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RESEARCH REPORT

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RESEARCH SUMMARY

Developmental Milestones and Daily Living Skills in Individuals with Angelman Syndrome

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WHAT WAS THE RESEARCH ABOUT?

Angelman syndrome (AS) is a neurodevelopmental disorder that is caused by the lack of expression of the *UBE3A* gene on chromosome 15. Normally, two copies of this gene are inherited (one from each parent). In AS, the mother's copy of this gene does not function correctly due to one of the following four reasons: deletion, *UBE3A* mutation, paternal uniparental disomy (UPD), or imprinting defect (ImpD), with the latter three classified as non-deletion causes.

Previous research has shown that people with AS develop more slowly relative to their neurotypical peers, but that they do make progress over time. The severity of developmental delays varies depending on which of the four mechanisms caused AS in the individual. Generally, individuals with a deletion tend to have more severe delays and achieve developmental milestones at a later age than those without a deletion.

The current study used data from a large-scale, longitudinal study to determine the likelihood and typical age range at which children with AS achieve various developmental milestones and daily living skills, as well as how these ages vary depending on molecular subtype.

WHAT DID THE RESEARCH TEAM DO?

Participants in this study were from the AS Natural History Study. The study included individuals with a confirmed molecular diagnosis of AS and an age between one day and 60 years. Participants

were assessed annually at one of six study sites across the U.S. At each visit, caregivers filled out a questionnaire about their child's developmental milestones in areas such as motor skills (gross and fine) and language (receptive and expressive communication).

Knowing when children with AS typically reach developmental milestones helps clinicians and caregivers set realistic goals and expectations for development and identify any medical issues that may be causing additional delays.

WHO WAS IN THE STUDY?

Participants were 261 individuals with a molecular diagnosis of AS, ranging in age from 4 months to 40 years at the baseline visit. There were an equal number of male and female participants in the sample.

Participants were evaluated annually at one of six sites in the US, with the number of visits per participant ranging from 1 to 9 (Mean = 3.7).

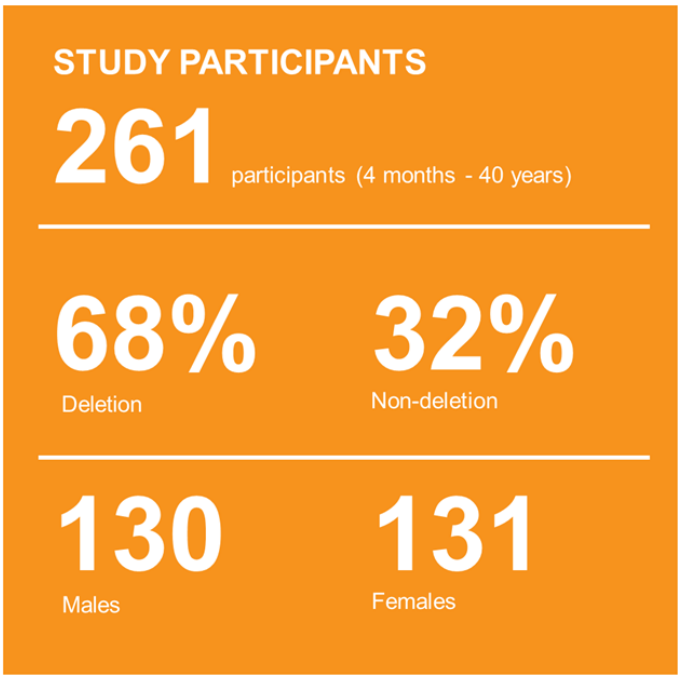
	Age at Baseline Visit (years)	Age at Final Visit (years)
Class I Deletion	5.7	8.6
Class II Deletion	5.2	8.0
UBE3A Mutation	5.7	8.2
Uniparental Disomy	6.7	8.8
Imprinting Defect	5.9	9.7

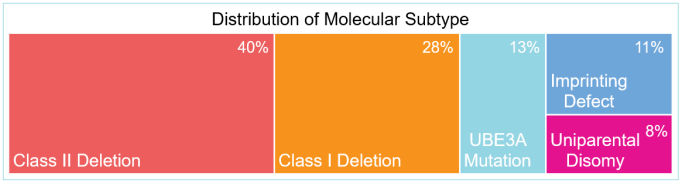
WHAT DID THE RESEARCH TEAM LEARN?

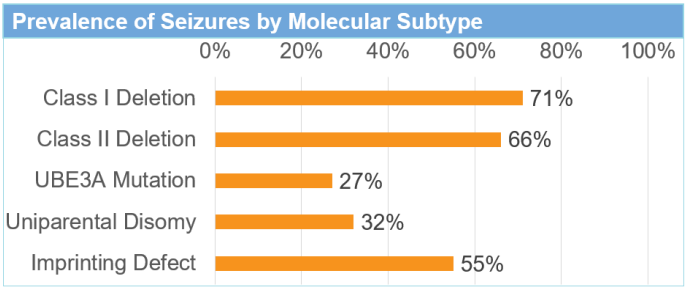
Skill development in individuals with AS

Most individuals with AS, regardless of molecular subtype, developed a majority of skills at a later age compared to neurotypical individuals.

Regardless of molecular subtype, skills such as sitting and walking with support are likely to be achieved within a narrow age range. By age 3.5 years, many participants could hold an object, and by age 5 years, most participants had achieved gross motor skills such as walking with support. Toileting and feeding skills are







Toileting and feeding skills are less likely to be acquired and have more variability in age of achievement. **Most AS participants struggled to acquire essential daily living skills such as brushing teeth, bathing, and dressing without assistance, all of which are necessary for independent living.**

Differences in development by genetic subtype

Individuals with AS caused by a deletion are less likely to acquire skills and acquire skills more slowly compared to those without a deletion.

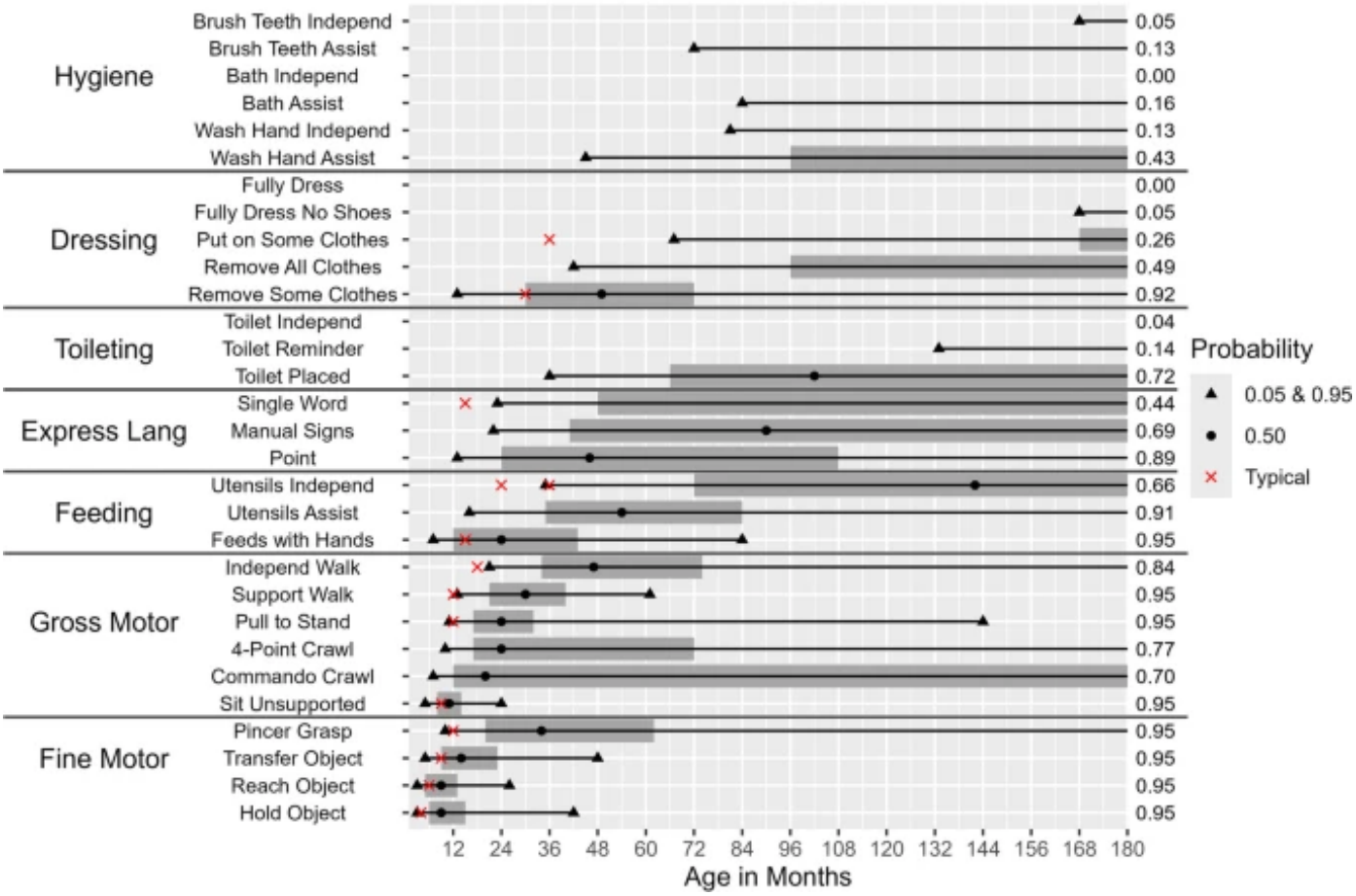
Individuals with a deletion have more variable age ranges for achieving many developmental milestones and daily living skills. Within non-deletion subtypes, the development of individuals with *UBE3A* mutations and ImpD subtypes was similar, achieving most skills and milestones earlier than those with deletion. UPD individuals were less likely to achieve skills compared to those with *UBE3A* mutations and ImpD, but more likely than those with deletion. **Individuals without a deletion are overall likely to acquire more developmental skills compared to those with deletion.**

Probability of skill achievement by molecular subtype

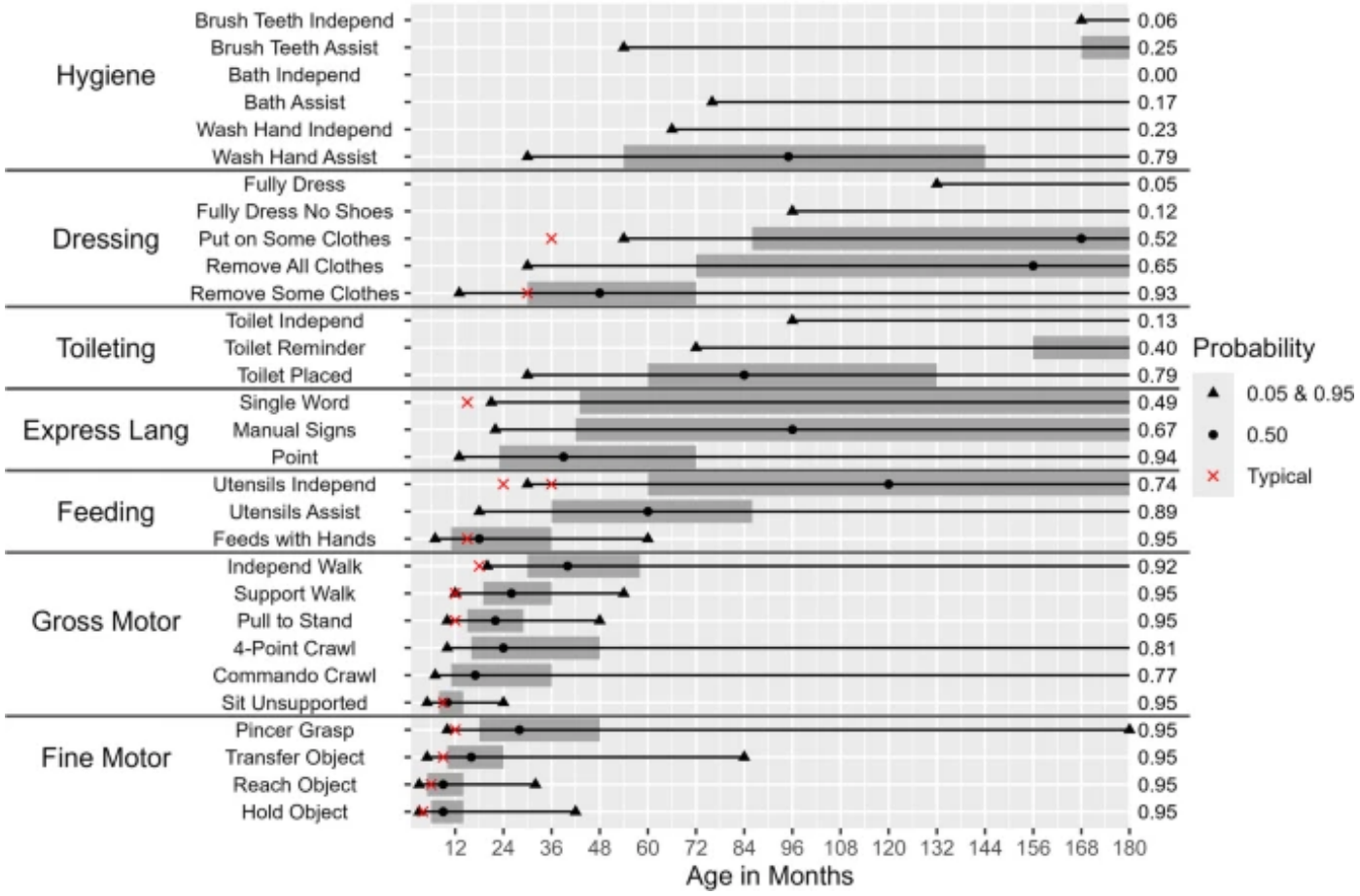
The following five figures display the probability of skill achievement across class I deletion, class II deletion, *UBE3A* mutation, UPD, and ImpD. In these figures, from left to right, the first black triangle represents a probability of 0.05, or a likelihood of 5% that the skill will be achieved by this age. The beginning of the shaded gray bar represents a probability of 0.25, the black circle represents a probability of 0.50, the end of shaded gray bar on the right represents a probability of 0.75. The second black triangle on the right represents a probability of 0.95. The red X indicates the age at which the milestone is achieved by at least 75% children in the general population.

The axis on the right indicates the probability of skill achievement in individuals with AS. This value is either 0.95, or the probability of skill achievement at 15 years of age in cases where the probability did not reach 0.95. For example, the probability that someone with a class I deletion will be able to remove some clothes by 15 years of age is 92%, whereas the probability that they will be able to wash their hands independently is only 13%.

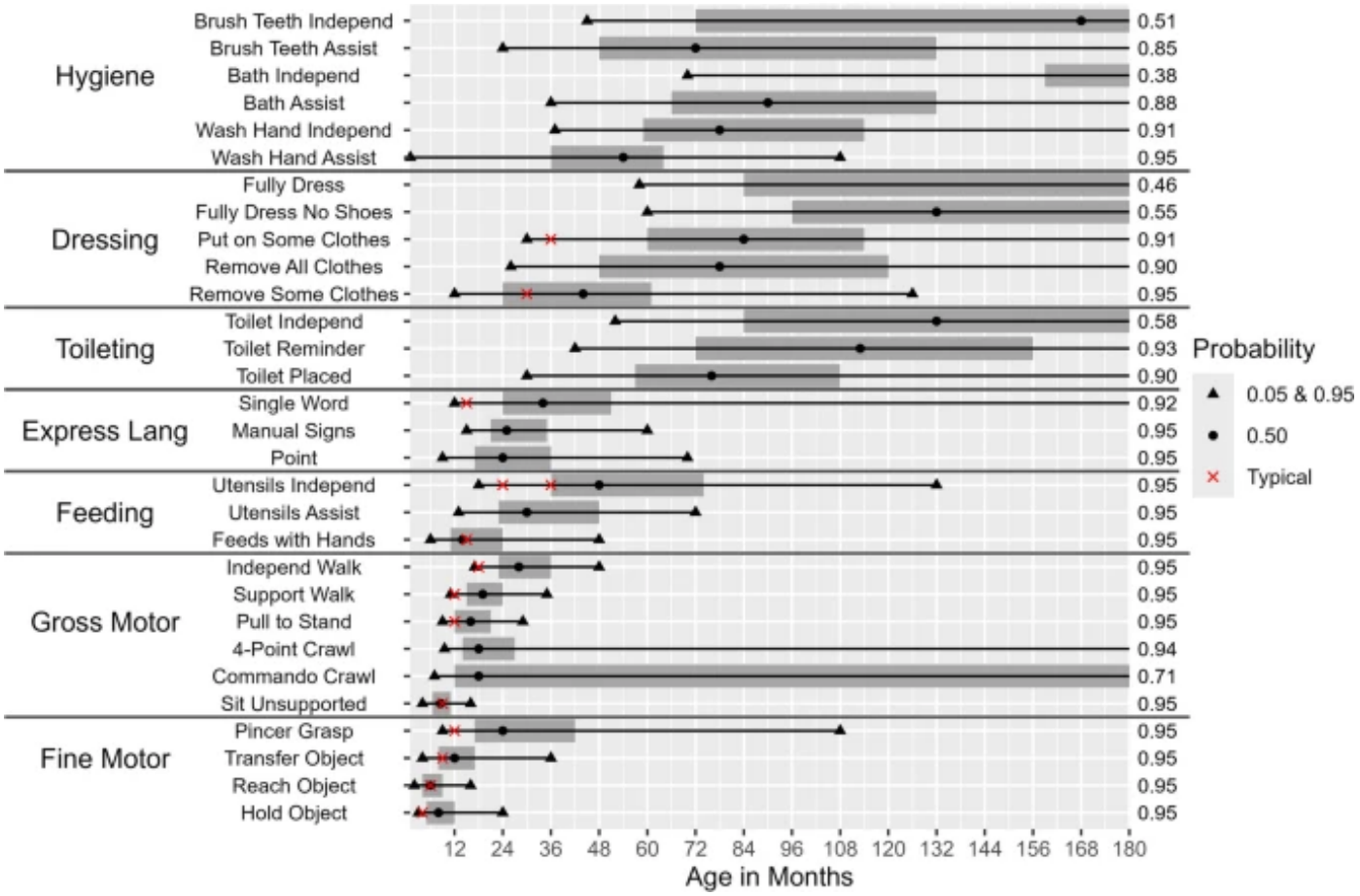
Probability of Skill Achievement in Class I Deletion



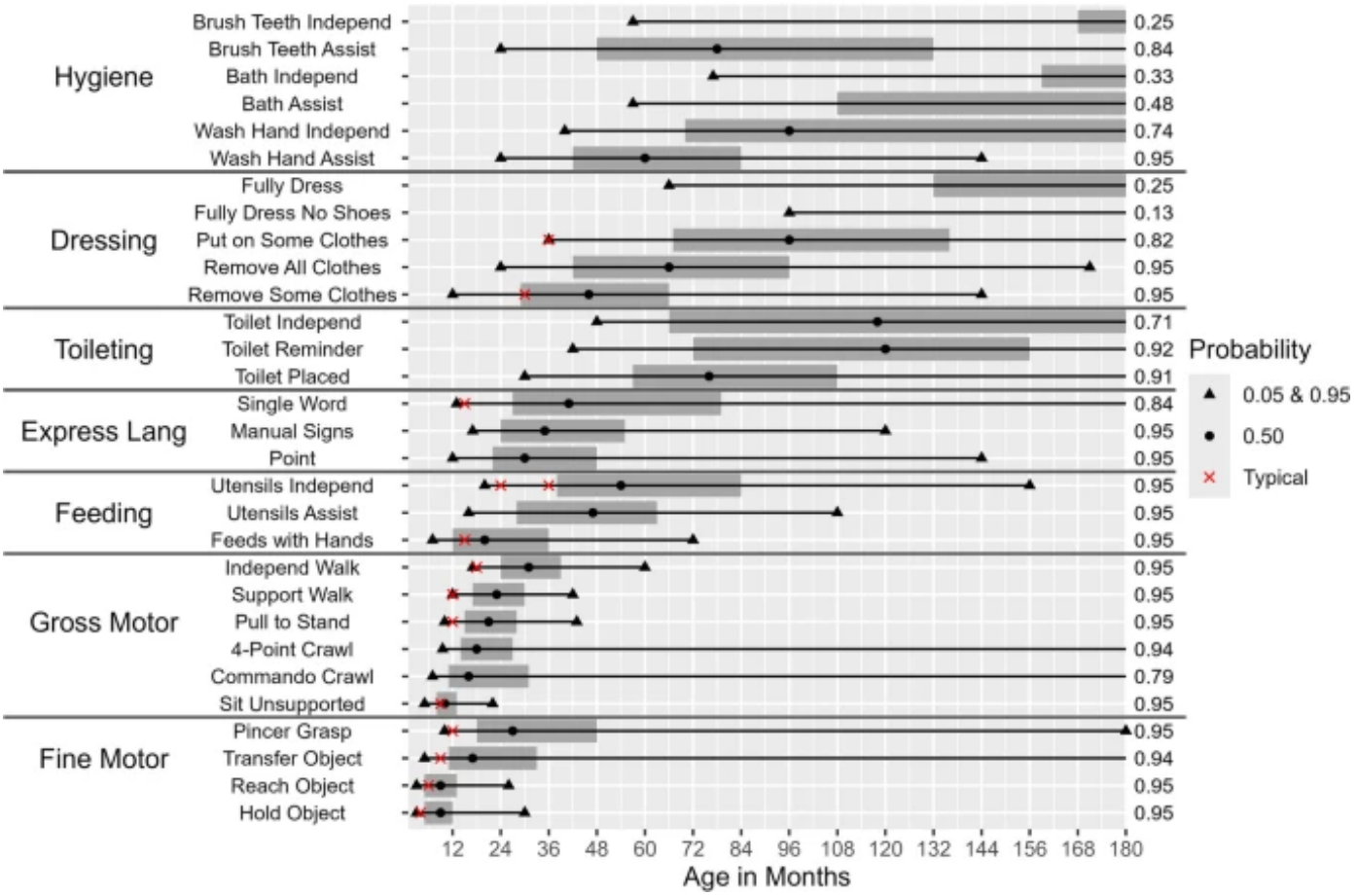
Probability of Skill Achievement in Class II Deletion



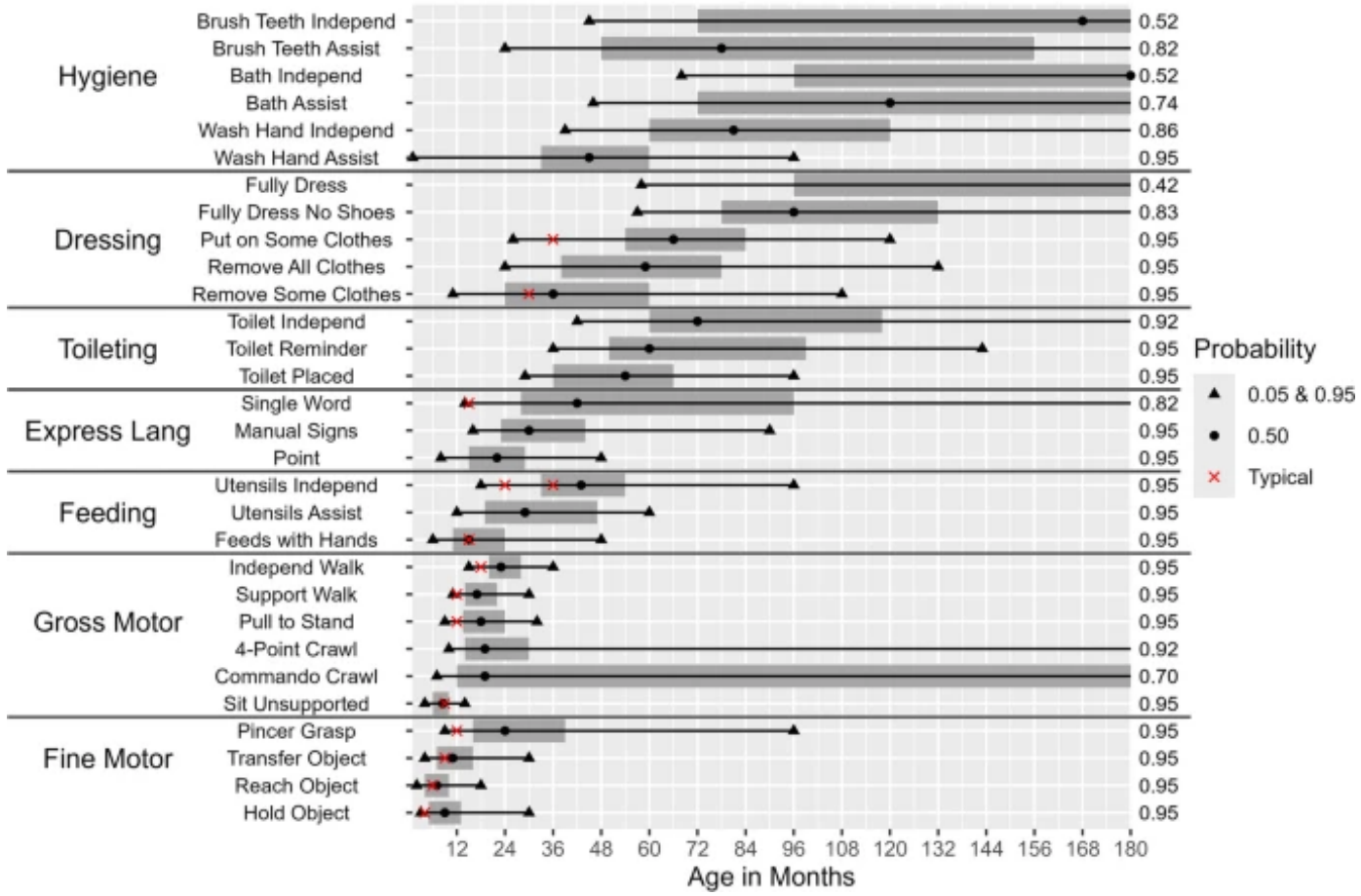
Probability of Skill Achievement in *UBE3A* Mutation



Probability of Skill Achievement in Uniparental Disomy



Probability of Skill Achievement in Imprinting Defect



WHAT DOES THIS MEAN FOR FAMILIES?

Teaching daily living skills from an early age through adulthood is important for individuals with AS to minimize potential caregiver burden. Daily living skills can be taught by breaking a larger task down into smaller, more manageable tasks. The study highlights the importance of including the teaching of daily living skills in Individualized Education Plans for children with AS. Clinicians and families can use the findings of this study to monitor developmental progress and plan interventions.

Full article by Dr. Sadhwani and colleagues:
Read here

Sadhwani A, Powers S, Wheeler A, Miller H, Potter SN, Peters SU, Bacino CA, Skinner SA, Wink LK, Erickson CA, Bird LM, Tan WH. Developmental milestones and daily living skills in individuals with Angelman syndrome. J Neurodev Disord. 2024 Jun 15;16(1):32. doi: 10.1186/s11689-024-09548-7. PMID: 38879552; PMCID: PMC11179294.

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