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RESEARCH REPORT

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RESEARCH SUMMARY

Developmental Skills of Individuals with Angelman Syndrome Assessed Using the Bayley-III

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WHAT WAS THE RESEARCH ABOUT?

Even though Angelman syndrome (AS) was initially described over 50 years ago, little is known about how skills, such as communication and cognition, develop over time in children with AS. AS is caused by a lack of function of a gene called UBE3A on chromosome 15. In about 70% of cases, AS results from a deletion of UBE3A on the copy of chromosome 15 that is inherited from the mother. The size of this chromosomal deletion in most individuals with AS is either 6 Mb (i.e., 6 million "letters" of DNA), which is known as a "class I deletion", or 5 Mb (i.e., 5 million "letters" of DNA), which is known as a "class II deletion". Of note, although these sound like large numbers, each of us has over 3 billion "letters" of DNA, so this is actually a very small percentage of DNA to lose. However, there are also less common non-deletion subtypes of AS, caused by either a mutation (pathogenic variant) in UBE3A on the maternal copy of chromosome 15, an imprinting defect on the maternal copy of chromosome 15, or paternal uniparental disomy, in which two copies of chromosome 15 are inherited from the father. Past research shows that children with AS due to a deletion experience greater delays across all developmental domains compared to children with non-deletion AS, but the difference in development of skills among non-deletion subtypes of AS is unclear. In this study, we looked at developmental profiles of children with AS using an assessment measure called the Bayley Scales of Infant and Toddler Development (Bayley-III), which measures a child's development in multiple areas, including cognition, communication, and motor skills.

WHAT DID THE RESEARCH TEAM DO?

We analyzed Bayley-III data obtained from children between the ages of 12 months and 12 years who were evaluated in the AS Natural History Study. The Bayley-III was designed to assess developmental skills in infants and toddlers, but it is also commonly used to assess developmental skills in older children with severe cognitive impairments, including individuals with AS.

We examined how cognition, receptive and expressive communication, and gross and fine motor skills develop over time in children with AS. We also looked at differences in these developmental domains among five molecular subtypes of AS and described patterns of strengths and weaknesses for children with AS based on these molecular subtypes. Documenting how developmental skills vary by molecular subtype is important for future studies that are focused on the needs and prognoses of these children, as well as for future treatment studies that may potentially improve developmental skills in one or more domains.

WHO WAS IN THE STUDY?

236 participants with a molecular diagnosis of AS between the ages of 1 and 12 years were included in the study. There was an equal number of male and female participants in the sample. On average, children had approximately three study visits. Overall, approximately 60% of the children in the sample had a history of seizures.

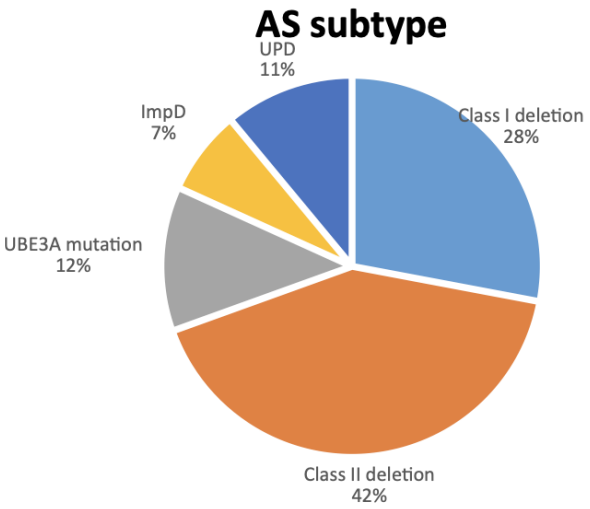
STUDY PARTICIPANTS

236 participants 1-12

50% male

50% female

~60% had history of seizures



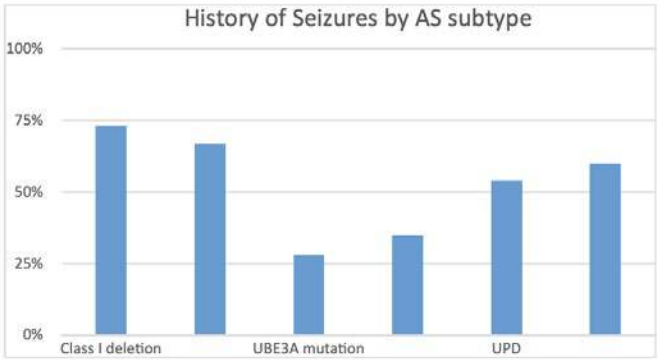


Table 1. Average age of participants at first and final study visits

	Class I deletion	Class II deletion	*UBE3A* mutation	ImpD	UPD	Overall
Average age at visit 1 (years)	4.0	4.2	5.0	5.4	5.8	4.5
Average age at final visit (years)	6.4	6.9	6.9	8.2	7.8	6.9

ImpD: imprinting defect; UPD: paternal uniparental disomy

WHAT DID THE RESEARCH TEAM LEARN?

At six years of age, most children with AS were functioning at the developmental level of a 14- to 27-month-old child across developmental domains. Children with AS made slow gains in development through at least 12 years of age, developing at a rate of about 1-2 months a year.

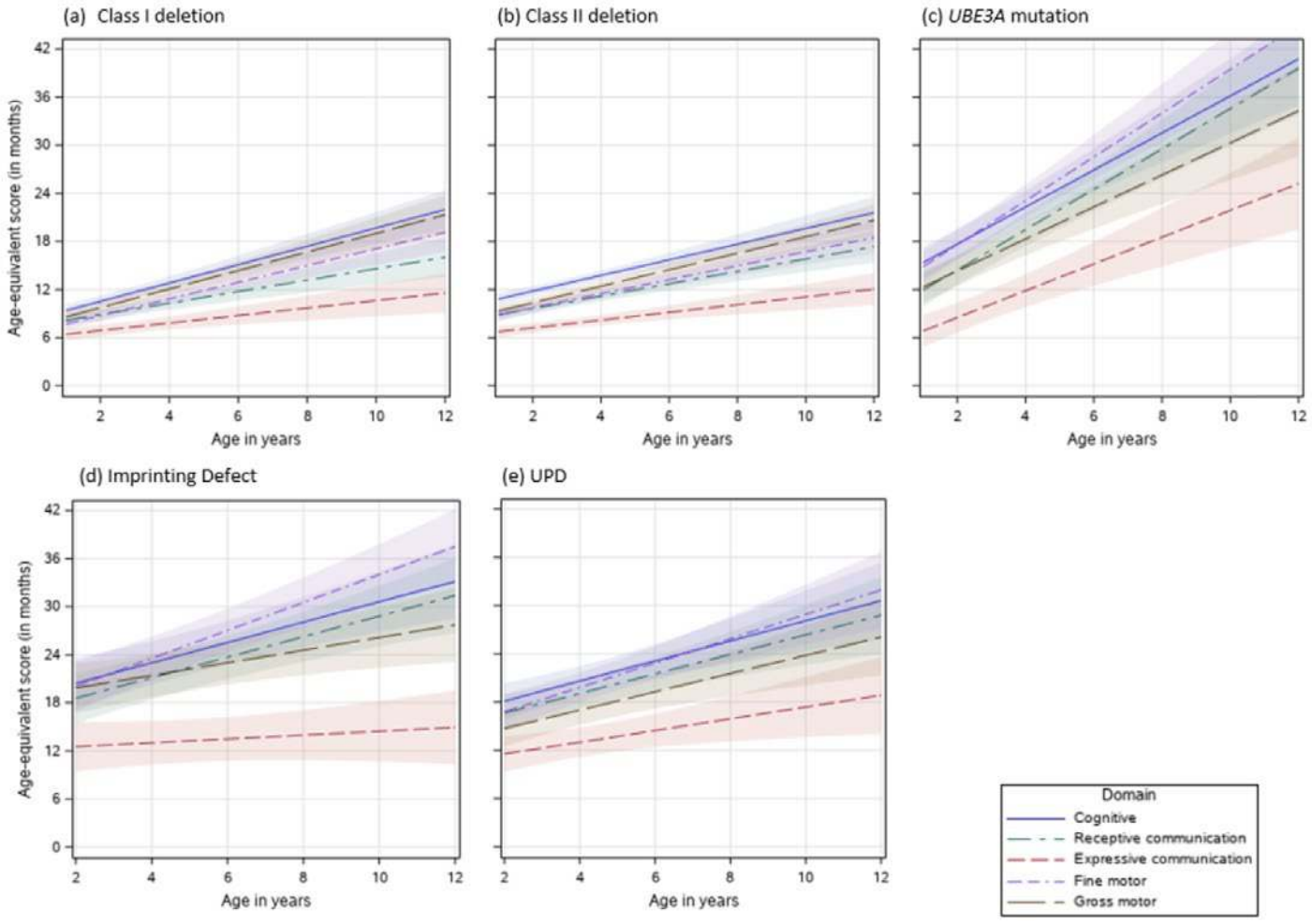
Children with a non-deletion AS subtype had better developmental skills compared to those with a deletion subtype

Consistent with previous studies, children with Class I and Class II deletions had lower scores on the Bayley-III and a slower rate of gaining skills compared to children with non-deletion AS. Children with a UBE3A mutation had higher scores and a greater rate of skill attainment compared to children with the other subtypes of AS. Children with an imprinting defect and paternal uniparental disomy had similar developmental profiles, typically demonstrating a lower level of skills and slower growth in skills compared to children with a UBE3A mutation but performing better than children with a Class I or Class II deletion.

Expressive communication was a significant weakness compared to the other developmental domains

Regardless of AS subtype, expressive communication was the most impaired developmental domain.

Figures 5a-e. Effects plots of Bayley-III Age-equivalent scores for each developmental domain and molecular subtypes



WHAT DOES THIS MEAN FOR FAMILIES?

This study provides evidence that children with AS continue to learn and gain skills throughout childhood and into early adolescence. Therefore, intensive developmental interventions that target areas of developmental concern, including physical, occupational, and communication therapies, should continue to be provided to children with AS regardless of subtype. Given the substantial delays in expressive communication in AS, and in spoken language in particular, speech-language therapy should include augmentative and alternative communication (AAC) systems. The use of AAC provides these children with a crucial modality for expressing their wants and needs.

Full article by Dr. Sadhwani and colleagues:
Read here

Sadhwani A, et al. Developmental Skills of Individuals with Angelman Syndrome Assessed Using the Bayley-III. J Autism Dev Disord. 2021 Jan 30:10.1007/s10803-020-04861-1. doi: 10.1007/s10803-020-04861-1. Epub ahead of print.