

# Angelman syndrome phenotype: ages 5-12 yo

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# Pre-Angelman Syndrome Foundation

## 1982: C. Williams, MD

- ▶ 6 cases meeting description of Harry Angelman – 5 were adults
- ▶ One 11 yo girl described with **following features:**
  - episodes of laughter & prominent tongue protrusion
  - “petit mal seizures since age 1.5 yo which have been difficult to control”
  - began walking at age 6 yo
  - said “mamma” at age 9 and no other words
  - “robot-like” gait with marked ataxia
  - lack of arm coordination
  - flat occiput, mandibular prognathism
  - lightly pigmented iris
  - both feet externally rotated
  - mild thoracic scoliosis and lumbar lordosis
  - normal muscle tone and stretch reflexes

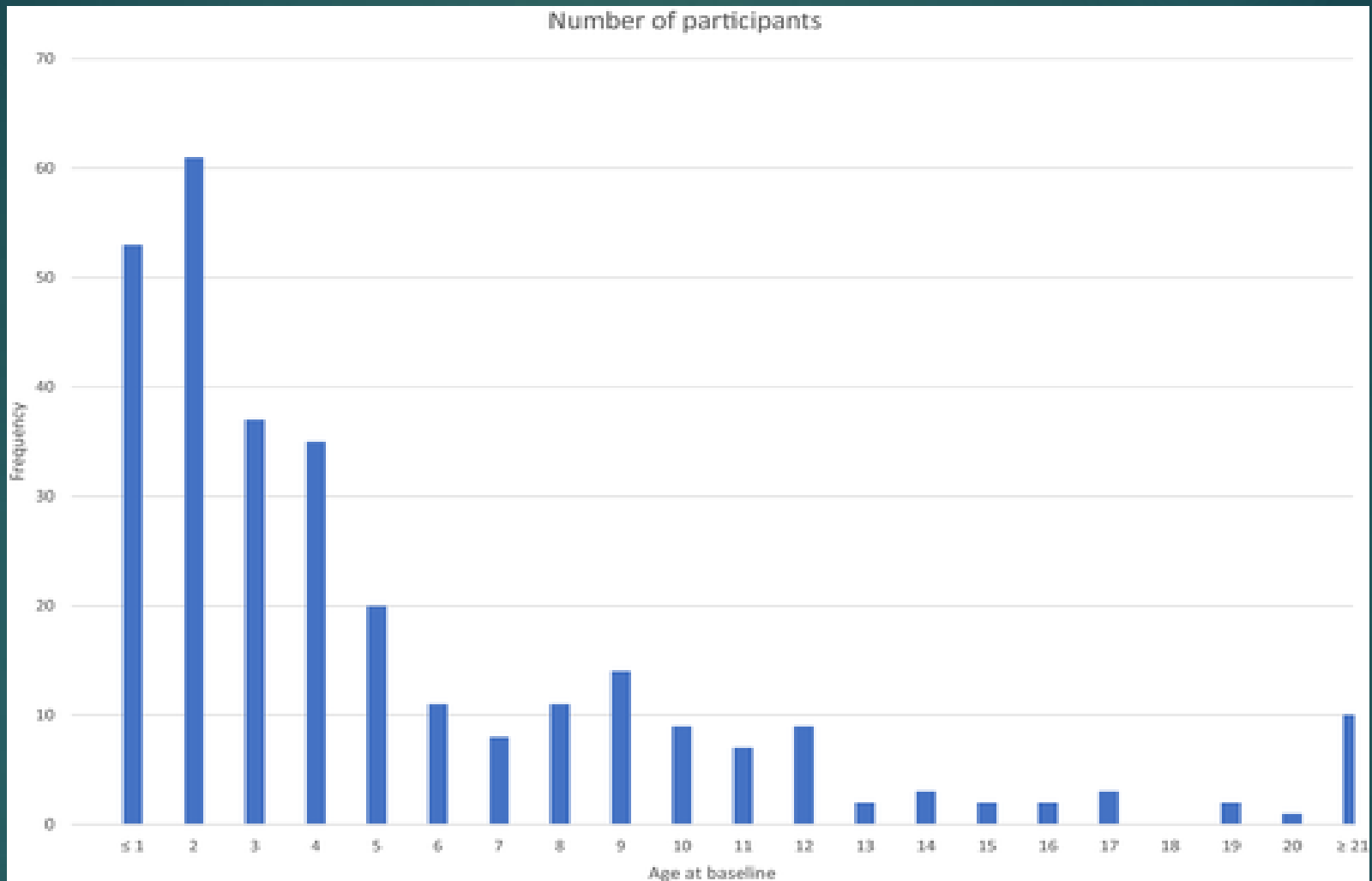
Williams CA & Frias JL Am J Med Gen 1982; 11, 453

# Additional features of **many** children with AS usually present before age 5 and persist

- ▶ Happy smiling demeanor
- ▶ Microcephaly
- ▶ Light hair and skin color (del+)
- ▶ Wide mouth, wide spaced teeth
- ▶ Drooling
- ▶ Mouthing behaviors
- ▶ Strabismus (may be corrected)
- ▶ Uplifted arms esp w/ walking
- ▶ Sensitivity to heat
- ▶ Brisk muscle stretch reflexes at knees/ankles
- ▶ Hyperkinetic behavior
- ▶ Jerky quality to movements
- ▶ Abnormal sleep wake cycles overall reduced total sleep time
- ▶ Attraction to water and “crinkly things”

# What features are prominent in the age group of 5-12 years old?

- ▶ Published descriptions
- ▶ Book: Angelman Syndrome    Bernard Dan, MD
- ▶ Natural history study data gathered
- ▶ Personal experience from seeing numerous patients via NHS, treatment trials, regular neuro clinic in San Diego, and Angelman clinic past 1.5 years
- ▶ Input from parents



# Parent Priorities from unpublished survey in age group 5-12

- ▶ Communication

- ▶ Sleep

- ▶ Seizures

# Growth

- ▶ Height on average is lower than mean but usually within the normal range
- ▶ Head size tends to continue to follow similar curve as present in preschool years
- ▶ Weight – children will often start gaining weight in later school age and obesity an issue often in children with imprinting defect genotype

# Skeletal features

- ▶ Scoliosis can be present in a minority as children advance in age
- ▶ Foot pronation may be more evident



# Gastrointestinal Issues 5-12 yo

- ▶ Common age when constipation problems emerge especially
- ▶ More of an issue for children with limited mobility
- ▶ More of an issue for kids who have preference for “white food”
- ▶ The early life dysphagia and feeding associated irritability often improves
- ▶ Reflux may be present – challenge to diagnose – low threshold for referring to GI especially to rule out Eosinophilic Esophagitis
- ▶ Up to 30% of AS patients may achieve toilet training – often in this time frame

# Sleep problems

- ▶ 30-60% continue to have problems initiating or maintaining sleep
- ▶ Issue may fluctuate – doing well for long stretches then sleep difficulties return
- ▶ Newer info ? Iron deficiency

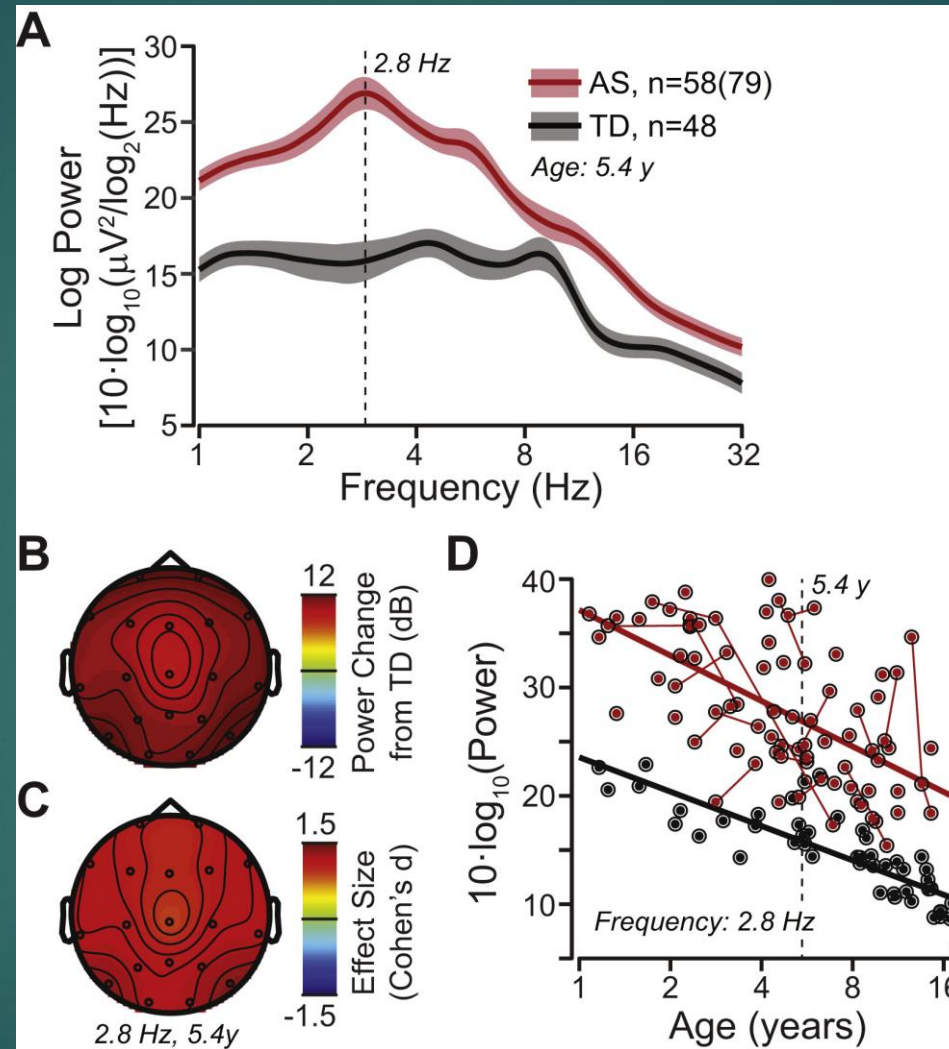
# Communication & Cognition 5-12 yo

- ▶ Couple of consistent words may emerge in a few kids
- ▶ Greater understanding over time of child's gestures by care providers, school personnel who are open and attentive enough
- ▶ This is age range in which it is evident to me that many AS children have remarkable receptive language skills and remarkable abilities to navigate a variety of electronic devices
- ▶ Continued emphasis on enhanced natural gestures as well as recurrent attempts at AAC worthwhile

# Neurological Issues 5-12 yo – Seizures and EEG

- ▶ Traditional literature – seizures often improve as children get into this age group – true for some not true for others
- ▶ Distinction between clinic-based and population-based data
- ▶ Uemura 2005 N= 23: 80% of deletion + pts were seizure free from “childhood to age 30”
- ▶ EEG stated to improve over time but specific data lacking until recently

Figure 2



# Seizures: When can I go off seizure medication? Or off diet therapy?

- ▶ Common criteria for judging success in going off med is 2 yrs seizure free plus normal EEG results in 70% chance of remaining seizure free for 2-3 years
- ▶ Latter criteria not really applicable in kids with AS as EEG almost never is normal
- ▶ Decision best made with face to face discussion with your treating physician
- ▶ For benzodiazepines extremely slow taper needed

# Neurological Issues age 5-12 yo

- ▶ Gait – 10% of AS patients never walk independently; most increasingly stable over time but some may have decline in stability
- ▶ Tremors/myoclonias may become an issue problematic
- ▶ Non-epileptic myoclonus (NEM) rare in this age group – older 11-12 yo when present
- ▶ Dystonia – rarely reported

# Behavior – vignette – age 9

*“he went into the bathroom & when we went to check on him he had squeezed all the shampoo and all of the toothpaste all over the place. It took just two minutes. He seemed to enjoy what he had done”*



# Behavior

- ▶ Hyperactivity and irritability increase over time in children with AS
- ▶ Is it an issue of size and strength making this more problematic?
- ▶ Is it an issue of strong desire for social contact?
- ▶ Is it an issue of needs/desires not being able to be communicated?
- ▶ Is it an expression of anxiety?

# Some parent reported changes 5-12 yo

- ▶ “Gagging began – thought was reflux – learned years later was behavioral”
- ▶ Constipation worsened
- ▶ Developed some compulsive repetitive behaviors not present before
- ▶ Walking did not change much
- ▶ “Sleep a little worse” but we’re used to it now
- ▶ “Was toilet trained age 6”
- ▶ “Constipation improved”
- ▶ “Improved initiation of social contact”
- ▶ “Improved gestural communication and increased interest in communication”
- ▶ “More interested in looking at picture books with me”
- ▶ “More aware of other kids near her”
- ▶ “Sleep a little better now that we found a good medicine”