 6.32$, $p < 0.001$, 95% CI [3.28, 9.37]) had greater ABR phase values as newborns than the comparison group. The same pattern was also observed in the left ear: children with ASD ($M_{difference} = 5.80$, $p < 0.001$, 95% CI [0.82, 10.79]) and SI ($M_{difference} = 4.67$, $p < 0.001$, 95% CI [1.48, 7.87]) had greater ABR phase values as

Table 2 Descriptive statistics for phase (in degrees) in a 2 (sex) × 5 (group) design

Sex	Group					All Groups
	Comparison	DD	SI	LI	ASD	
	M (SD)	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*	*M (SD)*
Right ear						
Female	138.40 (33.36)	137.26 (34.15)	142.83 (33.91)	138.37 (31.52)	142.99 (32.45)	138.41 (33.36)
Male	148.43 (33.51)	148.11 (35.02)	152.90 (36.25)	149.24 (32.09)	153.20 (35.65)	148.48 (33.59)
Both sexes	143.40 (33.81)	145.04 (35.11)	149.72 (35.82)	145.82 (32.28)	150.88 (35.17)	
Left ear						
Female	120.32 (35.19)	119.10 (34.22)	121.90 (36.55)	122.53 (37.38)	124.04 (33.62)	120.32 (35.19)
Male	130.40 (35.00)	130.01 (36.02)	133.76 (35.67)	131.43 (36.53)	133.23 (35.09)	130.43 (35.05)
Both sexes	125.34 (35.46)	126.93 (35.85)	130.01 (36.35)	128.63 (37.00)	131.14 (34.93)	

DD developmental delay, *SI* speech impairment, *LI* language impairment, *ASD* autism spectrum disorder, *M* mean, *SD* standard deviation

Table 3 ANCOVA results using right ear phase as the dependent variable

	SS	*df*	MS	*F*	*p*	η^2
Predictor						
Group	66,694.33	4	16,673.58	14.88	< 0.001	< 0.001
Sex	3,332,277.00	1	3,332,276.84	2974.22	< 0.001	0.022
Group × Sex	543.27	4	135.82	0.12	0.975	< 0.001
Covariate						
Age	14,886.12	1	14,886.12	13.29	< 0.001	< 0.001
NICU Status	37,682.06	1	37,682.06	33.63	< 0.001	< 0.001
Error	149,013,600.00	133,002	1120.39			

Analysis of Covariance results for the right ear

SS sum of squares, *df* degrees of freedom, *MS* mean square

Table 4 ANCOVA results using left ear phase as the dependent variable

	SS	*df*	MS	*F*	*p*	η^2
Predictor						
Group	44,641.17	4	11,160.29	9.06	< 0.001	< 0.001
Sex	3,370,162.00	1	3,370,161.95	2735.81	< 0.001	0.020
Group × Sex	1051.11	4	262.78	0.21	0.931	< 0.001
Covariate						
Age	72,588.13	1	72,588.13	58.93	< 0.001	< 0.001
NICU Status	113,180.30	1	113,180.28	91.88	< 0.001	0.001
Error	163,841,300.00	133,002	1231.87			

Analysis of Covariance results for the right ear

SS sum of squares, *df* degrees of freedom, *MS* mean square

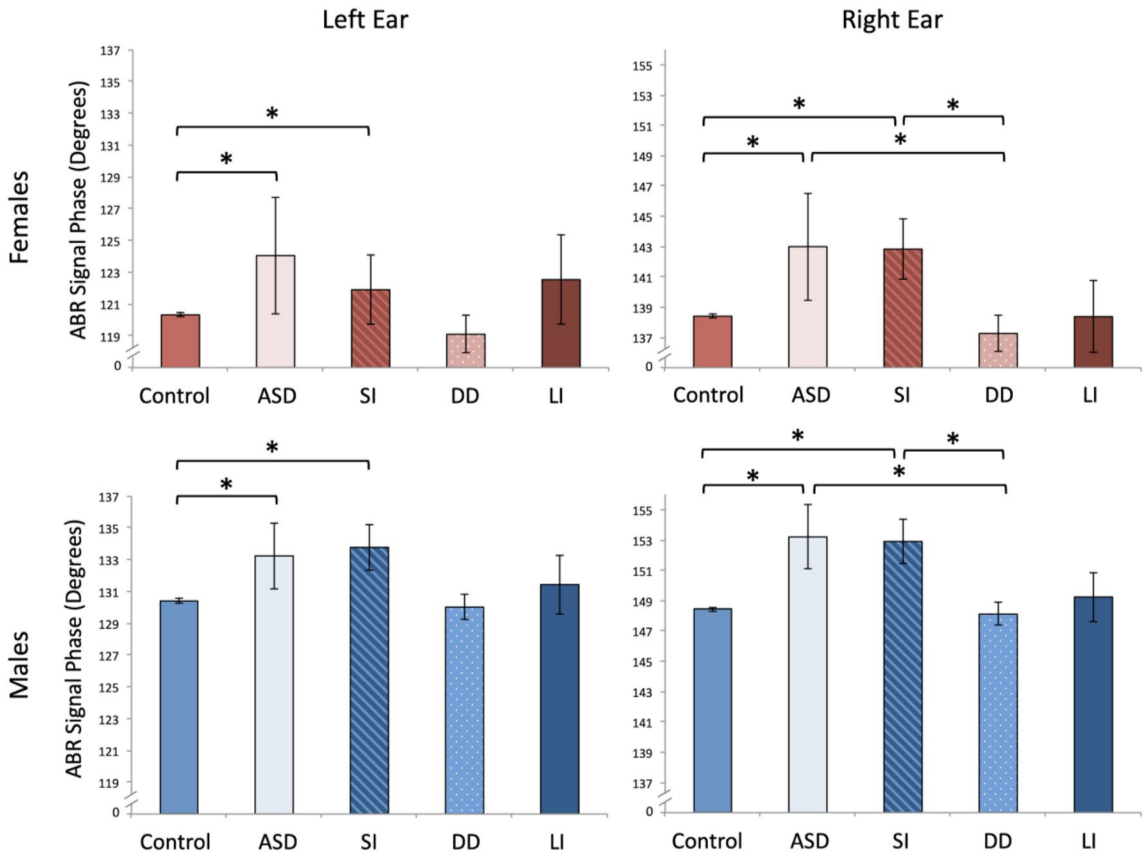

Fig. 2 Signal phase for female (top) and male (bottom) newborns recorded for the left and right ears for each group. *Control* comparison group, *ASD* autism spectrum disorder, *SI* speech impairment, *DD* developmental delay, *LI* language impairment. Error bars reflect standard error of the mean. *$ps < 0.05$. Phase values were consistently greater in the right ear compared to the left ear for both males and females, reflecting the different stimulation rates used to test each ear. The scales for the Y-axis are therefore different for the left and right ears to accommodate for this difference

newborns than the comparison group. Phase values for children with ASD and SI did not differ from each other (right ear, $p = 0.980$; left ear, $p = 0.985$). Moreover, the right ear ABR phase values in newborns later diagnosed with ASD ($M_{difference} = 5.84$, $p = 0.013$, 95% CI [0.80, 10.87]) and SI ($M_{difference} = 4.67$, $p = 0.002$, 95% CI [1.21, 8.14]) were higher than those who were later diagnosed with DD. Such differences were not significant for the left ear ($ps > 0.10$). We detected no other effects, $ps > 0.05$.

Given the differences in ABR phase between the ASD and SI groups relative to the comparison group, we further examined the practical importance of ABR phase values

in predicting disability diagnoses with a tenfold cross-validation logistic regression classification including ABR phase in both ears, infants' sex, age, and NICU status. The model selection used the custom made functions in the R "caret" package (Kuhn, 2020). We combined the ASD and SI groups to maximize the classification power to distinguish them from the comparison group in terms of the area under the receiver operating characteristic (ROC) curve. To address the problems of collinearity among phase values in the right and left ears ($r = 0.44$), we first centered these predictors, and then performed the principal component transformation for them. Then, we randomly split the sample into a training set (75%) and a testing set (25%). Model training used the training set and we measured the predictive power of the best model with the testing set. To address the problem of class imbalance (99% comparison, 1% ASD and SI), the built-in random up-sampling process in the "caret" package matched the class sizes in each step of cross-validation.

The final model indicated that all five predictors contributed to disability classifications (Table 5). We then tested the predictive power of the trained model in the testing set. The McNemar's Test indicated that the predictive performance was better than chance, $p < 0.001$. The results showed an AUC of 0.64 (95% CI [0.61, 0.67]), balanced accuracy of 0.62, sensitivity of 0.72, and specificity of 0.51 (Fig. 3). In addition, the final model showed a positive predictive value of 0.014 in the testing set, given the sample prevalence rate of 0.010, and a negative predictive value of 0.995, using the 50% criterion in classification. These findings indicate a small to medium level of predictive performance. The final model improved the sensitivity of prediction (i.e., the ability to detect a true ASD or SI case) while accuracy and specificity remained similar to random guesses. Negative predictive accuracy—the probability of a negative prediction (the accuracy of prediction that the infants are in the comparison group)—was high. However, positive predictive accuracy—the probability of positive prediction (the accuracy of prediction that the infants are in the ASD or SI groups)—was low, which is likely due to the low rates of ASD and SI in the sample and our use of a minimum classification criteria (0.50).

Table 5 Unstandardized coefficients, standard error, and significance of the trained logistic model to classify ASD and SI from the comparison group

Predictor	Estimate	*SE*	*z*	*p*
(Intercepts)	−0.48	0.008	−59.65	< 0.001
Right Phase	0.09	0.004	23.50	< 0.001
Left Phase	−0.07	0.006	−11.43	< 0.001
Sex	0.82	0.010	85.09	< 0.001
NICU Status	0.06	0.021	2.86	0.004
Age	−0.02	0.002	−8.73	< 0.001

ASD autism spectrum disorder, *SI* speech impairment, *SE* standard error

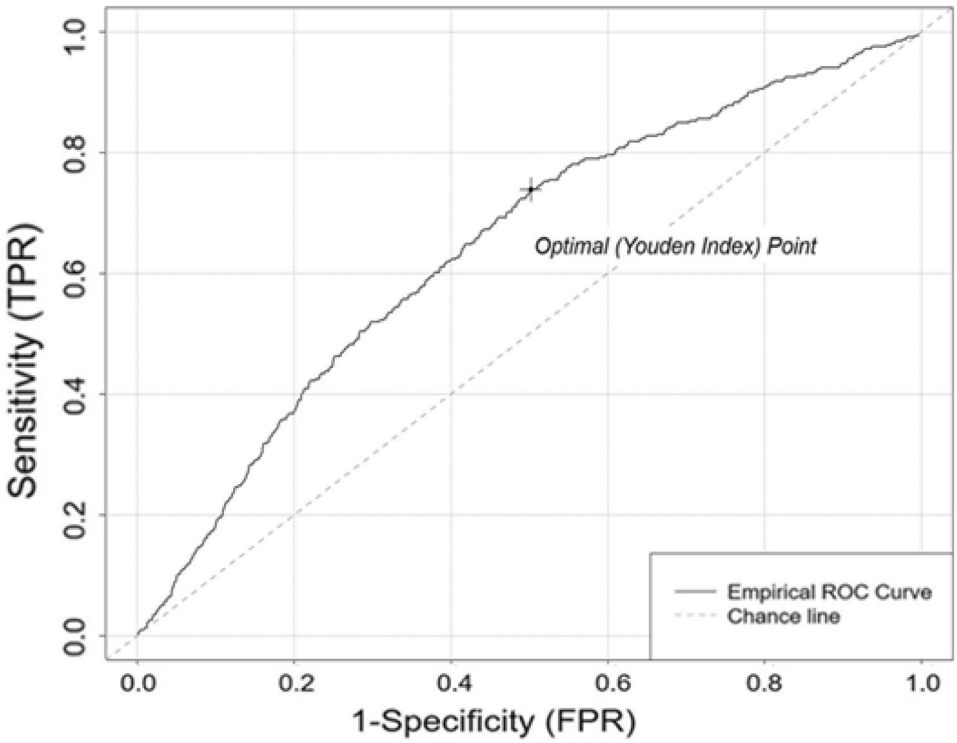

Fig. 3 Receiver operating characteristic (ROC) curve plotting sensitivity-true positive rate (TPR) over 1—specificity-false positive rate (FPR), evaluating the predictive power in the testing set. Dashed line reflects chance. Area under curve equals 0.64. The optimal point indicates the optimal cutoff point for the testing set

Discussion

Our findings demonstrate that neurological anomalies in response to sound are present soon after birth for children with ASD and SI, and that these sensory differences can be detected using newborn ABR screening methods. These results add to a growing body of research indicating that neurological abnormalities associated with ASD are present in newborns (Cohen et al., 2013; Karmel et al., 2010; Miron et al., 2016, 2021). Much like with ASD, we report, for the first time, similar newborn ABR latency delays for children later classified with SI. Children with ASD and SI appear to process acoustic signals at the brainstem level differently as newborns compared to other children.

Speech and language deficits are one of the defining characteristics of ASD. Disruptions in the brain development of children with ASD have been identified in cortical regions associated with ASD as well as in regions associated with communication and language (Stoner et al., 2014). Speech processing and speech production abnormalities are common in children with ASD (Russo et al., 2008, 2009; Stroganova et al., 2020). Our results suggest some neural commonality across those disorders at the level of the brainstem. Alterations in the development of the brainstem could have cascading effects on brain development that could lead to disabilities such as ASD and SI (Dadalko & Travers, 2018; Geva et al., 2017; Inui et al., 2017). Additionally, subcortical processes may interact with cortical processes associated with auditory processing and attention (Banai & Kraus, 2008). ABR is an effective, noninvasive way to measure auditory pathway deficits. ABR measures the brain's processing of sound, linked to the development of various abilities, including encoding speech sounds and verbal communication, theorized to be core deficits of ASD and SI (Roth et al., 2012; Russo et al., 2009).

Previous research indicted ABR differences for children with language impairments (Gabr & Darwish, 2016; Mason & Mellor, 1984; Roth et al., 2012), intellectual disability (Ferri et al., 1986; Mochizuki et al., 1986), and learning impairments (Hornickel & Kraus, 2013; King et al., 2002); however, these studies measured ABR in older children with an identified developmental disability. Based on our findings, children with LI do not appear to show ABR differences as newborns; however, these differences may develop later during infancy and childhood. We did not examine intellectual disability and specific learning impairment due to an insufficient number of cases in our preschool-aged sample. Children with these impairments were likely included in the DD group. Intellectual disability and specific learning impairment are the two most common future eligibility classifications for preschool children originally identified with DD who continue to receive special education services in elementary school (Delgado, 2009; Delgado et al., 2006). In our study, children with DD had similar ABR latencies to children in the comparison group and significantly shorter ABR latencies (right ear only) compared to children with ASD or SI. It is possible that we did not detect ABR differences for children with DD because the ABR anomalies associated with intellectual disability and specific learning impairment develop later. Alternatively, heterogeneity in the type and degree of impairment among children in the DD group may have impeded our ability to detect ABR differences. Children with DD are later diagnosed with a wide variety of developmental disabilities and many young children with DD no longer meet criteria for special education placement by third or fourth grade (Delgado, 2009; Delgado et al., 2006).

Both prenatal and postnatal factors contribute to the formation of developmental disabilities (Huang et al., 2016; Shultz et al., 2018). Animal and pathological studies suggest that ASD has foundations in the prenatal and/or perinatal periods (Careaga et al., 2017; Nakagawa et al., 2019; Stoner et al., 2014). Our findings support prenatal and/or perinatal origins for SI as well. Even though we did not detect ABR latency differences for LI and DD relative to the comparison group, developmental disabilities such as these likely originate in the prenatal period (Huang et al., 2016; Steer et al., 2015) and may be detectable using other neurological assessments (e.g., electroencephalogram (EEG) or magnetic resonance imaging (MRI); Lohvansuu et al., 2018). However, postnatal experiences also contribute to developmental disabilities. Brain injury, poor nutrition, exposure to high levels of stress, exposure to environmental toxins, maltreatment, and insufficient stimulation negatively affect brain development and can lead to developmental disabilities (Delgado & Ullery, 2018; Ergaz & Ornoy, 2011; Lozoff et al., 2006; Rosenbaum & Simon, 2016). Detecting increased risk for developmental disabilities in newborns and young infants is ideal for early intervention and favorable outcomes, but continued monitoring remains important as postnatal factors continue to impact brain development.

The average age at diagnosis varies across developmental disabilities. Although ASD can be accurately diagnosed by 14 months (Pierce et al., 2019), the median age for diagnosis is developmentally quite late, at 4 years of age (Baio et al., 2018; Brett et al., 2016). Behavioral signs of ASD are sometimes present before 12 months of age (Cohen et al., 2013; Jones & Klin, 2013) and neurological assessments such as EEG (Bosl et al., 2018; Dickinson et al., 2021) and MRI (Emerson et al., 2017; Hazlett et al., 2017) conducted in the first year of life can reliably predict infants who will later meet criteria for ASD. Although promising, EEG and MRI are time-consuming

and costly, and therefore, are not feasible for screening ASD at a population level. Because ABR-based newborn hearing screening is already prevalent in many countries, this technique presents an ideal opportunity to evaluate infants for neurological-based disorders such as ASD and SI. Although our ROC analysis did not meet the traditional predictive threshold for a clinical screening tool (Metz, 1978; Murphy et al., 1987), our findings indicate that newborn ABR latency measures, if further refined, have the potential to *improve* the prediction of which newborns will go on to develop ASD and SI. For example, predictive accuracy may be improved by using higher intensities and stimulation rates (Delgado, 2004) or more "speech-like" stimuli (e.g., syllable rather than click stimuli, Russo et al., 2009) with the ABR. If successful, then children identified at high-risk based on newborn ABR findings could be referred for additional evaluations and closely monitored throughout infancy. Additional evaluations could include existing screening tools, such as neurophysiological evaluations (e.g., EEG, MRI, and/or magnetoencephalography (MEG)), biomarkers (Celis et al., 2021), physiological indicators (Bonnet-Brilhault et al., 2018; Elder et al., 2008), and early behavioral indicators (Cohen et al., 2013; Denisova & Zhao, 2017; Jones & Klin, 2013).

Although the integration of secondary datasets provides information on large samples that is difficult to obtain in other ways, this procedure has limitations. The use of secondary datasets restricted methodological flexibility (e.g., we were limited to the ABR acquisition parameters available) and provided limited information (e.g., additional details about risk factors or the nature or severity of a child's disability were unavailable). Although we examined primary exceptionality, some children may have been diagnosed with more than one developmental disability (Rosenbaum & Simon, 2016). Future studies should examine the relations between ABR and comorbid disabilities. For example, although children with an identified primary exceptionality of hearing loss were excluded from the study, it is possible that some children had hearing impairment comorbid with a different primary exceptionality. It is also possible that mild hearing impairments may not have yet been identified in some of the children in this preschool-aged sample. Evaluation of threshold and/or frequency-specific ABR, which could identify mild hearing loss, was not part of the newborn screening protocol in this study. Additionally, we lacked data on risk factors for developmental disabilities, such as prematurity, family history, fetal infection, hearing loss, and related abnormalities and syndromes (Joint Committee on Infant Hearing, 2019). Future research is therefore needed to evaluate the role of these risk factors.

Conclusions

We found that children with ASD and SI had slower neurological responses to click sounds as newborns. Our findings indicate that there may be sensory differences at birth. While not yet ready to be a stand-alone screener, these neurological differences in newborns' sound processing suggest that ABR, a commonly used newborn screening test, may help identify differences in newborns and, in conjunction with early behavioral signs, may facilitate earlier diagnoses of ASD and SI. A better understanding of the developmental mechanisms of developmental disabilities will aid in earlier identification, earlier and better interventions, and ultimately better outcomes for children.

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Author Contributions CFD conceptualized and designed the study, drafed the initial manuscript, supervised data linkage, processed data, conducted data and statistical analyses, interpreted findings, reviewed and revised the manuscript. EAS conceptualized and designed the study, drafted the intial manuscript, conducted data and statistical analyses, interpreted findings, and reviewed and revised the manuscript. GZ conducted data and statistical analyses, interpreted findings, and reviewed and revised the manuscript. OM and RED conceptualized and designed the study, interpreted findings, and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Declarations

Conflict of interest The authors have no conflicts of interest relevant to this article to disclose.

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