Speech and language in DDX3X–neurodevelopmental disorder: A call for early augmentative and alternative communication intervention

Elana J Forbes [1 2], Lottie D Morison [1], Fatma Lelik [1], Tegan Howell [1], Simone Debono [1], Himanshu Goel [3 4], Pauline Burger [5], Jean-Louis Mandel [5 6], David Geneviève [7], David J Amor [1 8], Angela T Morgan [1 9]

Affiliations + expand

PMID: 38421120 DOI: 10.1002/ajmg.b.32971

Abstract

Pathogenic variants in DDX3X are associated with neurodevelopmental disorders. Communication impairments are commonly reported, yet specific speech and language diagnoses have not been delineated, preventing prognostic counseling and targeted therapies. Here, we characterized speech and language in 38 female individuals, aged 1.69-24.34 years, with pathogenic and likely pathogenic DDX3X variants (missense, n = 13; nonsense, n = 12; frameshift, n = 7; splice site, n = 3; synonymous, n = 2; deletion, n = 1). Standardized speech, language, motor, social, and adaptive behavior assessments were administered. All participants had gross motor deficits in infancy (34/34), and fine motor deficits were common throughout childhood (94%; 32/34). Intellectual disability was reported in 86% (24/28) of participants over 4 years of age. Expressive, receptive, and social communication skills were, on average, severely impaired. However, receptive language was significantly stronger than expressive language ability. Over half of the assessed participants were minimally verbal (66%; 22/33; range = 2 years 2 months-24 years 4 months; mean = 8 years; SD = 6 years) and augmented speech with sign language, gestures, or digital devices. A quarter of the cohort had childhood apraxia of speech (25%; 9/36). Despite speech and language impairments, social motivation was a relevant strength. Many participants used augmentative and alternative communication (AAC), underscoring the need for early, tailored, and comprehensive AAC intervention.

Keywords: DDX3X; developmental delay; intellectual disability; language; neurodevelopment; speech.