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PREDICTING AUTISM FROM INFANT CHARACTERISTICS: A SYSTEMATIC REVIEW

An Undergraduate Honors Thesis Submitted in Partial fulfillment of University Honors Program Requirements University of Nebraska-Lincoln

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March 11, 2022

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Abstract

A literature review was conducted of 73 articles to explore 12-month-old characteristics in infants that predicted later diagnosis with autism (ASD). Articles were reviewed if they discussed ASD, infants with siblings diagnosed with autism (high-risk) and/or infants later diagnosed with autism without known family history of ASD (low risk). Articles were not reviewed if the participants were 36 months or older at the start of the study. More factors were identified that discriminate characteristics associated with later ASD diagnosis in infants between 12-24 months compared to characteristics of infants below 12 months. Characteristics of infants under 12 months that were associated with later autism diagnosis include social behaviors, communication behaviors, eye gaze, abnormal movements, and auditory brainstem responses.

Key Words: Autism; Infants; Communication Sciences and Disorders

Predicting Autism from Infant Characteristics: A Systematic Review

Importance of Early Prediction of Autism

Predicting communication disorders in infancy improves parent access to support systems, child access to intervention services, and the development of later diagnostic tools. Research on early prediction of autism (ASD) is critical to developing later diagnostic and screening tools (Goin & Myers, 2004). Conducting research is informative of ASD characteristics present in infancy that can later lead to earlier diagnoses (Goin & Myers, 2004).

Early prediction of ASD is critical for improving parent access to support systems. In a focus group of parents raising children with disabilities, there was a theme of fear and guilt over society's existing viewpoints about disability (Goddard et al., 2000). For example, parents experienced guilt from others questioning their prenatal care, ability to manage atypical behaviors, and toilet training. Receiving an early diagnosis for communication disorders may alleviate the parents' guilt because it provides evidence that their actions did not cause their child's disability. Additionally, many parents described difficulty with their experience in navigating in a different culture where most parents raise children without disabilities (Goddard et al., 2000). Parents of children with disabilities described how they often felt conflicted between viewing their children with acceptance and society viewing their children with sorrow. When parents receive a diagnosis, they can then find support groups to connect with other parents who have similar experiences. Additionally, they will then be able to educate themselves on their child's disability and be a better advocate for their child in the future.

Predicting ASD is essential to improving child access to intervention services. Achieving a diagnosis can also help parents secure funding to receive intervention services for their

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children. In a focus group of parents raising children with disabilities, one parent expressed her frustration when she encountered a pediatrician who was reluctant to give a diagnosis even though the parent needed to secure intervention funding (Goddard et al., 2000). Early intervention for ASD may also allow children with ASD to function within the typical range and reduce the presence of communication-based secondary symptoms such as aggression, selfharm, anxiety, and depression (Koegel et al., 2014). Currently, many ASD diagnostic tools are targeted for 3-year-old or older children (Goin & Myers, 2004). Lack of early detection means children may be missing out on beneficial intervention services (Goin & Myers, 2004). Increased emphasis in early intervention has decreased the rate of individuals with ASD who are nonverbal throughout their life from 50% in 1980 to less than 10% in 2014 (Koegel et al., 2014).

Tools for Identifying Autism

Various tools can be used to assess skills or identify ASD in infants. The Communication Symbolic and Behavior Scales (CSBS) significantly discriminates 12- to 18-month-old infants with ASD from typically developing age-matched peers through lower scores (Roemer et al., 2019; Wetherby et al., 2004). The Mullen Scales of Early Learning (MSEL) significantly discriminates 14- to 24-month-old high-risk infants with ASD from typically developing age-matched peers (Landa & Garrett-Mayer, 2006). The Autism Observation Scale for Infants (AOSI) significantly discriminates 14-month-old high-risk infants later diagnosed with ASD from typically developing high-risk and low-risk age-matched peers through higher scores (Gammer et al., 2015). The Autism Diagnostic Observation Schedule (ADOS) identified ASD in 15- to 24-month infants when parents indicated communication concerns with a 100% retest stability rate (Guthrie et al., 2013). Primary care provider screening tools allow parents to assess their infants' skills and engage in follow-up and ongoing reflection of their infant's behaviors (Zwaigenbaum et al., 2009). The First Year Inventory (FYI) can also be used to discriminate children with ASD. 12- to 24-month-old infants who were later diagnosed with ASD from the ADOS also produced significantly less gesture on the FYI compared to typically developing age-matched peers (Gordon & Watson, 2015).

Discrimination of Autism From Other Language Disorders

Coordinated communication and gaze are predictors that discriminate children with autism from children with other language disorders. The 14-month-old high-risk infants later diagnosed with ASD displayed significantly less growth in their productions of coordinated communication efforts compared to 14-month-old high-risk infants later diagnosed with language delay (Parladé & Iverson, 2015). Three studies reviewed in a literature review of home movies found that 12-month-old infants later diagnosed with autism displayed lower quality of affect, less frequent orientation to name, and less looking at others compared to typically developing age-matched peers later diagnosed with developmental disorders (Saint-Georges et al., 2010).

Autism Predictors for General Population Infants Above 12 Months

Predictors for children above 12 months at low risk for ASD are social and communication behaviors and expressive language.

Social and Communication Behaviors

Home video studies reviewed footage samples of social and communication behaviors collected from parents of children who received an ASD diagnosis. Home videos of infants over 12 months later diagnosed with ASD demonstrated less maintenance of social engagement and accepting social invitation from adults compared to typically developing age-matched peers (Muratori et al., 2011). Home videos of 12-month to 30-month-old infants later diagnosed with pervasive developmental disorder not otherwise specified (PDD-NOS) (a condition on the autism spectrum that has historically been seen as less severe) demonstrated more behaviors than the ASD group of looking at faces, alternating gaze, following verbal directions, and imitating words but less of these behaviors than their typically developing age-matched peers (Mars et al., 1998). Home videos of play behaviors (using a toy in a way that is consistent with its function, stacking toys or having two different toys interact with each other) of 24-monthold infants later diagnosed with ASD significantly predicted later Vineland Adaptive Behavior Composite scores (Thorsen et al., 2008).

Studies with participants in lab settings also found similar significant social and communication behavior predictors for low-risk children with ASD. The 18- to 24-month-old infants later diagnosed with ASD utilized significantly more behavior regulation and social interaction but had a significantly lower mean rate of communicative gestures compared to typically developing age-matched peers (Shumway & Wetherby, 2009). The 26-month-old infants later diagnosed with ASD also demonstrated significantly lower effortful control, surgency (this includes behaviors such as activity level, high-intensity pleasure, and positive anticipation), and higher negative emotionality compared to typically developing age-matched peers (Macari et al., 2017). A literature review of studies exploring response-to-name behavior found 19 studies that identified significantly atypical response-to-name behaviors in children with ASD (Zhang et al., 2018). Parents of 18- to 24-month-old twin-children who failed the Modified Checklist for Autism in Toddlers (M-CHAT) also rated their children poorly in typical reciprocal behavior compared to video references of typical reciprocal behavior (Marrus et al., 2015).

Expressive Language

Expressive language is a predictor of ASD for 12-month-old or above low-risk children. ASD Composite scores of pre-speech behaviors and nonverbal intelligent quotient on the Childhood Autism Rating Scale on children with ASD collapsed from scores collected between 6-53 months predicted growth of children's expressive language (Bopp & Mirenda, 2011). The number of right-handed gestures in 26- to 36-month-old children diagnosed with ASD was positively associated with expressive language one year later (Dimitrova et al., 2020). Toddlers diagnosed with autism who did not produce their first word by 18 months received significantly lower scores on the MSEL compared to typically developing age-matched toddlers who produced their first word before 18 months (Mayo et al., 2013).

Autism Predictors for High-Risk Infants at or Above 12 Months

Predictors that discriminate 12- to 24-month-old high-risk children for autism from peers are social behaviors, communication behaviors, and sounds.

Social Behaviors

Affect behaviors during 12-14 months are predictive of later ASD diagnosis. The 12month-old and 18-month-old high-risk infants later diagnosed with ASD displayed significantly lower responsivity and attention when observing another adult undergoing distress compared to typically developing age-matched peers (Hutman et al., 2010). By 18 months, typically developing high-risk infants could no longer be discriminated from age-matched controls with low-risk. The 14-month-old high-risk toddlers who received an earlier ASD diagnosis displayed significantly less affect compared to age-matched peers who received a later ASD diagnosis and typically developing age-matched peers (Landa et al., 2007). The 14-month-old high-risk infants later diagnosed with ASD displayed significantly less smiling and laughter behaviors compared to typically-developing low-risk age-matched peers (Clifford et al., 2012; Pijl et al., 2019). The 12- to 24-month-old high-risk infants displayed significantly less social and non-social smiling behaviors without discrimination of later ASD diagnosis compared to typically developing agematched peers (Nichols et al., 2014). The 18-month-old high-risk infants displayed significantly more withdrawal behaviors without discrimination of later ASD diagnosis when novel objects were introduced compared to typically developing age-matched peers (Cornew et al., 2012).

Several studies examined infants' initiation of joint attention behaviors around toys to determine risk of later ASD diagnosis. Initiating joint attention was defined as the infant alternating gaze between the toy and experimenter or making eye contact with the experimenter while manipulating the toy (Cassel et al., 2007). The 14- to 15- month-old highrisk infants later diagnosed with ASD displayed significantly less initiation of joint attention bids compared to typically developing age-matched peers (Cassel et al., 2007; Heymann et al., 2018; Landa et al., 2007). The 12-month-old high-risk infants who displayed atypical performance on the ADOS in initiating joint attention had an increased risk of a diagnosis of ASD or other developmental disorder (Macari et al., 2012).

Overall joint attending behaviors (adults and children sharing attention to the same event) are also predictive of ASD diagnosis. The 18-month-old high-risk infants later diagnosed with ASD displayed significantly less response to joint attention bids from adults compared to age-matched typically developing peers (Cassel et al., 2007). Response to joint attention was defined as the infant following an examiner's combined dietic gesture and vocalization (Cassel et al., 2007). The 13-month-old high-risk infants later diagnosed with ASD displayed significantly less joint attending to objects and increased disengagement compared to typically developing age-matched peers (Bedford et al., 2012, 2014). High-risk infants with a mean age of 15 months displayed a significantly delayed response to joint attention compared to typically developing age-matched peers (Yoder et al., 2009). The 12-month-old high-risk infants displayed significantly less shifting attention from objects to caretakers compared to typically developing high-risk and low-risk age-matched peers (Kadlaskar et al., 2019). The 24-month-old infants later diagnosed with ASD displayed low attention level shifting compared to typically developing high-risk and low-risk age-matched peers (Garon et al., 2009).

Eye contact is predictive of ASD diagnosis. The 12- to 14-month-old high-risk infants later diagnosed with ASD displayed significantly less eye contact compared to typically developing high-risk and low-risk peers (Nichols et al., 2014). Parents self-reported their children at 18.8 months who received a later ASD diagnosis displayed poor eye contact (Becerra-Culqui et al., 2018).

Activity level and movements are also predictive of ASD diagnosis during the 12-24 months period. The 12-month-old and 24-month-old high-risk infants later diagnosed with ASD were significantly more likely to display high activity levels than peers who did not receive a later ASD diagnosis (Garon et al., 2009; Macari et al., 2012). Compiled data of high-risk infants at 6, 12, 18, 25, and 36 months later diagnosed with ASD displayed higher activity levels compared to typically developing high-risk peers (Rosario et al., 2014). Mean age 32.95-month-

old high-risk infants displayed more repetitive stereotyped body and object movements compared to typically developing age- and mental age-matched peers (Damiano et al., 2013).

Communication Behaviors

Several studies found language in 12-24-month-old infants predicted later diagnosis of ASD. Compiled scores on the MSEL of high-risk infants at 6 and 36 months later diagnosed with ASD had a significant association with low verbal expression and low verbal reception or language/motor acquisition skill delay (Franchini et al., 2018; Landa et al., 2012). The 14-monthold high-risk infants later diagnosed with ASD had significantly lower scores on MSEL on the receptive and expressive language, gross motor, visual reception, and adaptive behavior compared to typically developing high-risk and low-risk age-matched peers (Estes et al., 2015; Lazenby et al., 2016). The 14-month-old high-risk infants who received an early ASD diagnosis at 14 months on the MSEL displayed significantly lower expressive language scores compared to atypically developing age-matched peers who received a late ASD diagnosis after 14 months (Landa et al., 2013). The 12- to 18-month-old high-risk infants scored lower on the MSEL in gesture and language without discrimination of later ASD diagnosis compared to typically developing age-matched peers (Roemer et al., 2019). The 18- to 36-month-old high-risk toddlers diagnosed with ASD produced significantly fewer consonants and lower mean syllable structure of their vocalizations but significantly more nonverbal squeal utterances compared to typically developing age-matched peers (Schoen et al., 2011).

Studies that utilized other screening tools also found significant communication behavior predictors in infancy for later ASD diagnosis. The 12-month-old high-risk infants later diagnosed with ASD scored lower on the CSBS in use of communication, use of gestures, and eye gaze compared to typically developing age-matched peers (Veness et al., 2012). However, the differences in scores could not discriminate the children with ASD from children with other language disorders or developmental delays until 24 months. The 12-month-old high-risk infants later diagnosed with ASD demonstrate significantly slower growth in coordinated communication efforts than typically developing age-matched peers (Parladé & Iverson, 2015). The 18-month-old high-risk infants diagnosed by researchers with ASD utilizing the ADOS and MSEL had a positive predictive diagnosis stability rate of 93% when retested at 3-years-old (Ozonoff et al., 2015). However, some children that passed these 18-month screeners were still candidates for receiving a later ASD diagnosis when retested at 3-years-old.

Sounds

Sound analysis of infants above 24 months can discriminate infants who later receive ASD diagnosis from typically developing peers. The 15-month-old high-risk infants later diagnosed with ASD had significantly higher fundamental frequency of crying during the strange situation procedure compared to typically developing age-matched peers (Esposito et al., 2014). The 18- to 42-month-old toddlers who received an ASD diagnosis in auditory brain stem response (ABR) screening tests displayed ABR latencies and prolongations compared to typically developing age-matched peers (Miron et al., 2021).

Autism Predictors for General Population Infants Below 12 Months

Predictors of autism for low-risk infants below 12 months are social behaviors, abnormal movements, and auditory brainstem responses.

Home videos of 0- to 6-month-old infants later diagnosed with ASD displayed significantly fewer social behaviors and syntony (the ability to express affect and the ability to

repeat, attend, or read the affective states of others) compared to age-matched typically developing infants (Maestro et al., 2005; Muratori et al., 2011). A significant difference in social behaviors (looking, orienting, and vocalizing towards a person) were no longer shown in 7- to 12-month-old infants (Maestro et al., 2005). The 9-month-old infants later diagnosed with ASD on the well-baby checklist passed "laughs" and "understanding objects" significantly less frequently compared to typically developing age-matched peers (Davidovitch et al., 2018). A literature review of home film studies found six studies that indicated infants 6-month-old and under retrospectively diagnosed with ASD had significantly less anticipation of others' aims, social attention, pointing, and attuning behaviors compared to typically developing agematched peers (Saint-Georges et al., 2010).

Eye gaze in infants is predictive of ASD diagnosis and later emotional traits. A literature review found six studies that indicated infants 12-month-old and under displayed reduced gazing at others compared to typically developing age-matched peers (Saint-Georges et al., 2010). The 6-month-old infants later diagnosed with ASD regardless of high-risk or low-risk history displayed less gazing at others' faces compared to typically developing age-matched peers (Chawarska et al., 2013). The 7-month-old infants that displayed eye gaze preference for human faces as opposed to scrambled face stimuli were significantly less likely to demonstrate callous emotional traits at 48 months (Peltola et al., 2018).

Specific motor and neurosensory factors have been implicated in ASD prediction for infants under 6 months. Videos of 0- 6-month-old infants later diagnosed with ASD were significantly more likely to display abnormal writhing or fidgeting movements than typically developing age-matched peers (Zappella et al., 2015). Retrospectively obtained auditory brainstem tests from infants with a mean age of 3.2 months later diagnosed with ASD had significantly prolonged ABR in both ears and significant ABR latency in the right ear compared to typically developing gender-matched and corrected chronological age-matched peers (Miron et al., 2016). Computer classification analysis software correctly classified infant diagnosis status based on ABR latency with 78% positive predictive validity (Miron et al., 2016).

Autism Predictors for High-Risk Infants Below 12 Months

Predictors that discriminate infants below 12 months at high risk for autism from peers are social behaviors, communication behaviors, and eye gaze.

Social Behaviors

Various screening tools can discriminate high-risk infants with ASD from typically developing infants. The 8-month-old high-risk infants later diagnosed with ASD in the Early Social Communication Scale displayed significantly less initiation and response to joint attention compared to typically developing high-risk age-matched peers (Ibañez et al., 2013). The rate of growth of requesting behaviors was significantly slower for all high-risk infants compared to age-matched peers. The 4-month-old high-risk infants later diagnosed with ASD displayed less synchrony in infant-initiated interactions during mother-child free play compared to typically developing age-matched controls (Yirmiya et al., 2006). The 9- and 12-month-old high-risk infants later diagnosed with autism displayed significantly lower total scores on the CSBS compared to typically developing age-matched peers (Bradshaw et al., 2021). The 6-month-old high-risk infants on the MSES had significantly lower gross motor and visual reception scores and significantly lower scores on the Vineland without discrimination of later ASD diagnosis compared to typically developing peers (Estes et al., 2015). Social behaviors that can predict ASD in infants below 12 months also include affect behaviors. Parents of 7-month-old high-risk infants regardless of ASD diagnosis reported significantly less smiling and laughter compared to typically developing age-matched controls (Clifford et al., 2012). The 6-month-old high-risk infants later diagnosed with ASD displayed less smiling and laughter during observed play and the still-face procedure compared to typically developing high-risk and low-risk age-matched peers (Cassel et al., 2007; Paterson et al., 2019).

Communication Behaviors

Early communication behaviors similar to characteristics in older infants above 12 months have been predictive of later ASD diagnoses in high-risk infants under 12 months. The 9- to 12-month-old high-risk infants displayed significantly less canonical syllable production and canonical babbling ratios compared to typically developing age-matched peers (Patten et al., 2014; Paul et al., 2011). Parents rated the cries of 1-month-old infants later diagnosed with ASD as displaying fewer total utterances with more variable utterance and inter-utterance length compared to neurotypical age-matched infants likely exposed to drug substances (English et al., 2019).

Gestures can also be used to discriminate high-risk infants under 12 months with ASD from typically developing peers. The 9-month-old high-risk infants later diagnosed with ASD on the Communication Development Inventory exhibited a significantly slower growth rate of early gestures compared to typically developing age-matched peers (Iverson et al., 2018). The 12month-old high-risk infants later diagnosed with ASD displayed a significant positive correlation score on the Repetitive Behavior Scale and Sensory Experiences Questionnaire (Wolff et al., 2019).

Eye Gaze

Eye gaze behaviors can predict later ASD diagnosis in high-risk infants under 12 months. The 6-month-old high-risk infants later diagnosed with ASD displayed a significant correlation between MSES language scores and gaze fixation on their mother's mouths (Young et al., 2009). The 8-month-old high-risk infants later diagnosed with ASD displayed a less reliable preference for infant-directed speech through eye gaze compared to typically developing age-matched peers (Droucker et al., 2013). The 9-month-old infants later diagnosed with ASD displayed lower gaze preference for eyes over mouths compared to typically developing high-risk age-matched peers (Rutherford et al., 2015). The 10-month-old girl infants later diagnosed with ASD displayed significantly less eye gaze after an adult made eye contact compared to typically developing girl age-matched peers (Nyström et al., 2017). The 10-month-old high-risk infants later diagnosed with ASD displayed less differentiation between asynchronous audio and visual stimuli and synchronous audio and visual stimuli compared to typically developing high-risk and low-risk age-matched peers (Falck-Ytter et al., 2018).

Conclusion

This literature review found 39 studies that significantly discriminated characteristics that predicted later ASD diagnosis in infants between 12-24 months compared to 26 studies that discriminated predictors of ASD in infants below 12 months. The lower amount of literature for ASD predictors in infants below 12 months is likely due to the less diverse types of communication behaviors that can be observed in infants. For example, detecting language delays in 6-month-old infants is extremely difficult because 6-month-old infants are not producing words. Despite the difficulty in detecting communication disorders below 12 months, many studies of eye gaze, vocal behavior, social interaction, and movement have emerged that have successfully discriminated infants with ASD under 12 months from typically developing infants. The field should strive to conduct further research for ASD predictors in infants below 12 months to increase parent access to support systems, child access to intervention services, and the development of later diagnostic tools.

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