The role of computer-aided facial recognition technology in accelerating the identification of Angelman syndrome

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Angelman syndrome (AS) is characterized by severe intellectual disability, seizures, absent or severely limited speech, and a distinctive behavioral profile which includes easily provoked laughter, reduced need for sleep, and mouthing of objects. There is subtle facial dysmorphism (midface recession, prognathism, broad mouth, thin upper lip vermilion and deeply set eyes) that can be appreciated in the AS adolescent and adult, but the young child with AS is usually non-dysmorphic. While early diagnosis may improve prognosis through early provision of appropriate interventions, such as alternative communication strategies, the average age of AS diagnosis is 2½ years. The diagnosis is often delayed, specifically in individuals who lack microcephaly, seizures, or the characteristic behavioral profile.

We previously showed http://www.ashg.org/2013meeting/abstracts/fulltext/f130121627.htm that a computer-aided facial analysis technology (developed by FDNA, Inc.) is highly accurate in distinguishing individuals with AS from controls (both normal individuals and those with other syndromes) when applied to a large population with diverse ages. In this study, we evaluate how such technology performs separately for distinct age groups, and whether FDNA technology can assist in recognizing the AS phenotype in infants less than 2 years of age.

We divided the previous data set comprising 210 facial images of individuals with molecularly proven AS, 520 images of normal controls, and 808 images of individuals with other syndromes into 3 distinct age groups: (i) 2-4 years, (ii) 4-6 years, and (iii) 6-8 years. We added a fourth group, comprising a set of 50 images of children less than 2 years of age, including 15 children with AS, 15 normal children and 20 children with other syndromes.

Our results demonstrate the "strength" of the computer-aided technology in discerning AS from other control groups at different age groups and suggest that this technology may be implemented in clinical settings to assist clinicians in recognizing AS at younger ages. These results also support new insights into the progression of the AS phenotype over time.

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Disclosure

- No financial interest
- FDNA facial recognition software not FDA approved
- Co-author Wolf = co-founder of FDNA

Angelman syndrome

- Functionally severe intellectual disability
- Seizures, abnl EEG
- Microcephaly
- Absent/minimal speech, movement disorder
- Characteristic behavioral profile
  - Easily provoked laughter
  - Mouthing behaviors
  - Sleep disturbance
  - Fascination with water, plastic

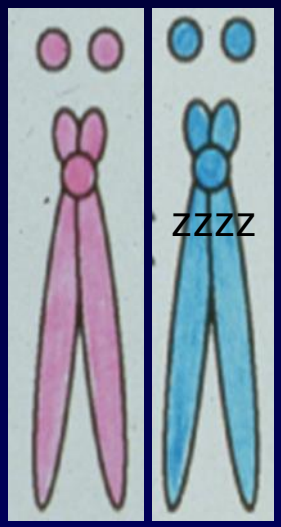
Angelman syndrome

- Young child with AS is usually non-dysmorphic

- Facial dysmorphism in adolescent
  - midface recession
  - prognathism
  - broad mouth
  - deeply set eyes
  - thin upper lip vermilion

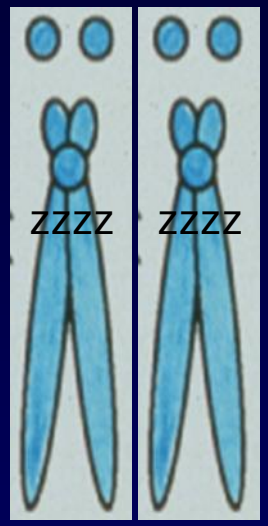
UBE3A deficiency

normal



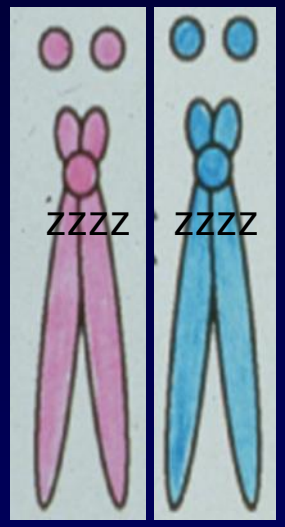
deletion

70-75%



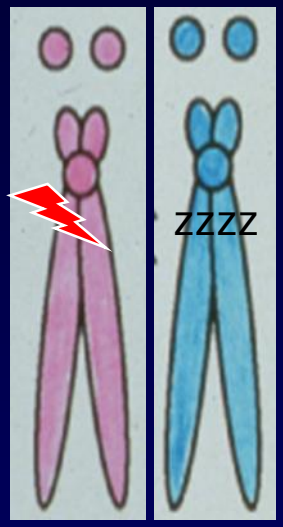
paternal disomy

5-10%



Imprinting defect

5-10%



UBE3A mutation

10-15%

Angelman syndrome

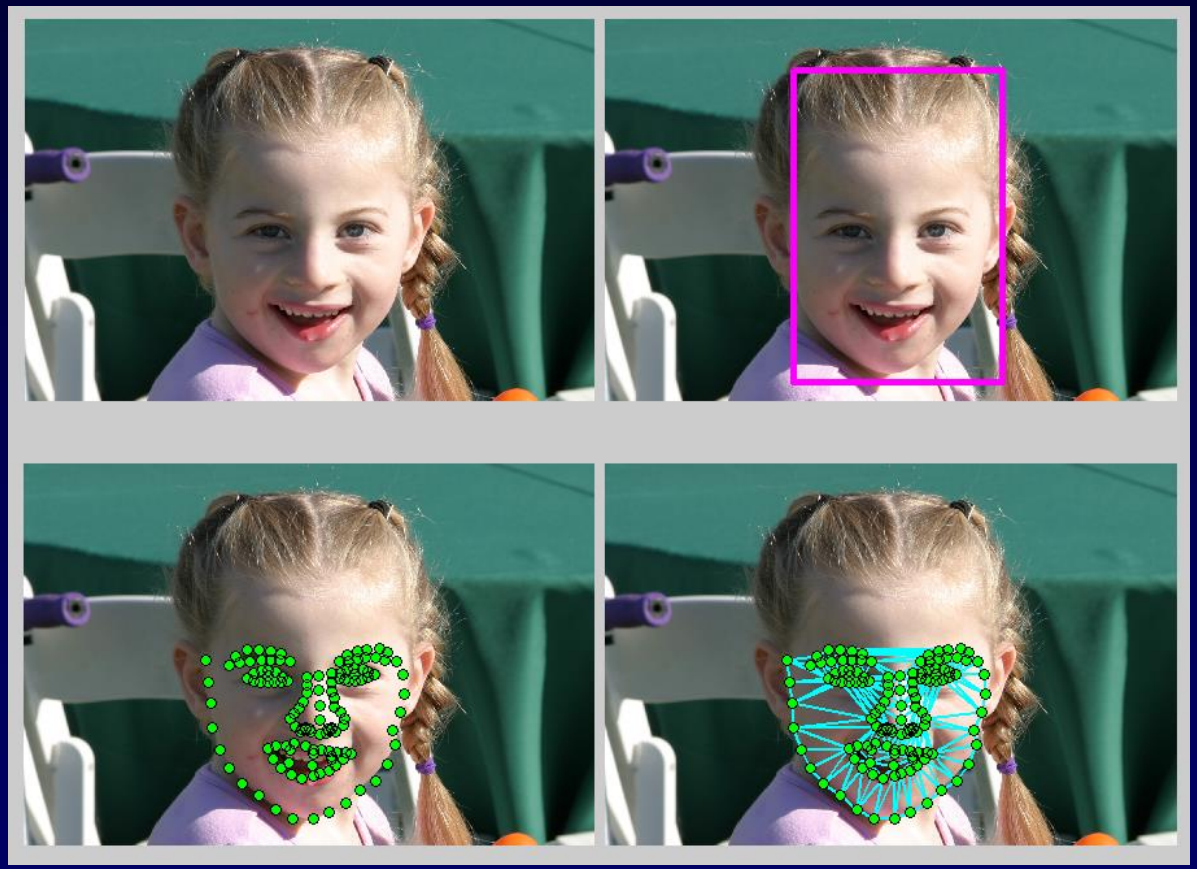
- Natural History study
  - Annual visits
    - clinical, neuropsych, socio-economic, EEG, behavior, other data
  - Photographs

Age at Diagnosis

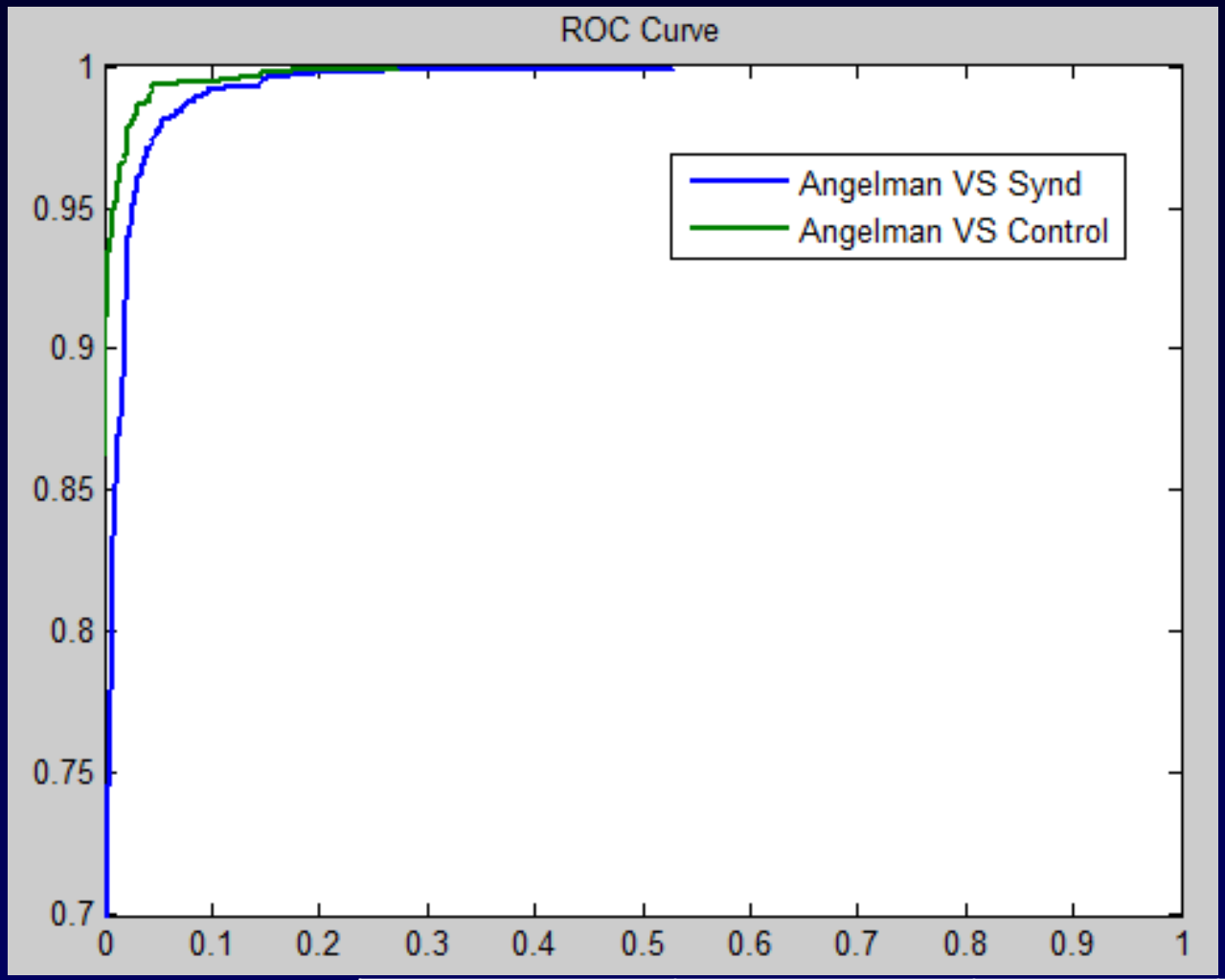
Molecular Class	Number	Age
All types	300	30 months
Deletion	210	25 months
Non-deletion	86	41 months
UPD	29	35 months
UBE3A	32	40 months
Imprinting defect	22	49 months

Age range	Number	% deletion
0-12 months	55	96%
13-24 months	128	78%
25-36 months	53	57%
37-48 months	18	39%
>48 months	38	42%

Image Analysis



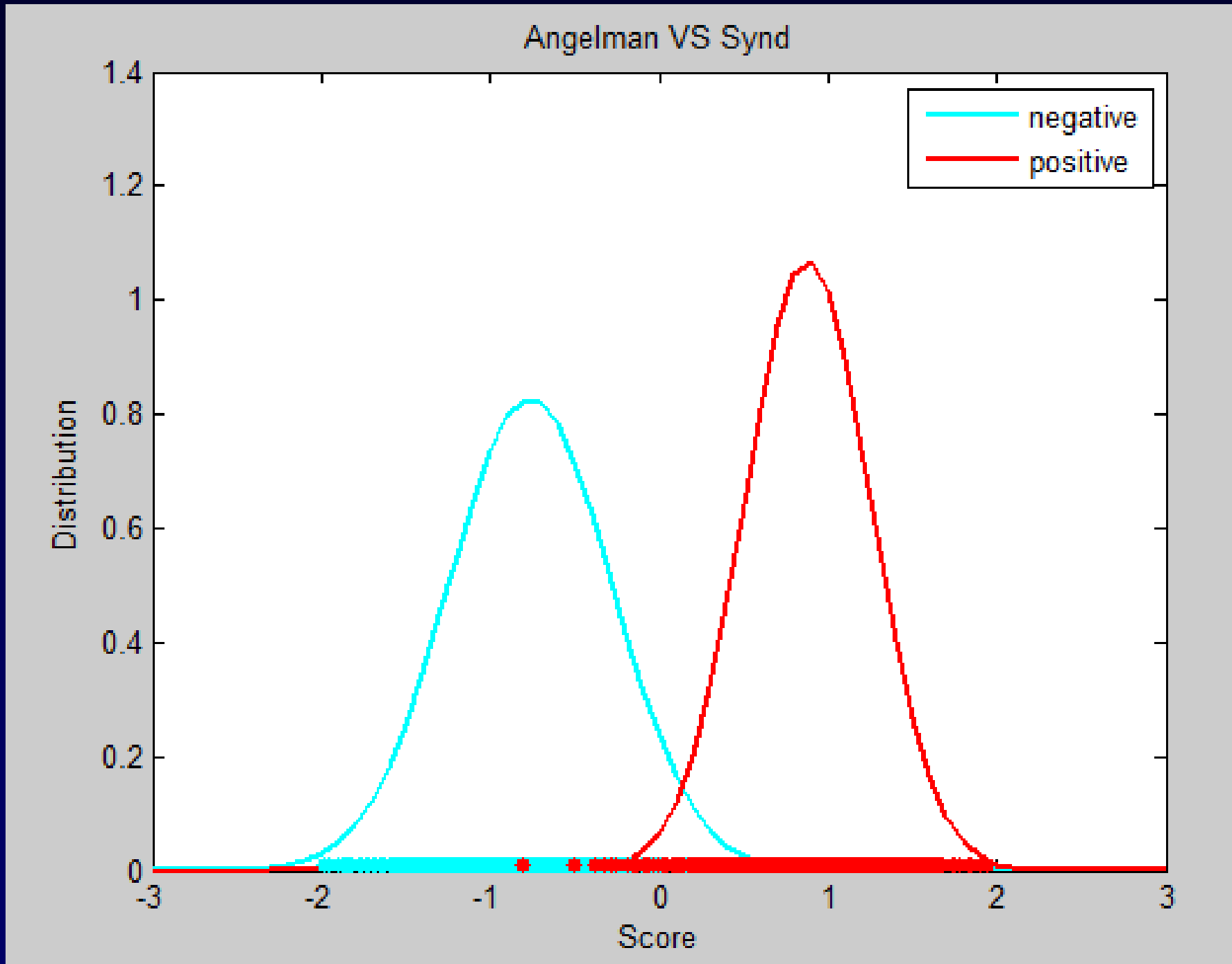
FDNA
Accessible Genetics



Other syndromes n=780

Controls n=550

Compared to Other Syndromes	Area Under Curve	Equal Error Rate	Sensitivity at 95% specificity	Specificity at 99% sensitivity
All AS	99.2%	3.3%	97.6%	90.8%
Del+	99.2%	3.9%	97.0%	89.0%
UPD	99.1%	2.7%	95.6%	92.1%
Imprinting	**99.4%**	**1.7%**	**99.1%**	**95.3%**
UBE3A	99.1%	2.8%	98.4%	93.9%


Angelman VS Synd
negative
positive
Distribution
Score
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-3
-2
-1
0
1
2
3

Accuracy re: molecular type

Compared to other syndromes	Area Under Curve	Equal Error Rate	Sensitivity at 95% specificity	Specificity at 99% sensitivity
All AS	99.2%	3.3%	97.6%	90.8%
AS Del+	99.2%	3.9%	97.0%	89.0%
UPD	99.1%	2.7%	95.6%	92.1%
Imprinting	**99.4%**	**1.7%**	**99.1%**	**95.3%**
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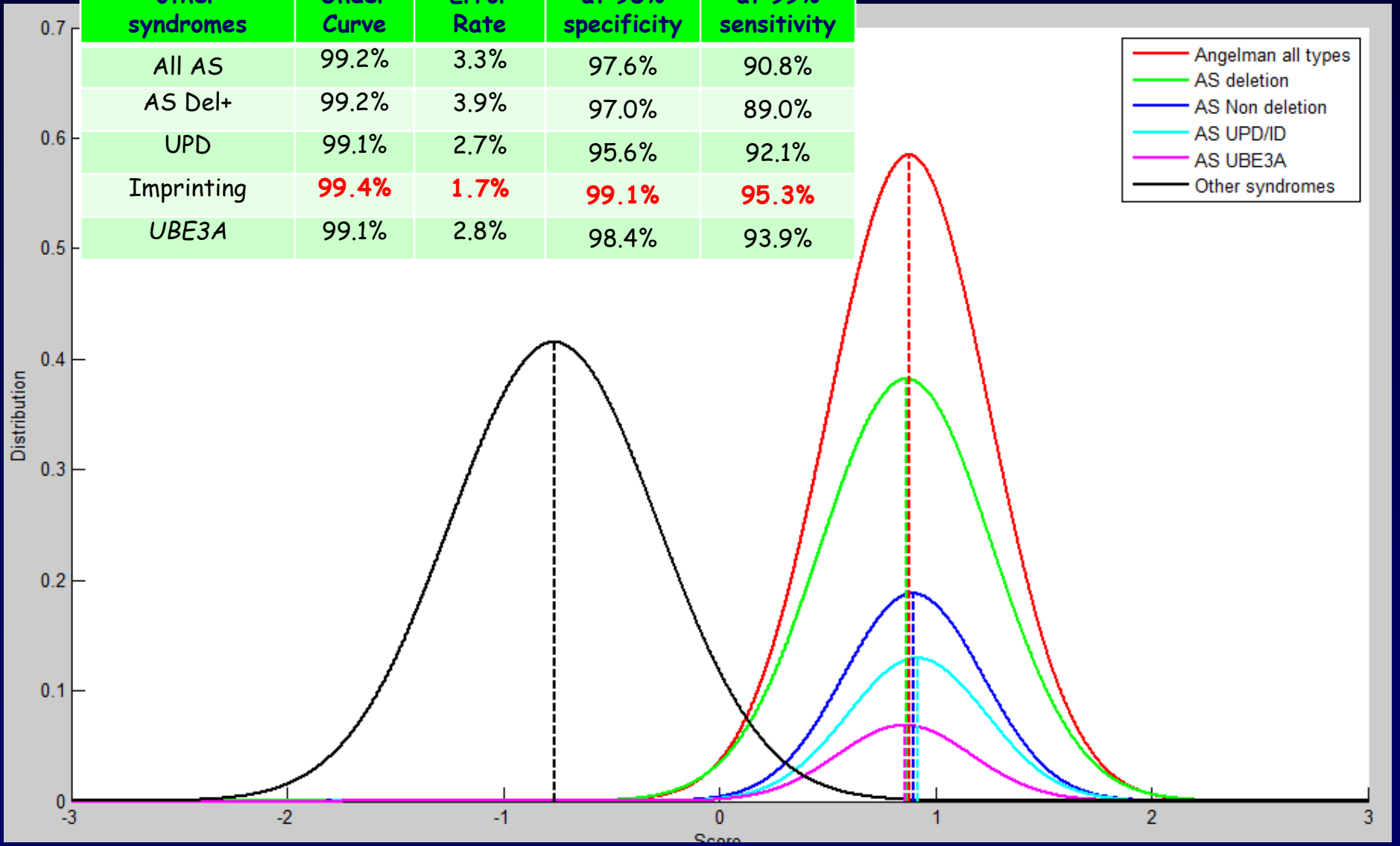
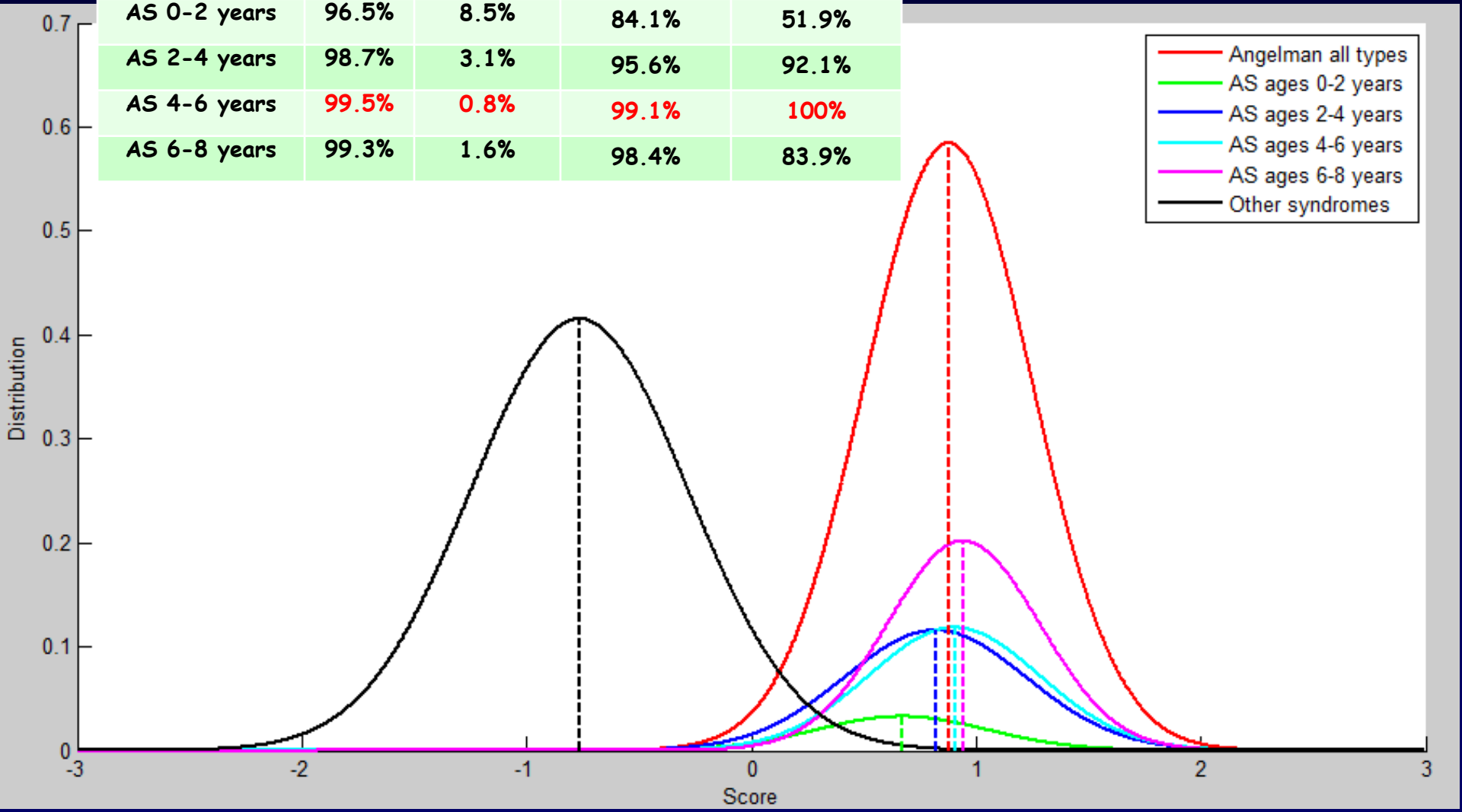


Accuracy re: age

Compared with other syndromes	Area Under Curve	Equal Error Rate	Sensitivity at 95% specificity	Specificity at 99% sensitivity
AS all ages	99.3%	2.2%	95.5%	86.9%
AS 0-2 years	96.5%	8.5%	84.1%	51.9%
AS 2-4 years	98.7%	3.1%	95.6%	92.1%
AS 4-6 years	99.5%	0.8%	99.1%	100%
AS 6-8 years	99.3%	1.6%	98.4%	83.9%



Sample heat maps

Conclusions

- FDNA technology is able to discriminate reliably between Angelman syndrome and other syndromes, regardless of molecular subclass

- The accuracy of FDNA technology in discriminating Angelman syndrome from other syndromes improves with the age of the individual through early childhood.

Contributors

- Baylor/Texas Childrens
- Boston Children's Hospital
- Cincinnati Children's
- Greenwood Genetic Center
- Vanderbilt
- UCSD/Rady Children's Hospital San Diego

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and Angelman families.