# Neurobehavioral Approaches to Maximize Health and Behavioral Functioning in Individuals with Angelman Syndrome: Lessons Learned (Part II)

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# What you will learn about today

- Range of factors that are associated with physical and behavioral concerns in individuals with AS
- How knowledge about these factors can be used to improve physical and emotional health and reduce challenging behavior in individuals with AS

# About Us

- Jane Summers, PhD (psychologist), Toronto
- Erick Sell, MD (neurologist), CHEO in Ottawa
- Melissa Carter, MD (clinical geneticist, developmental pediatrician), CHEO in Ottawa
- Mutual interest in seeing people with AS
- Neurology + behavior = Neurobehavioral approach
- Clinical aims:
  - Improve physical and emotional health, reduce occurrence of challenging behaviour
  - Enable individual with AS to reach full potential, maximize quality of life

# Information sources for presentation

- Health Watch Table for Individuals with AS (AS-HWT)
- Clinic in Ottawa
- On-line Behavior Modules
- Recent literature on AS

**Health Watch Table — Angelman Syndrome (AS)**
*Forster-Gibson, Berg and Korossy 2015*

# AS Health Watch Table (AS-HWT)

- Developed in 2015 by Cynthia Forster-Gibson, Joseph Berg and Marika Korossy
- Purpose is to provide anticipatory guidance for health/mental health concerns, monitor health/mental health needs across all ages/stages
- Reviews physical and behavioral/mental health issues and provides recommendation or guidance for how to manage them

**www.surreyplace.on.ca/documents/Primary%20Care/HWT-AS10Sep2015.pdf**

**Health Watch Table — Angelman Syndrome (AS)**
*Forster-Gibson, Berg and Korossy 2015*

# Areas covered in AS-HWT*

* We have added our own information in italics

- Genetics
- Neurology
- Musculoskeletal
- HEENT (Head, Eyes, Ears, Nose, Throat)
- Gastrointestinal
- Dental
- Endocrine & Sexuality
- **Mental health/behavioral**

**(includes sleep and communication)**

* ***Toileting***
* **Safety**
* ***Pain/discomfort***
* ***Family support needs***

# Ottawa Clinic: Behavior & Skills Assessment

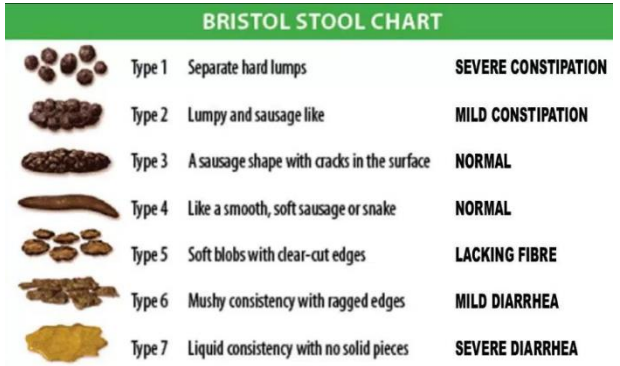
- Service history
- Behavior/mental health issues
- Safety concerns
- Presence of challenging behavior, related factors
- Skill building approaches
- Parents' needs for support and information

# Toileting

# *Toileting*

- *Daytime bladder incontinence and nocturnal enuresis are common, more so in younger children and those with seizures. Incontinence can lead to physical discomfort, UTIs, dependence on caregivers and expense. Hesitancy, straining and interrupted stream have been found. Bladder may not be emptied entirely. Constipation may occur and be associated with mobility impairment, side effects of anti-convulsant medication.*

# *Toileting* (continued)




*<u>RECOMMENDATIONS</u>: Toilet training programs can help with urinary continence and reduce accidents. Relaxed state on the toilet may make voiding easier. Reward for fully emptying bladder. For constipation, increase exercise, fibre and fluid; upright position on toilet, establish consistent habit time when defecation is likely. Track frequency, size and consistency of bowel movements if needed.*

# What we have learned

## Lessons

- Many taken to toilet on schedule
- Constipation is common
- More are urine trained than bowel trained

## Implications

- Constipation can be associated with pain and discomfort, can affect skills and functioning
- Lack of toilet skills can increase burden of care, expense

# Case example: Lindsay – Severe constipation

Lindsay is a 20-year-old female with AS, del+. She has a seizure disorder and takes 4 anti-convulsant medications daily. She has reflux and doesn't like to drink fluids. Lindsay is mobile and walks independently. She is time trained and will stay dry between trips to the bathroom.

Lindsay has a history of constipation. She was taken to the hospital 3 times in the past year in relation to constipation/bowel impaction. She was seen by a GI who was concerned about an expanded colon.

# Lindsay (continued)

Lindsay's mother noticed her abdomen becomes very bloated, her food consumption drops and her cognitive skills decline when she is constipated.

Lindsay is now taking Metamucil, mineral oil, restoralax, prune juice and prunes to prevent constipation. Her mother tries to get her to drink several glasses of water daily and maintain a regular exercise routine.

# Pain and Discomfort

# *Pain and Discomfort*


*Pain and discomfort can present as distress, sleep disturbance or behavioral changes, such as an increase in aggression or irritability. Facial expression and vocalizations can change.*

RECOMMENDATIONS:

*Investigate and treat possible physical cause (GERD, headache, toothache, sore foot, uncomfortable clothing, etc.). Look for and address environmental factors (too loud, too hot/cold, too crowded).*

# What we have learned

## Lessons

- Many lack concept of danger
- Some have swallowed hazardous items or choked
- Many show signs of pain

## Implications

- Safety proofing and supervision
- Look for changes in typical behavior
- Failure to cry doesn’t mean there isn’t a problem

# Non-Communicating Children's Pain Checklist

(NCCPC; Breau et al., 2002)

- **Vocal** (moaning, whining, whimpering, crying, screaming)
- **Eating/sleeping** (eating less, increase or decrease in sleep)
- **Social** (cranky, irritable, less interaction, seeking comfort or contact)
- **Facial** (furrowed brow, not smiling, lips tight or puckered, clenching or grinding teeth, chewing)
- **Activity** (not moving, less active, agitated, fidgety)
- **Body/limb** (floppy, stiff, gesture to part of body that hurts, flinch or move body part away)

# Sleep

**Health Watch Table — Angelman Syndrome (AS)**
*Forster-Gibson, Berg and Korossy 2015*

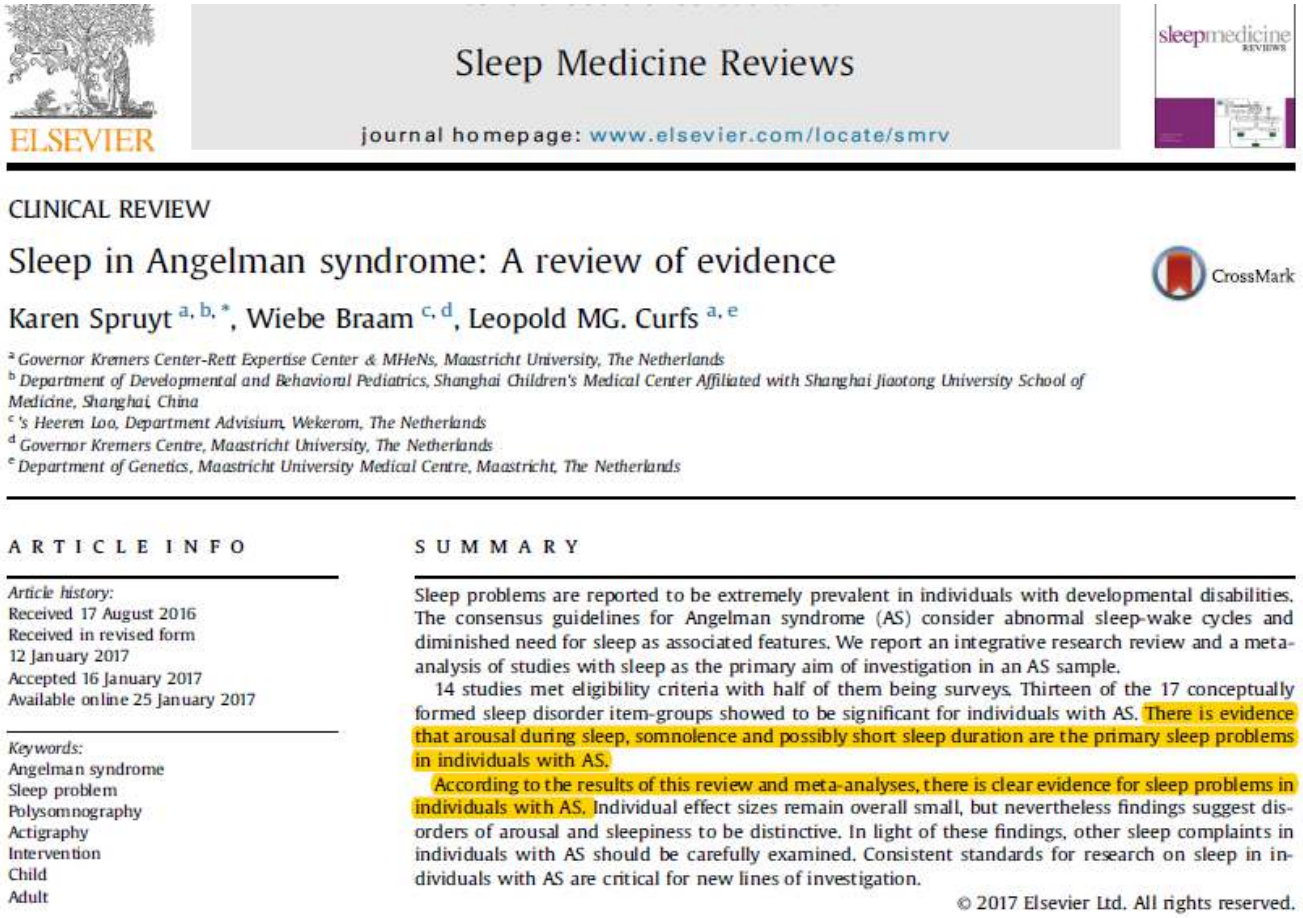
# Sleep Disturbance

*High rates of sleep problems. Problems include decreased need for sleep, abnormal sleep-wake cycle, difficulties falling asleep or remaining asleep, reduced total sleep time, disruptive bedtime behaviors. Problems can have a significant impact on family functioning. Sleep is most affected in infancy and middle childhood and tends to improve in adolescence and adulthood.*

RECOMMENDATIONS:

Implement consistent nighttime routine; *modify sleep environment;* consider trial of melatonin; possible referral to sleep specialist or clinic. *Consider referral to behavioral specialist to assess parent-child interactions. Sleep apnea may be an issue but can be difficult to diagnose and treat. Removal of tonsils/adenoids, weight loss may help.*

# Meta-analysis of sleep studies



Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

## Sleep in Angelman syndrome: A review of evidence

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SUMMARY

Sleep problems are reported to be extremely prevalent in individuals with developmental disabilities. The consensus guidelines for Angelman syndrome (AS) consider abnormal sleep-wake cycles and diminished need for sleep as associated features. We report an integrative research review and a meta-analysis of studies with sleep as the primary aim of investigation in an AS sample.

14 studies met eligibility criteria with half of them being surveys. Thirteen of the 17 conceptually formed sleep disorder item-groups showed to be significant for individuals with AS. There is evidence that arousal during sleep, somnolence and possibly short sleep duration are the primary sleep problems in individuals with AS.

According to the results of this review and meta-analyses, there is clear evidence for sleep problems in individuals with AS. Individual effect sizes remain overall small, but nevertheless findings suggest disorders of arousal and sleepiness to be distinctive. In light of these findings, other sleep complaints in individuals with AS should be carefully examined. Consistent standards for research on sleep in individuals with AS are critical for new lines of investigation.

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**Key Findings:**

- Problems with short sleep duration, length of time taken to fall asleep, awakening during the night and poor sleep efficiency were found from reviewing the literature

# Health concerns and sleep problems

RESEARCH Open Access

## A cross-syndrome cohort comparison of sleep disturbance in children with Smith-Magenis syndrome, Angelman syndrome, autism spectrum disorder and tuberous sclerosis complex

J. Trickett[1,2*], M. Heald[2], C. Oliver[2] and C. Richards[2]

**Abstract**

**Background:** Sleep disturbance is common in children with neurodevelopmental disorders, with high rates identified in children with Smith-Magenis syndrome (SMS), Angelman syndrome (AS), autism spectrum disorder (ASD) and tuberous sclerosis complex (TSC). Phenotypic sleep profiles for these groups may implicate different pathways to sleep disturbance. At present, cross-group comparisons that might elucidate putative phenotypic sleep characteristics are limited by measurement differences between studies. In this study, a standardised questionnaire was administered across groups affording comparison of the prevalence and profile of sleep disturbance between groups and contrast to chronologically age-matched typically developing (TD) peers.

**Methods:** The modified version of Simonds and Parraga's sleep questionnaire, adapted for use in children with intellectual disabilities, was employed to assess sleep disturbance profiles in children aged 2–15 years with SMS ($n = 26$), AS ($n = 70$), ASD ($n = 30$), TSC ($n = 20$) and a TD contrast group ($n = 47$). Associations between sleep disturbance and age, obesity, health conditions and overactivity/impulsivity were explored for each neurodevelopmental disorder group.

**Results:** Children with SMS displayed severe night waking (81%) and early morning waking (73%). In contrast, children with ASD experienced difficulties with sleep onset (30%) and sleep maintenance (43%). Fewer children with ASD (43%) and AS (46%) experienced severe night waking compared to children with SMS (both $p < .01$). Higher sleep-disordered breathing scores were identified for children with SMS ($p < .001$) and AS ($p < .001$) compared to the TD group. Sleep disturbance in children with AS and TSC was associated with poorer health. Children experiencing symptoms indicative of gastro-oesophageal reflux had significantly higher sleep-disordered breathing scores in the AS, SMS and ASD groups (all $p < .01$). A number of associations between overactivity, impulsivity, gastro-oesophageal reflux, age and sleep disturbance were found for certain groups.

**Key findings for children with AS:**

- Night waking and early waking problems were common
- Night wakening appeared to decrease with age
- 71% were taking melatonin or other medication to improve their sleep quality
- Potential association between symptoms suggestive of reflux and sleep-disordered breathing (snoring, possible sleep apnea)

# Parental input about sleep issues

Research in Developmental Disabilities

journal homepage: www.elsevier.com/locate/redevdis

Research Paper

## Sleep in children with Angelman syndrome: Parental concerns and priorities

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ARTICLE INFO

Number of reviews completed is 2

*Keywords:*
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Parental perspectives

ABSTRACT

Angelman syndrome is a rare genetic syndrome, in which sleep disturbances are reported for 20–80% of individuals (Williams et al., 2006). This interview study delineated parental perceptions of sleep problems experienced by children with Angelman syndrome and the impact on parental sleep quality, health and wellbeing. The nature of desired interventions was also explored. Semi-structured interviews were completed with parents of 50 children, aged 16 months–15 years with Angelman syndrome who experienced current or historic sleep problems; predominantly night waking and settling problems. Parents were concerned by the impact of their child's sleep quality upon their own ability to function during the day. The importance of considering parental experiences was evidenced by variability in coping e.g. despite the persistence of sleep problems 20% of parents did not feel the need for any additional support. Amongst a range of types of further support desired, 27% cited further support with a behavioural intervention, and information about the trajectory of sleep problems in Angelman syndrome (18%). The results suggest that behavioural interventions supporting both children and parents in improving their sleep quality and well-being, and longitudinal research into sleep problems should be prioritised.

**Key findings:**

- Impact of sleep problems – affected parents' ability to function during the day, difficulty coping at work
- 68% of parents had tried behavioral approaches + medication
- 64% had seen a professional about child's sleep problem
- 27% wanted information and supports to develop a behavioral intervention for their child

# What we have learned

## Lessons

- Many have problems falling asleep or going back to sleep
- Many have tried sleep medications

## Implications

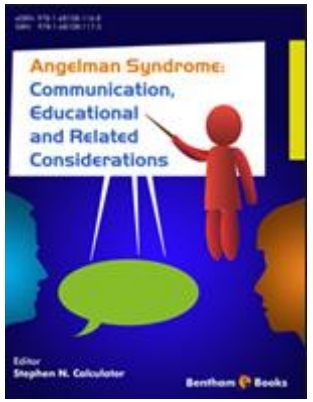
- Sleep problems may impact child's learning and behavior, affect parents' sleep and increase parent stress
- Consider link between pain/discomfort and sleep problems

# Mental Health/Behavioral: Communication

# Mental Health/Behavioral

- Language development is variably, though markedly impaired – majority do not develop speech; receptive language skills are always more advanced than expressive language skills and continue to improve even in adulthood.

RECOMMENDATIONS: Early and ongoing intervention by speech-language therapist is essential and should focus on nonverbal forms of communication. Use of augmentative and alternative communication aids, such as *Pragmatic Organization Dynamic Display*, picture cards, communication boards, *speech generating devices*, should be encouraged.




# What we have learned

## Lessons

- Most vocalize and use gestures
- Many use AAC
- Some words

## Implications

- Many individuals with AS use aided (PODD, Proloquo) and unaided (gestures, signs, vocalizations, speech) approaches
- AAC devices should be present across environments and modeled by a range of communication partners
- Communication challenges linked to behavior problems

# Challenging behavior

**Health Watch Table — Angelman Syndrome (AS)**
*Forster-Gibson, Berg and Korossy 2015*

# Mental Health/Behavioural

- Frequent laughter, apparently happy demeanor, easy excitability, hyperactivity, sleep disturbance, and aggressive behaviours such as grabbing and pulling, but not self-injury, are common

RECOMMENDATIONS: For hyperactivity, arrange consultation with occupational therapist for sensory issues, behavior therapist and then a psychiatrist to consider medication management for hyperactivity (atypical response to stimulant medication may occur). *Shape paying attention for longer periods of time; rearrange physical and teaching environment.*

# Challenging Behavior

AMERICAN JOURNAL OF medical genetics PART A WILEY

ORIGINAL ARTICLE

## Maladaptive behaviors in individuals with Angelman syndrome

Anjali Sadhwani[1] | Jennifer M. Willen[2,3] | Nicole LaVallee[4] | Miganush Stepanians[4] | Hillary Miller[5] | Sarika U. Peters[6] | Rene L. Barbieri-Welge[7] | Lucia T. Horowitz[8] | Lisa M. Noll[9] | Rachel J. Hundley[6] | Lynne M. Bird[10,11] | Wen-Hann Tan[2]

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Maladaptive behaviors are challenging and a source of stress for caregivers of individuals with Angelman Syndrome (AS). There is limited information on how these maladaptive behaviors vary over time among individuals with AS due to different genetic etiologies. In this study, caregivers of 301 individuals with AS were asked questions about their child's behavior and completed the Aberrant Behavior Checklist-Community version (ABC-C). Developmental functioning was evaluated with either the Bayley Scales of Infant Development, Third Edition (Bayley-III) or the Mullen Scales of Early Learning (MSEL). Family functioning was assessed using the parent-completed Parenting Stress Index (PSI) and the Family Quality of Life questionnaire (FQoL). Approximately 70% of participants had AS due to a deletion on the maternally-inherited copy of chromosome 15q11q13. Results revealed that at baseline, individuals with AS had low scores in the domains of lethargy (mean: 2.6–4.2 depending on genotype) and stereotypy (mean: 2.3–4.2 depending on genotype). Higher cognitive functioning was associated with increased irritability ($r = 0.32$, $p < .01$). Hyperactivity ($p < .05$) and irritability ($p < .05$) increased with age across all genotypes and should be ongoing targets for both behavioral and pharmacological treatment. Concerns for short attention span were endorsed by more than 70% of caregivers at baseline. Maladaptive behaviors, particularly hyperactivity, irritability and aggression, adversely affected parental stress, and family quality of life.

KEYWORDS
behavior rating scale, behavioral symptoms, developmental disabilities, problem behavior

**Key Findings**

- Easy excitability, mouthing and fascination with water and short attention span were commonly reported by caregivers
- On ABC-C, irritability is a problem and increased over time
- Hyperactivity and short attention span are also significant concerns
- Aggressive behavior increased over time and changed in form (↑pinching ↓biting)
- Problems could be related to seizures, poor sleep, communication problems

# Challenging Behaviors in Young Children with AS

Journal of Autism and Developmental Disorders (2019) 49:1717–1726
https://doi.org/10.1007/s10803-018-3853-x

BRIEF REPORT

## Brief Report: Challenging Behaviors in Toddlers and Preschoolers with Angelman, Prader–Willi, and Williams Syndromes

Wei Siong Neo[1] · Bridgette L. Tonnsen[1]

Published online: 12 December 2018
© Springer Science+Business Media, LLC, part of Springer Nature 2018

**Abstract**
Children with neurogenetic syndromes (NGS) experience comorbid challenging behaviors and psychopathology. We examined challenging behaviors in 86 toddlers and preschoolers across three NGS [Angelman syndrome (AS), Prader–Willi syndrome (PWS), and Williams syndrome (WS)] and 43 low-risk controls (LRC), using the Child Behavior Checklist for Ages 1½–5. Challenging behavior profiles differed across NGS, with generally elevated behaviors in AS and WS, but not PWS, relative to LRC. Withdrawn and autism spectrum symptoms were particularly elevated in AS. Although several profiles were similar to those previously reported in older children and adults, we also observed inconsistencies that suggest non-linear developmental patterns of challenging behaviors. These findings underscore the importance of characterizing early challenging behaviors to inform atypical phenotypic development and targeted intervention.

**Key Findings for children with AS**:

- CBCL concerns – speech problems, chews on things that aren't edible, can't concentrate for long
- Withdrawn behavior and symptoms of autism were prominent concerns in children with AS

# What we have learned

## Lessons

- Top behavioral concerns – aggression, short attention span
- Aggression – hair pull, grab, pinch, bite, slap

## Implications

- Relationship between behavior and skill deficits
- Behavior can serve as a form of communication

# Aggressive behavior

- Behavior that can result in harm to oneself, others or the environment
- Common forms of aggression in AS: hair pulling, grabbing, pinching, kicking, slapping
- In the absence of verbal and motor skills, aggression may be a way to "tell" people:
  - to pay more attention or stay connected
  - wants something
  - don't like/don't want something
  - not feeling well or unhappy

# On-Line Behavior Modules


- Social and environmental influences on aggressive behavior
- Aggression as a communicative behavior
- Cognitive and sensory issues
- Mental health influences on aggressive behavior
- Neurologic and medical influences on aggressive behavior

**www.angelmanbehaviors.org**

# Emotional and Mental Health

# Mental Health/Behavioral

(continued)

- Emotional needs are often neglected in severe disability combined with limited communication

RECOMMENDATIONS: Work with the individual and family to optimize opportunities for inclusion, participation and friendship. *Watch for changes in behavior that can occur in relation to stressors or major life events (moves, end of school, loss of family, friends, workers). Use tools that have been developed to identify possible signs of mental health problems in individuals with severe intellectual disability. Signs may include increased irritability and agitation or changes (increase/decrease) in sleep, energy, appetite and mood. Consider referral to psychologist or psychiatrist.*

# Anxiety symptoms and separation distress

JIDR Journal of Intellectual Disability Research
Published on behalf of mencap and in association with IASSID

Journal of Intellectual Disability Research doi: 10.1111/jir.12635

**Anxiety-associated and separation distress-associated behaviours in Angelman syndrome**

A. C. Wheeler,[1,2] K. C. Okoniewski,[1,2] A. Wylie,[1] M. DeRamus,[2] L. S. Hiruma,[2] D. Toth[1] & R. B. Christian[2]

1 *Center for Newborn Screening, Ethics and Disability Studies, RTI International, Durham, NC, USA*
2 *Carolina Institute for Developmental Disabilities, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA*

**Key findings:**

- Created a questionnaire to assess anxiety and separation distress in children and adults with AS
- 41% of caregivers expressed concerns regarding anxiety; can happen if preferred caregiver is busy with someone else, tries to leave or someone gets in the way
- Fewer anxiety-related behaviors for deletion group
- Anxiety scores highest for adolescents and lowest for children under 5 years
- Sleep difficulties and aggressive behaviors predicted anxiety scores

# Medication treatment for anxiety symptoms

**Buspirone for the treatment of anxiety-related symptoms in Angelman syndrome: a case series**

Kayla Balaj[a], Lisa Nowinski[b,c], Brianna Walsh[b], Jennifer Mullett[b], Michelle L. Palumbo[b,c], Ronald L. Thibert[b,c,d], Christopher J. McDougle[b,c,d] and Christopher J. Keary[b,c,d]

*Objectives* Angelman syndrome (AS) is a neurogenetic disorder associated with impaired expression of the ubiquitin-protein ligase E3A gene on chromosome 15. AS results in intellectual disability with limited expressive language, epilepsy, ataxia, sleep impairment, and problematic behavior which may include anxiety. Buspirone is a serotonin $(5\text{-HT})_{1A}$ receptor partial agonist used in the treatment of anxiety disorders and may, therefore, have a treatment role for patients with AS.

*Methods* We describe three patients who were given open-label buspirone for the treatment of behaviors thought to be related to anxiety.

*Results* We found significant improvement in symptoms of anxiety with buspirone. Patients tolerated long-term usage of the medication.

*Conclusion* The findings of this study suggest that buspirone may be effective for the amelioration of behaviors related to anxiety in patients with AS, and well tolerated. Limitations include the open-label nature of these treatments, the small sample size and the absence of a control group. *Psychiatr Genet* 29:51–56 Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Psychiatric Genetics 2019, 29:51–56

Keywords: Angelman, anxiety, buspirone, treatment

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Accepted 21 December 2018

**Key findings:**

- 3 adult cases
- Anxiety and distress symptoms - excessive swallowing and vomiting; sweating and loud vocalizations; pacing; aggression, self-harm and property destruction; sleep disturbance
- Triggers or contributing factors – separation from preferred caregiver; stressful environment; pain and discomfort; sensory overload; expressive communication deficits; limits being set
- Buspirone was associated with reduction in symptoms

# Skill Building

# Mental Health/Behavioral
(continued)

- **Interventions based on applied behavior analysis (ABA) are being used to teach adaptive and communication skills to improve individuals' functioning** and address behaviours that challenge people and services.

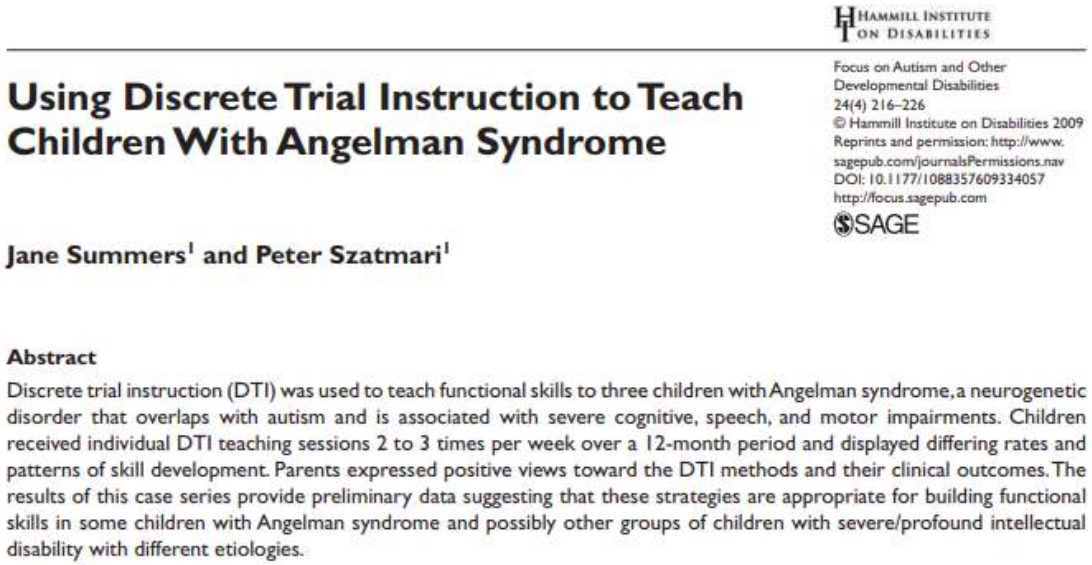
RECOMMENDATIONS: Visit www.angelmanbehaviors.org.

If behavior changes/occur, evaluate for medical cause. *Consider emotional needs and possible mental health issues*.

# Why are skill building approaches important?

- Increase individual's independence and sense of competence
- Reduce care needs
- More skills = better emotional health and quality of life, reduction in challenging behavior

# One example of a skill building approach



HAMMILL INSTITUTE ON DISABILITIES

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SAGE

## Using Discrete Trial Instruction to Teach Children With Angelman Syndrome

Jane Summers[1] and Peter Szatmari[1]

**Abstract**

Discrete trial instruction (DTI) was used to teach functional skills to three children with Angelman syndrome, a neurogenetic disorder that overlaps with autism and is associated with severe cognitive, speech, and motor impairments. Children received individual DTI teaching sessions 2 to 3 times per week over a 12-month period and displayed differing rates and patterns of skill development. Parents expressed positive views toward the DTI methods and their clinical outcomes. The results of this case series provide preliminary data suggesting that these strategies are appropriate for building functional skills in some children with Angelman syndrome and possibly other groups of children with severe/profound intellectual disability with different etiologies.

**Key findings:**

- Behavioral strategies were used to teach functional skills (motor imitation, visual matching, following instructions) to 3 children with AS
- Parents reported positive changes in child's development after intervention
- Had favorable views toward the intervention (worth time and effort, would recommend to other parents, more hopeful about child's future afterward)

# Impact of skill building approach

*Developmental Neurorehabilitation*, August 2012; 15(4): 239–252

informa
healthcare

## Neurodevelopmental outcomes in children with Angelman syndrome after 1 year of behavioural intervention

JANE SUMMERS[1,2]

[1]*McMaster Children's Hospital, Hamilton Health Sciences, Hamilton, Ontario, Canada, and* [2]*McMaster University, Hamilton, Ontario, Canada*

*(Received 4 February 2012; revised 11 March 2012; accepted 11 March 2012)*

**Abstract**

*Objective*: To examine the impact of teaching approaches based on the principles of applied behaviour analysis (ABA) on neurodevelopmental outcomes in children with Angelman syndrome (AS).

*Methods*: A non-randomized pre-test–post-test control group design was used. The intervention group consisted of four children with AS aged 3.1–9.2 years. Controls were other children with AS who were individually matched on the basis of chronological age, gender and molecular sub-type. Children in the intervention group were provided two-to-three ABA-based therapy sessions per week over a 1-year period. Standardized measures of cognitive, adaptive and language functioning were administered at baseline and after 1 year.

*Results*: There were no statistically significant differences between the two groups at baseline or after 1 year. However, positive trends were observed in the intervention group for some cognitive and adaptive measures.

*Conclusion*: ABA-based intervention improved aspects of neurodevelopment for some children with AS and warrants further study.

**Key findings:**

- 4 children with AS received 1 year of behavioral intervention, compared to 4 children with AS who did not
- Children in intervention group showed non-significant trend toward improved fine motor and receptive language scores on a cognitive measure after 1 year

# Clinical and Information Needs

# Unmet clinical needs

REVIEW Open Access

## Unmet clinical needs and burden in Angelman syndrome: a review of the literature

Anne C. Wheeler[1*], Patricia Sacco[2] and Raquel Cabo[3]

**Abstract**

**Background:** Angelman syndrome (AS) is a rare disorder with a relatively well-defined phenotype. Despite this, very little is known regarding the unmet clinical needs and burden of this condition, especially with regard to some of the most prevalent clinical features—movement disorders, communication impairments, behavior, and sleep.

**Main text:** A targeted literature review using electronic medical databases (e.g., PubMed) was conducted to identify recent studies focused on specific areas of the AS phenotype (motor, communication, behavior, sleep) as well as epidemiology, diagnostic processes, treatment, and burden. 142 articles were reviewed and summarized. Findings suggest significant impairment across the life span in all areas of function. While some issues may resolve as individuals get older (e.g., hyperactivity), others become worse (e.g., movement disorders, aggression, anxiety). There are no treatments focused on the underlying etiology, and the symptom-based therapies currently prescribed do not have much, if any, empirical support.

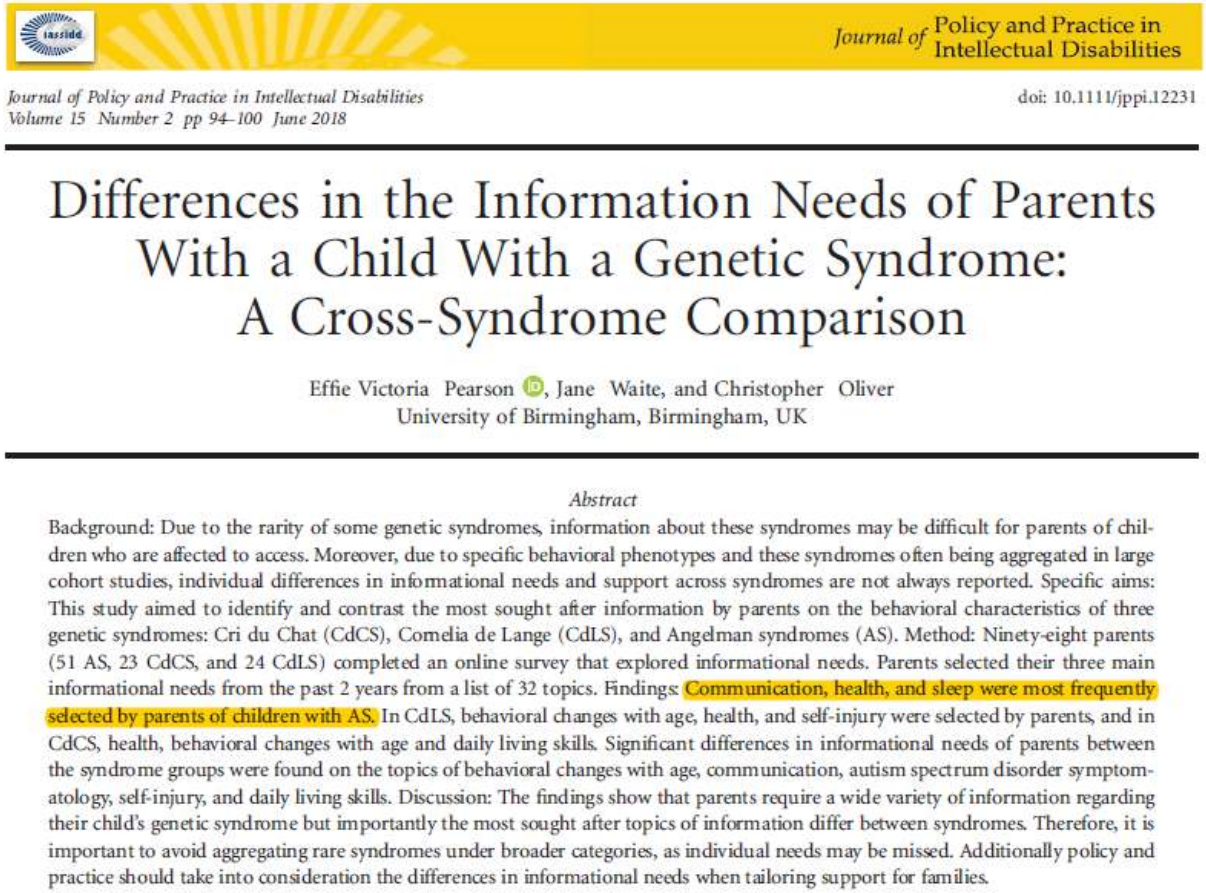
**Conclusions:** The lack of standardized treatment protocols or approved therapies, combined with the severity of the condition, results in high unmet clinical needs in the areas of motor functioning, communication, behavior, and sleep for individuals with AS and their families.

**Keywords:** Angleman syndrome, Burden, Unmet clinical needs, Clinical features, Treatments

**Key findings:**

- Literature review
- Found that some issues get better with age (hyperactivity) while some issues can get worse (movement disorders, aggression and anxiety)
- High unmet clinical needs in the areas of motor functioning, communication, behavior and sleep for individuals with AS and their families

# Parent information needs



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## Differences in the Information Needs of Parents With a Child With a Genetic Syndrome: A Cross-Syndrome Comparison

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*Abstract*

Background: Due to the rarity of some genetic syndromes, information about these syndromes may be difficult for parents of children who are affected to access. Moreover, due to specific behavioral phenotypes and these syndromes often being aggregated in large cohort studies, individual differences in informational needs and support across syndromes are not always reported. Specific aims: This study aimed to identify and contrast the most sought after information by parents on the behavioral characteristics of three genetic syndromes: Cri du Chat (CdCS), Cornelia de Lange (CdLS), and Angelman syndromes (AS). Method: Ninety-eight parents (51 AS, 23 CdCS, and 24 CdLS) completed an online survey that explored informational needs. Parents selected their three main informational needs from the past 2 years from a list of 32 topics. Findings: Communication, health, and sleep were most frequently selected by parents of children with AS. In CdLS, behavioral changes with age, health, and self-injury were selected by parents, and in CdCS, health, behavioral changes with age and daily living skills. Significant differences in informational needs of parents between the syndrome groups were found on the topics of behavioral changes with age, communication, autism spectrum disorder symptomatology, self-injury, and daily living skills. Discussion: The findings show that parents require a wide variety of information regarding their child's genetic syndrome but importantly the most sought after topics of information differ between syndromes. Therefore, it is important to avoid aggregating rare syndromes under broader categories, as individual needs may be missed. Additionally policy and practice should take into consideration the differences in informational needs when tailoring support for families.

**Key findings:**

- Highest information needs for health (specifically seizures, reflux, bone/joint problems), communication (expressive communication) and sleep issues
- Mobility issues were also identified

# Clinical Trials

# Parent perceptions and priorities about clinical trials

Journal of Intellectual Disability Research
Oral Presentation

**HOPES, FEARS AND BELIEFS ABOUT CLINICAL TRIALS FOR CHILDREN WITH ANGELMAN SYNDROME, 22Q11.2 DELETION SYNDROME AND OTHER RARE GENETIC DISORDERS**

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**Background**: The rapid growth in genomic medicine has led to advances in potential treatments for a number of rare syndromes. However, little is known about what parents of children with such syndromes think and feel about these trials and their priorities for treatment. **Methods**: Parents of 89 children with Angelman ($n = 42$), 22q11.2 deletion syndrome ($n = 20$) and other syndromes ($n = 27$) completed an online survey. Questions asked about their knowledge and perspectives on clinical trials and the specific areas they feel should and should not be targeted by treatments. **Results**: The majority (91%) felt that clinical trials aiming to reduce symptoms associated with their child's syndrome were positive, but there were significant differences between groups in the proportion that felt that such trials should be aiming to 'cure' their child's syndrome ($\times 2(4) = 28.9$, $P < .001$). Although less than half of parents reported feeling at least 'moderately' confident in their knowledge about clinical trials, nearly half of the parents reported being keen to take part in clinical trials, even if the treatment had not been trialled in humans. Behaviour and IQ were identified as priority target areas by 33.3–45% and 15–19% of parents (respectively) across all three groups. However, other target areas were syndrome-specific, with mental health being identified as a priority by 50% of the 22q11 group and speech/communication by 73.8% of the Angelman group. Almost one-third identified personality as the one characteristic they would not want to be changed. **Conclusion**: This expands the limited knowledge on parent's perceptions and priorities for treatment trials. Parents of children with rare genetic syndromes are motivated and keen to take part in trials to reduce the symptoms of their child's syndrome, despite potentially not being fully informed of what this means. It is important that researchers, clinicians and trial coordinators work together to increase parental knowledge prior to trials commencing.

**Key Findings**:

- Assessed parents' knowledge and perspectives on clinical trials for AS and other rare genetic disorders
- In general, parents viewed trials to reduce symptoms associated with their child's syndrome in a positive light
- Many identified behavior and IQ as priority areas
- Speech/communication was identified as priority area for ~75% of AS group

# Possible outcome measures for clinical trials

DEVELOPMENTAL NEUROREHABILITATION
https://doi.org/10.1080/17518423.2019.1619857

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## Using Behavioral Approaches to Assess Memory, Imitation and Motor Performance in Children with Angelman Syndrome: Results of a Pilot Study

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**ABSTRACT**

**Purpose:** This study was designed to assess memory, imitation of motor actions and motor performance by 12 children (age range 40–151 months) with Angelman syndrome (AS), a rare neurogenetic disorder associated with learning and memory impairments. **Methods**: Children's functioning was assessed at several time points over a 3-month period. **Results**: Memory and motor performance tests had acceptable test-retest and inter-rater reliability whereas the motor imitation test did not. Children were able to recall action sequences after a 24-h delay. Memory and motor performance scores were correlated with children's chronological age and raw scores on subdomains of the Vineland-II. **Conclusions**: These behavioral tests require further development and evaluation but may show promise to accompany standardized assessments that are currently in use with children with AS.

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**KEYWORDS**
Angelman syndrome; intellectual disability; memory; motor imitation; motor performance


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