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The Teenage Years: Angelman Syndrome

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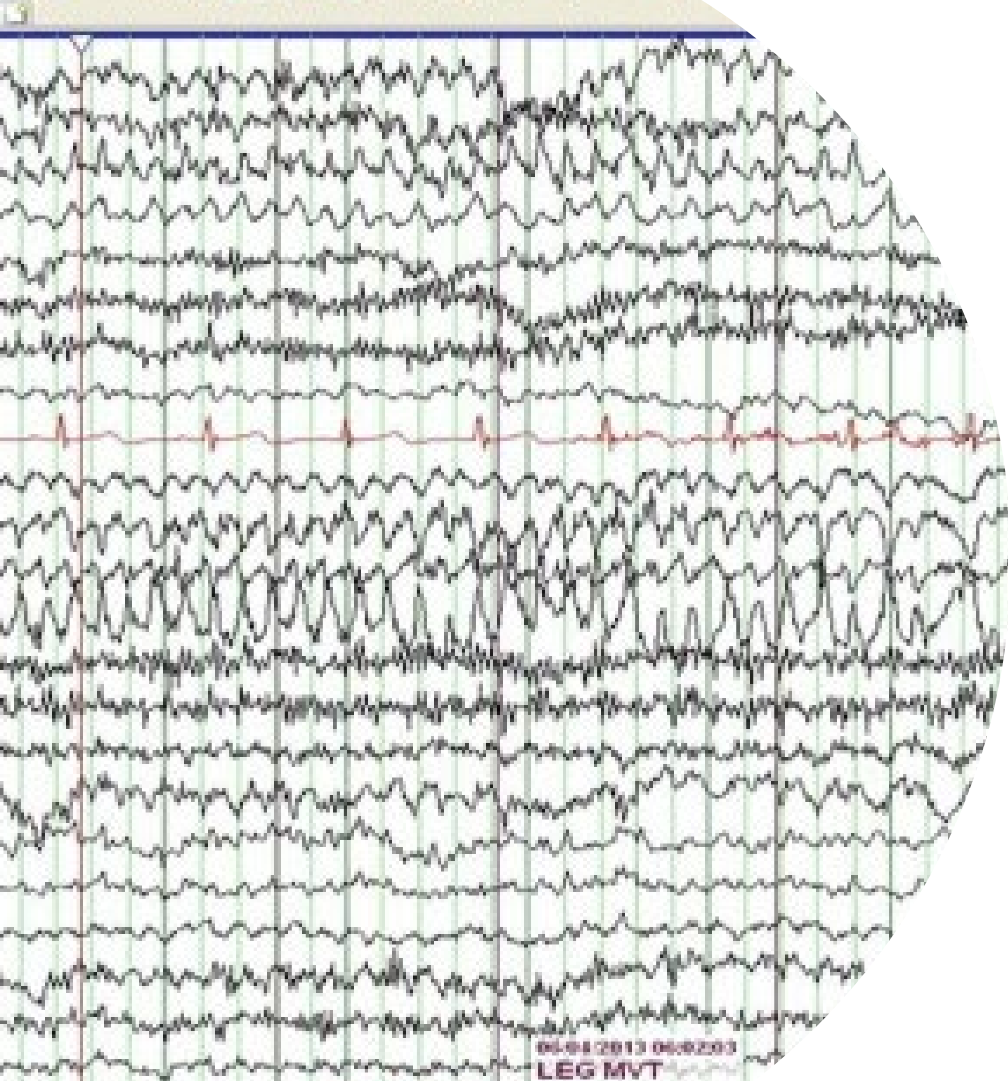
Concerns in the teenage years

1. Puberty
2. Anxiety
3. Behaviors
4. Non-epileptic myoclonus
5. Mobility
6. Transition of care



Considerations Around Puberty

- Seizures can come after a long period of stability and be difficult to treat
- New movement disorders can start
- New behaviors can start sometimes more related to environmental changes rather than body changes
- Lots of considerations regarding hormonal therapies
  - IUD
  - Implanon
  - Depoprovera
  - Oral contraceptives

Common Behavioral Challenges Presenting in the Clinic

1. Sensory seeking
2. ADHD
3. Aggression
4. Anxiety

Behavior	Deletion % (N=211)	UPD / ImpD % (N=56)	UBE3A % (N=33)	Difference in genotypes
Mouthing behaviors	92	89	70	0.002
Short attention span	89	88	73	0.069
Hyperactivity	69	59	55	0.155
Aggressive behavior				
Overall	51	84	70	<.001
Biting	27	45	49	0.012
Hair pulling	44	55	36	0.161
Pinching	23	43	27	0.025
Anxiety	19	45	36	<.001

Sadhwani et al., 2019

Changes in Problem behaviors over time

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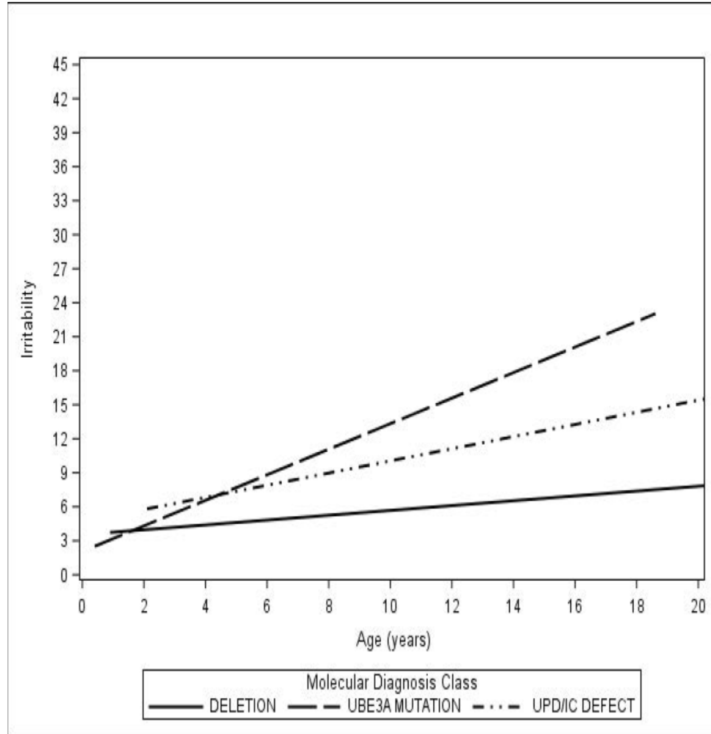
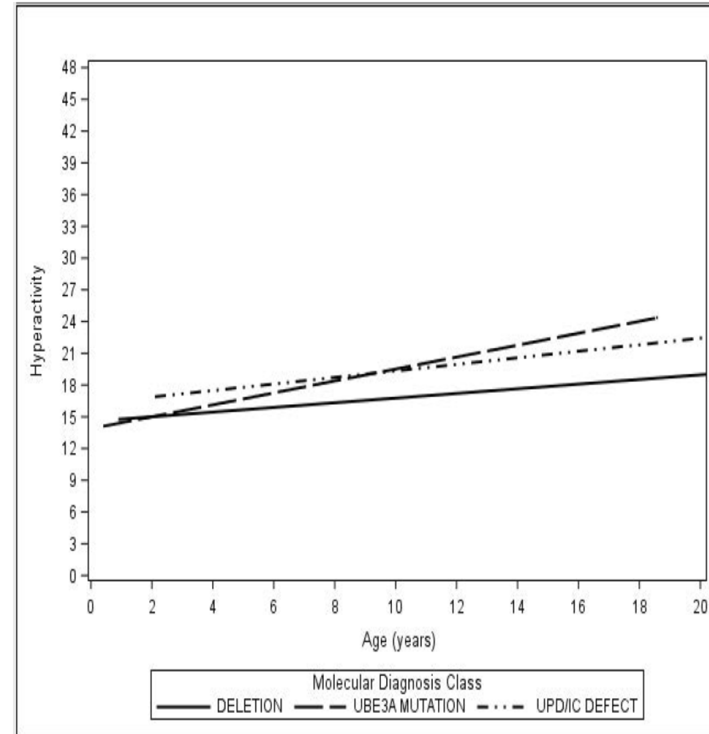
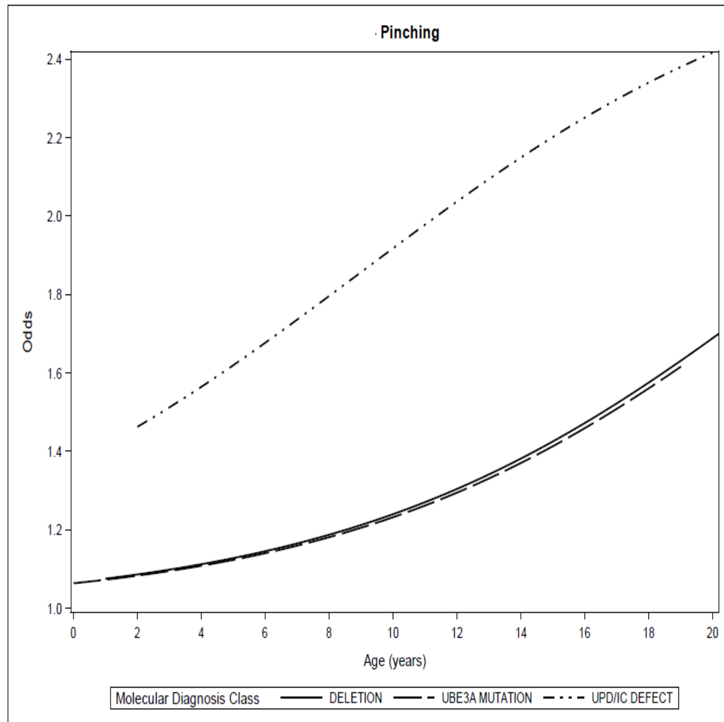
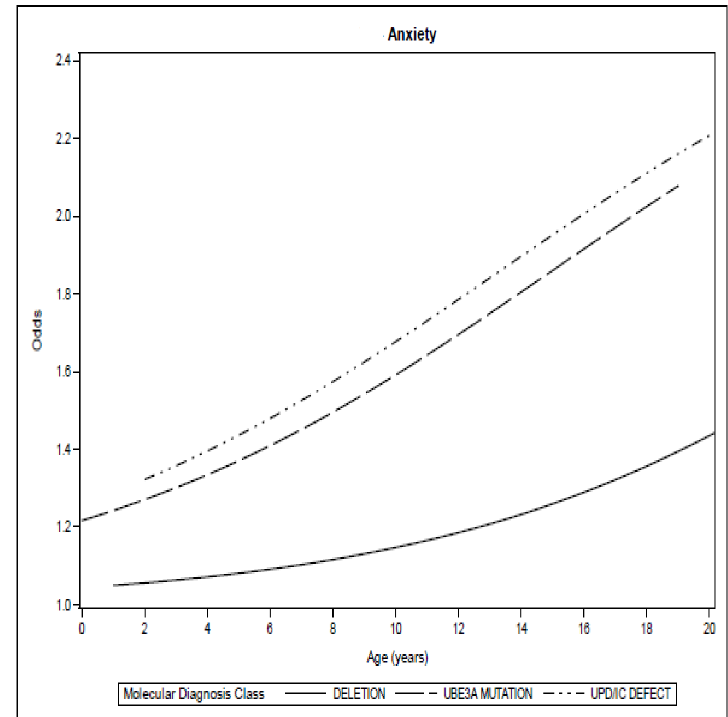




Sadhwani et al., 2019





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Anxiety Concerns by Subtype

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100%
80%
60%
40%
20%
0%

UPD
UBE3A
Deletion
Other

Anxiety…
Caregive…
Agitation…
Agitation…
Agitation…
Caregive…

Findings of Anxiety in AS are atypical

1. Aggression (e.g. biting, hitting, hair pulling)
2. Shutting down
3. Challenges around transition, rigidity, insistence on sameness (particularly a preferred caretaker)
4. Gagging, vomiting, other somatic manifestations including tremor
5. Change in sleep patterns

Case 1

14 year old deletion + male with recent increases in aggression including biting and hitting, awakening at night screaming, worsening constipation, and gagging particularly when parents take him to restaurants or events with a lot of noise or people.

Purpose of Disruptive Behaviors

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Purpose of Disruptive Behaviors

Purpose	Percentage
Attention Seeking	45.7
Avoidance	22.3
Communication	57.4
Craving Sensory Input	30.5

Data from ongoing FDA Natural History Study

What triggers the behavior?

1. Changes in his caretakers
2. Transitions in the school or home setting
3. Attention seeking

Treatment

- Behavioral interventions – functional behavioral assessment at school, routine, reward (especially attention) for positive behaviors, ignoring negative behavior as long as safe, visual prompts/schedules
- Applied behavioral analysis
- Consistency of para professional, training on AS
- Treatment for anxiety
- Communication support

Consider medical concerns such as GI issues (GERD), pain, dental problems, allergies, medications, school routine, new aides, transitions, etc.

Hyperactivity

- Behavioral intervention: routine, visual schedules, use of timers, reinforcement of positive behaviors with rewards
- Behavioral/Occupational therapy interventions
- Medication trial tier 1: clonidine, guanfacine, atomoxetine, stimulant, amitriptyline, SSRI
- Medication trial tier 2: Antipsychotics (e.g., risperdal)

Anxiety

- Rule out causes, may be helpful to ask for a functional behavioral assessment in school, visual schedules, timers, keep a diary to note when this is occurring
- Therapy interventions (Speech/AAC; OT, behavioral)
- Amantadine
  SSRI (start very low dose)
- Consider clonidine or guanfacine
- Consider Lamictal or clobazam, cannabidiol
- Atypical antipsychotic
  Prochlorperazine

Sensory Seeking

- Keep a diary of when this is occurring, may be related to anxiety. Consider substitutions such as chewys, vibrating toys
- Occupational/behavioral therapy
- Trial of treatment of drooling (e.g. scopolamine patch), amantadine, SSRIs

Aggression

- Functional behavioral assessment at school, new caretakers, transition difficulties, keep diary of events and circumstances
- Behavioral therapy/Speech/AAC
- Treat underlying cause, amantadine, clonidine/guanfacine, SSRI could help with irritability such as trazodone
- Atypical antipsychotic, AED (Lamictal, clobazam)

Repetitive behaviors

- Behavioral Therapy
  Occupational therapy

Case 2

12 year old female with deletion + AS who presents with persistent episodes of shaking that starts on one side of the body and progressed to her whole body and can last for up to 1 hour. Mother notes she is leaning over a lot, walks with her knees bent and has more behaviors including biting and pulling hair. She recently started her menses. She awakens multiple times at night.

Important Considerations

1. Possible resurfacing of seizures around puberty
2. Change in mobility including a flexed knee gait pattern
3. Onset of non-epileptic myoclonus around the time of puberty
4. Behaviors may be an expression of other underlying concerns

Treatment

- Hormonal regulation – treatment with oral contraceptive or hormone secreting IUD
- Work up to rule out seizures may be appropriate
- Focus on treatment of underlying etiology ultimately will help NEM
- Evaluation for scoliosis, gait study to understand changes in mobility
- Therapy intervention with PT
- Behavioral therapy to co-treat with other specialists
- OT for sensory integration therapy
- AAC support and integration in all environments – increase choices
- Most often spasticity is not present and Botox can make things worse
- Treatment of underlying sleep concerns