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Trajectories of cognitive development in toddlers with language delays

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ABSTRACT

Background: Toddlers with early language delays (LD) are at risk for developmental difficulties, including autism spectrum disorder (ASD). However, little is known about early cognitive skill acquisition in this population.

Aims: To explore heterogeneity in cognitive development in toddlers with significant LD (n = 30) or typical development (n = 61), and how this relates to 36-month outcomes (ASD, non-ASD delays, or no delays).

Methods: Growth mixture modeling of nonverbal and verbal mental age (NVMA, VMA) scores from the Mullen Scales of Early Learning was conducted with data from 18, 24 and 36 months.

Results: A two-class NVMA solution was selected (Age Appropriate, 82%, Delayed, 18%); class membership was related to the no delay outcome, and although the proportion of toddlers with ASD in the Age-Expected class was 17% compared to 50% of toddlers with non-ASD delays, this difference was not statistically significant. The best-fitting model for VMA included three classes: Age Appropriate (66%), Delay Catch-Up (23%), Delayed (11%); class assignment differed by outcome. Children in the Delay Catch-Up class were more likely to have non-ASD delays compared to ASD, while the reverse was true in the Delayed class.

Conclusions: Cognitive development in toddlers with LD is heterogeneous, and delayed verbal trajectories relate to later ASD diagnosis.

1. Introduction

The importance of the early developmental course of children who are later diagnosed with autism spectrum disorder (ASD) cannot be overstated (Rogers, 2009). Apart from population-based methods, any prospective study of infants and toddlers who will be diagnosed with ASD requires that the researchers select some group of children who are more likely than the average child to develop ASD.

During the last 10 years when research using this high-risk design has accelerated, the population that has garnered the most attention is the younger siblings of children diagnosed with ASD. Prospective research on these infants, who have heightened genetic risk for developing the disorder, has critical implications for improving understanding of pathways to later outcomes (Szatmari et al.,

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2016). Importantly, however, there are limitations to generalizations of the findings from studies of infant siblings. Primarily, the unavoidable parental vigilance associated with having an older child already diagnosed with ASD may bias these studies.

Thus, complementary studies of children at risk for ASD due to factors other than familial genetic transmission alone are needed. Along with other risk groups, including infants with neonatal problems (Karmel et al., 2010) and infants already identified based on concerns about possible ASD (Lord, Luyster, Guthrie, & Pickles, 2012), toddlers with early language delays are good candidates for this purpose (Guthrie, Swineford, Nottke, & Wetherby, 2013). Toddlers with language delays are at increased risk for persistent developmental difficulties, and are diagnosed with ASD at a higher-than-average rate (Miniscalco, Nygren, Hagberg, Kadesjo, & Gillberg, 2006). Given that language delay is a commonly reported first concern of parents whose children are later diagnosed with ASD (Chawarska et al., 2007; Coonrod & Stone, 2004; Hess & Landa, 2012), language delay is a particularly relevant construct for creating a high-risk sample.

Nevertheless, the bulk of our knowledge about the early development of children later diagnosed with ASD comes from the infant sibling literature. A commonly explored potential predictor of interest in these toddlers at risk or already diagnosed is cognitive ability (Chawarska, Klin, Paul, Macari, & Volkmar, 2009; Jones, Gliga, Bedford, Charman, & Johnson, 2014). Research utilizing developmental measures that serve as a proxy for cognitive skills, such as the Mullen Scales of Early Learning (MSEL; Mullen, 1995), has helped elucidate the progression of verbal and nonverbal cognitive skill acquisition. For example, cognitive abilities in high-risk siblings have been shown to diverge from low risk infants by approximately 12–14 months (Landa & Garrett-Mayer, 2006; Landa, Gross, Stuart, & Bauman, 2012; Landa, Gross, Stuart, & Faherty, 2013; Ozonoff et al., 2010; Ozonoff et al., 2014). Rates of cognitive growth in infants later diagnosed with ASD leading up to the third year of life are variable, but often delayed (Brian et al., 2014; Estes et al., 2015; Landa & Garrett-Mayer, 2006; Landa et al., 2012). Despite the variability in developmental trajectories among the approximately 20% of high-risk infants who later receive an ASD diagnosis (Ozonoff et al., 2011), cognitive disparities compared to healthy controls tend to increase over time (Brian et al., 2014; Estes et al., 2015; Landa & Garrett-Mayer, 2006; Landa et al., 2012).

Importantly, research has also revealed significant heterogeneity in early cognition and its progression in these high-risk infant siblings. For example, one study documented differences in cognitive development between infants with earlier versus later diagnoses of ASD (Landa et al., 2013). Other studies have quantified this heterogeneity using latent variable methods, providing further evidence that cognitive development in infant siblings at risk for ASD is not monolithic. Two studies using similar statistical methodology found evidence for three types of trajectories: advanced, stable, and delayed (also called declining, whether it be general delay or specific to language/motor) (Brian et al., 2014; Landa et al., 2012). In both of these studies, the children who later received an ASD diagnosis were more frequently in the stable or declining classes versus the advanced trajectory, suggesting that at least among infant siblings of children with ASD, these trajectories of cognitive development may indicate higher likelihood of later ASD diagnosis.

These studies provide initial, clinically meaningful evidence about the presence of heterogeneity and patterns of early development in infants at increased genetic risk for ASD. However, as described, the limitations inherent to studying infant siblings require that complementary evidence be assembled. In this study, we sought to describe prospectively the development of cognitive ability in children with early language delay, who at 36 months would achieve age-appropriate development, exhibit non-ASD delays, or be diagnosed with ASD. Thus, we utilize growth mixture modeling (GMM), a method of identifying latent subpopulations in longitudinal data, to objectively quantify and describe the heterogeneity in MSEL nonverbal and verbal cognitive trajectories in toddlers with early language delay.

We hypothesized that the heterogeneity in verbal and nonverbal cognitive development of our combined sample of toddlers with language delay (LD) and typical development (TD) would be best explained by more than one trajectory class. We expected that this would include an age-appropriate class and likely two classes with different patterns of delays, consistent with prior findings on trajectories in infant siblings (Landa et al., 2012). Since prior research in at risk samples has not specifically described relationships between nonverbal and verbal cognitive growth as measured by the MSEL, we also report the relationship between nonverbal and verbal MSEL class membership, which we expected to be strongly related. Finally, we expected that membership in both delayed verbal and nonverbal MSEL trajectory classes would predict ASD outcomes, as demonstrated in the infant sibling data (Brian et al., 2014; Landa et al., 2012).

2. Methods

2.1. Participants

Ninety-one toddlers participated in a longitudinal study examining language delay as a risk factor for outcomes such as ASD conducted across two sites: the National Institute of Mental Health and the University of Utah. The Institutional Review Boards at both sites approved this study, and all families gave written consent for study participation. Participants included toddlers with LD (n = 30) or TD (n = 61). Study recruitment was based on suspicion of LD as a risk factor for ASD and drew from pediatric practices, early intervention providers, and child development clinics. TD toddlers were recruited through flyers posted in community settings (e.g., doctors' offices, preschools) and word-of-mouth. Toddlers were initially evaluated at 12 or 18 months of age (± 2 months) to determine study eligibility. Participants who met inclusion criteria (described below) were evaluated at 18, 24, and 36 months. Given the limited number of participants with 12-month data, the focus of the present study is on the 18, 24 (n_{LD} = 28, n_{TD} = 59), and 36-month (n_{LD} = 24, n_{TD} = 56) intervals. Participant characteristics are shown in Table 1.

Based on inclusion criteria, all participants were born full term (≥36 weeks) and lived in households where English was the primary language. LD was determined upon study entry (12 or 18 months) using the Mullen Scales of Early Learning (MSEL; Mullen,