Fostering adaptive behaviors in individuals with Angelman syndrome

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Chapter 1

General introduction

Preamble

Research in the field of intellectual disability (ID) and genetic syndromes is evolving. More is now known about their origin, developmental path and medical and behavioral treatment options. Individuals with a genetic syndrome usually present with some unique features, both physically (e.g., distinct facial figures, short stature) and behaviorally (e.g., typical behaviors, preferences). Because of these shared features, individuals more or less face the same developmental possibilities and challenges. In an attempt to find support and increase their knowledge, parents have assembled into syndrome-specific parent associations. Parents of around 150 children with Angelman syndrome (AS) in the Netherlands are assembled in the Prader-Willi Angelman Association (PWAV), which originated in 1991.

Parents learned that there was little knowledge available concerning concerning medical aspects and behavioral characteristics of children with AS. Within the domein of education and care parents asked 'Why does our child not speak?', 'Can my child be taught to speak or to communicate nonverbally, and if yes, how?' Other questions of parents were related to development and growth of their child and topics such as sleep problems and toilet training. Parents were interested in the nature and prevalence of such problems, but above all how these problems may be addressed (see e.g., Braam, Didden, Smits & Curfs, 2008).

The present thesis is the result of a collaboration between parents who have a child with AS and researchers from the Radboud University Nijmegen and University of Maastricht. The collaboration was a type of co-partnership. This was accomplished by exploring parental preferences about their child's educational priorities, assessing children's challenging behaviors and implementing procedures to increase their adaptive skills (i.e., communication, toileting).

1. Angelman syndrome

Angelman syndrome is a neurodevelopmental disorder affecting approximately one in every 12.000-40.000 live births (Steffenburg, Gillberg, Steffenburg, & Kyllerman, 1996; Thomson et al., 2006). There are four genetic causes for AS, all leading to a deficient UBE3A gene: (a) deletion of chromosome 15q11-q13, (b) paternal uniparental disomy of chromosome 15, (c) a UBE3A mutation or (d) an imprinting defect (Williams, Driscoll, & Dagli, 2010). Generally, individuals with AS have a severe or profound intellectual disability (ID) and a movement disorder described as a combination of jerky, ataxic and/or tremulous movements (Williams, 2010). Epilepsy is present in more than 80% of the individuals and usually starts before the age of three (Williams et al., 2010). Individuals with AS display some unique behaviors, together making up their behavioral phenotype. Functional speech is usually absent and individuals often communicate through other modes of communication (Clayton-Smith & Laan, 2003; Williams et al., 2010). Individuals with AS are known for their happy demeanor (e.g., smiling behavior) and their interest in social contact (Pelc, Cheron, & Dan, 2008; Williams, 2010). Hypermotoric movements and hand flapping are also common, although these appear to decrease with age (Clarke & Marston, 2000; Clayton-Smith, 2001; Williams et al., 2010). Adaptive behavioral skills (e.g., communicative behaviors, toileting skills) are severely impaired and often absent while challenging behaviors (e.g., aggression, self-injury) are common (Arron et al., 2011; Di Nuovo & Buono, 2011; Gasca et al., 2010; Peters et al., 2004).

The occurrence of phenotypical behaviors in individuals with AS have shown to be related to environmental factors. For instance, Oliver, Demetriades and Hall (2002) and Horsler and Oliver (2006) verified that smiling behavior in AS occurred more frequently during social interaction than in situations without social interaction, and that this behavior occurred more

often when the adult actively interacted with the child than when no interaction took place. In a recent study, Heald, Allen, Villa and Oliver (2013) applied discrimination training in four children with AS. A novel stimulus was used to cue the availability of attention and the children showed more social approach behaviors in the presence than in the absence of this cue. Results of these studies strongly suggest that environmental and especially social events may influence phenotypical behavior in AS. Such behavioral responding is exemplary for gene-environment relationships and indicates that although certain behaviors appear to be genetically predisposed, they can be altered by changing the environment.

In their review, Tunnicliffe and Oliver (2011) found that many phenotypical behaviors of individuals with genetic syndromes were influenced by environmental factors. For instance, in 9 out of 17 participants with Cornelia de Lange syndrome, self-injurious behavior was related to level of attention (Arron et al., 2006); in a girl with Prader-Willi syndrome food stealing decreased to zero after an intervention for food stealing (Maglieri, DeLeion, Rodrigues-Carter, & Sevin, 2000); another case-study in Prader Willi syndrome showed that skin-picking was reduced after behavioral intervention (Radstaake, Didden, Bolio, Lang, Lancioni, & Curfs, 2011); and in Smith-Magenis syndrome self-injurious behavior was increased during low levels of adult attention (Taylor & Oliver, 2008). These studies show that environmental variables can influence the occurrence of phenotypical behavior, and this knowledge may be used to alter their occurrence (Tunnicliffe and Oliver., 2011).

2. Fostering adaptive behavior

2.1. Learning theory and Applied behavior analysis

Phenotypical and challenging behaviors in AS may be reduced using principles from learning theory. Applied Behavior Analysis (ABA) uses these principles and engages the notion that behavior is functionally related to antecedent and consequent environmental events. When a behavior leads to a desired outcome, the individual will likely repeat this behavior. Behavior and outcome are functionally related. Hanley, Iwata, and McCord (2003) conducted a review on functional analysis (i.e. methodology to assess the function of challenging behavior) in individuals with ID. Behaviors studied mainly included self-injury and aggression. Out of the 536 cases assessed, the behavior was maintained by escape from unpleasant situations (34.2%), by access to attention (25.3%) or tangibles (10.1%) and by automatic reinforcement (15.8%). In a minority of cases (14.6%) multiple functions were identified and in 4.1% no function could be identified.

Meta-analyses and reviews have shown that functional analysis prior to treatment significantly increases treatment effectiveness (see e.g., Didden, Duker, & Korzilius, 1997). Numerous studies have been published that show that challenging behavior may be decreased and adaptive behavior may be increased by implementing interventions based on ABA (Carr, Robinson, Taylor, & Carlson, 1990; Duker, Didden, & Sigafoos, 2004; Kurtz et al., 2003). Interventions can generally be distinguished in antecedent procedures (changing stimuli evoking the challenging behavior), and consequent procedures (changing the reinforcing consequences of the behavior). A well-established behavioral treatment package is functional communication training (FCT; Carr & Durand, 1985). In FCT, the child is taught to replace his or her challenging behavior by socially accepted communicative behavior (e.g., gestures or picture

exchange) that leads to the same reinforcement as the challenging behavior. FCT is an evidence-based intervention for challenging behaviors and increases communicative behaviors in individuals with ID (see e.g., Kurtz et al., 2003; Pat, 1997; Sturmey & Didden, 2014). In the past two decades, behavioral treatments have been increasingly implemented in home and school settings for children with ID (see e.g., Lydon, Healy, O'Reilly, & Lang 2012; Ringdahl & Sellers, 2000), promoting the generalization of the new behavior to other settings and persons (Matson, Mahan, & LoVullo, 2009; Stokes & Baer, 1977).

2.2. Function and behavioral treatment of challenging behavior in AS

Several studies have assessed types and prevalence rates of challenging behaviors in AS. Summers et al. (1995) reviewed 108 case reports and found that 10% engaged in aggressive behaviors and 27% engaged in self-injurious behaviors. They also conducted a questionnaire study in which all 11 children were reported to show some type of aggressive behavior. Common topographies were grabbing and hair pulling. Horsler and Oliver (2006) reviewed studies on behavioral characteristics in AS and reported on 6% of the cases (n = 846) to show aggressive behaviors and another 6% to show self-injury. Didden et al. (2009) assessed the form and function of communicative behaviors and found that 10-35% of their cases (n = 79) used challenging behaviors (e.g., pinching others and self-injurious behavior) to communicate with others. Most recent, Arron et al. (2011) showed that individuals with AS were three times more likely to show physical aggression than individuals with non-specific ID. Although the studies differ in methodology and purpose, they indicate that challenging behavior is relatively common in individuals with AS.

Communication deficits in AS might in part explain why individuals with AS show challenging behaviors. Functional speech is absent and communication deficits have proven to increase the risk of self-injurious or aggressive behavior in individuals with ID (McClintock, Hall, & Oliver, 2003). Indeed, in the study by Didden et al. (2009) parents reported that the problematic behaviors were mainly used to reject, protest or comment. When challenging behavior is reinforced in the absence of more socially accepted communicative behaviors (which is often the case in AS), a functional relationship between challenging behavior and the reinforcer (e.g. adult attention) is established. When the function of the challenging behavior is to acquire attention, this functional relationship may be particularly strong in AS due to their social disposition; social attention might be especially rewarding for them (Tunnicliffe & Oliver, 2011). Both the communication deficits and social disposition of individuals with AS places them at risk for challenging behavior.

Two studies have examined the function of challenging behavior in AS (Strachan et al., 2009). Stachan et al. made use of experimental functional analysis to assess the behavioral function of 10 children with AS. In experimental functional analysis, several conditions mimicking everyday situations are re-enacted while manipulating antecedent and consequent variables to assess the behavioral function of challenging behavior. Results showed that in one child aggressive behavior functioned to maintain attention, in two children to escape from a task and in three children to receive social attention. In the remaining children challenging behavior levels were very low or results were inconclusive. In this study, not all children showed challenging behavior to receive social attention. Apparently, social attention is not a reinforcer for challenging behavior in all individuals with AS.

After determining the behavioral function of challenging behavior, FCT can be implemented. In the process of FCT, challenging behavior is often placed under extinction (i.e. the reinforcer is withheld) and communicative behavior is prompted (i.e. the child is assisted in performing the task independently). This has two potential downfalls: a) when challenging behavior proceeds the prompting of communicative behavior, the individual can chain both behaviors together (Reichle & Johnston, 1993), restricting the child from learning to communicate independently, and b) the individual may experience pain, frustration or discomfort stemming from the challenging behavior. Both downfalls can be prevented by prompting communicative behavior upon the onset of a behavior occurring *before* the challenging behavior; that is the so-called precursor. Since precursors and challenging behaviors are maintained by the same variables and events, they are functionally equivalent (Carr & Durand, 1985; Petty, Allen & Oliver, 2011). This makes precursors candidates for the initiation of prompting in FCT. When the precursor is replaced for communicative behavior and this behavior is reinforced, challenging behavior is expected to cease since it was aimed at the same reinforcer. Borrero and Borrero (2008) provided evidence for the functional equivalence of precursor and challenging behavior and suggested that interventions aimed at precursors might be successful in the treatment of challenging behavior. Langdon, Carr and Owen-deSchryver (2008) demonstrated that precursor-based prompting was effective in decreasing challenging behavior in individuals with ID.

The effectiveness of precursor-based prompting has not been studied in AS yet, although the potential benefits are evident. Precursor-based prompting might especially be effective in individuals with AS as they often have problems with maintaining their attention and are likely to show non-compliance (Summers et al., 1995). Immediate prompting upon the onset of precursor behavior might lead to fewer opportunities for distraction and to more opportunities

per session to receive reinforcement, heightening the motivation of the child to show adaptive behavior.

We assessed the behavioral function(s) of challenging behavior in seven children with AS. Following experimental functional analysis we implemented FCT and evaluated the effectiveness of precursor-based prompting on challenging behavior in both therapeutical and naturalistic settings. We also used familiar trainers, as this could improve both the ecological validity and the generalization of the newly acquired adaptive behaviors (see e.g., Lang et al., 2008; Stokes & Bear, 1977). Aforementioned studies primarily used unknown researchers and clinical settings to assess the behavioral functions in the children. This could have altered the behavior of the child, possibly leading to a different behavioral function found in the research setting compared to the function of the same behavior in a natural setting (see Hanley et al., 2003).

2.3. Incontinence and toilet training in AS

Incontinence is common in AS and prevalence rates of incontinence vary between 12% and 63% (Buntinx et al., 1995; Laan, den Boer, Hennekam, Renier, & Brouwer, 1996), depending on type of incontinence (e.g., urine or feces) and individual's age. The topic of incontinence in AS has been largely neglected. A reason may be that incontinence is seen as a "symptom" stemming from the severe ID in AS or from AS itself. To assess this, comparisons have to be made between individuals with AS and individuals with severe or profound ID of other origin. This type of research will designate if incontinence is part of the behavioral phenotype of AS (Dykens, 1995). A study, however, has not yet been conducted. To date, risk

factors for incontinence in AS have not been studied either. When known, this could lead to effective prevention and/or treatment of incontinence in AS.

In individuals with ID, urinary incontinence was found to be positively associated with decreased mobility, fecal incontinence, a higher body mass index, urinary tract infections and severity of ID (Hannestad et al., 2003; Ouslander, Palmer, Rovner, & German, 1993; Van Laecke et al., 2010; Von Gontard & Néveus, 2006; Yang, Meng, & Chou, 2010). Incontinence may also be associated with voiding dysfunctions (e.g., abnormal voiding patterns and bladder volumes). Yang et al. (2010) and Van Leacke et al. (2001) examined voiding dysfunctions in children with ID and found that compared to children without ID, children with ID showed more abnormal voiding patterns, had smaller bladder capacities and were more often incontinent of urine during the day. To date, it is unknown if and how these factors are related to incontinence in AS.

Urinary incontinence has adverse consequences. It may cause urinary tract infections, pain and discomfort (Foxman, 2002; Kroeger & Sorenson-Burnworth, 2009). Next to this, being incontinent may lead to dependency on caregivers, stigmatization, and it can restrict an individual from taking part in social activities (Cicero & Pfadt, 2002; Kroeger & Sorenson-Burnworth, 2009). Toilet training in AS is needed since the relatively high prevalence rate of urinary incontinence in AS implies that continence is not likely to develop when regular approaches are used. Further, phenotypical behavior might interfere with toilet training, emphasizing the need to develop training protocols that are attuned to individuals with AS.

Several toilet training procedures have been developed for individuals with severe ID (see Kroeger & Sorenson-Burnworth, 2009, for a review) including the Azin-Foxx toilet training program (Azrin & Foxx, 1971) and the response restriction toilet training method (Duker,

Averink, & Melein, 2001). To our knowledge, only one study on toilet training in AS has been conducted. Didden, Sikkema, Bosman and Duker (2001) successfully used a modified Azrin-Foxx toilet training procedure to toilet train six children with AS. Training included increased liquid intake, scheduled sittings, reinforcements for correct urinary voids and a time out from reinforcement and restitutional overcorrection upon an urinary accident. In their review, Kroeger and Sorenson-Burnworth observed a tendency towards least-aversive procedures to establish continence in individuals with ID. The response restriction toilet training method is an example of a method containing no aversive stimuli (such as overcorrection). This method is based on restricting all responses that interfere with correct toileting, gradually increasing the distance between the trainee and the toilet, increasing the fluid intake and providing reinforcement upon a correct void (Duker et al., 2001). It has not yet been investigated if this method can lead to urinary continence in AS.

We examined if incontinence is part of the behavioral phenotype of AS by comparing incontinence in AS with incontinence in individuals from a matched control group. Variables associated with incontinence in AS were assessed as well. We further assessed the effectiveness of individualized response restriction training protocols to foster urinary continence in children and adolescents with AS. The protocols were individualized as it could not be assumed that there is a "one size fits all" toilet training protocol for individuals with AS. Finally, we examined if voiding dysfunctions are apparent in AS using uroflowmetry, a non-invasive technique to measure the volume and the pattern of the urine flow (Néveus et al., 2006).

2.4. Parental preferences in the care for children with AS

In the Netherlands, goals (including fostering adaptive behaviors) for individuals with ID and the support they receive are documented in the "Individualized Support Plan" or "Individualized Education Plan" (IEP). The use of IEPs is mandatory for individuals with ID (Ministerie van Volksgezondheid, Welzijn en Sport (VWS) [Ministry of Public Health, Welfare and Sports], 2000) in the Netherlands. Key elements of an IEP are: a) the individualization of the plan, b) empowering the voice of the client and/or their legal representative(s), and c) goals aiming at the future in order to increase the quality of life. The IEP is the end product of a dialogue between the professional and the client and/or legal representative(s) (Buntinx, Herps, & de Ruiter, 2013).

This dialogue is of increasing importance in the Netherlands, since some major shifts in legislation and financing concerning care and support for individuals with ID are scheduled for the following years (VWS, 2013). Individuals with ID are viewed as individuals with wants and needs, just as any other individual in society. However, they need extra support on one or several life domains (Shalock & Verdugo, 2002; VWS, 2013). Prior to the enrollment in professional care, support should be sought in the home environment and in informal care circuits including family members, volunteers, and schools, further signifying the role of parents. Emphasis is also placed on the evaluation of the care and support as experienced by the client and/or legal representative(s). As individuals with AS have severe ID and severe communication deficits, parents are the main advocates of their child's care and welfare and efforts should be made to include them in their care.

Parental involvement is seen as essential and customary in the care for individuals with ID (Matson, Mahan, & LoVullo, 2009; Siebes et al., 2006). In the study by Siebes et al. (2006)

parents emphasized that involving them in goal setting would amount to "a better fit with practical difficulties encountered by the children in daily life, and services would be more 'in-tune' with the family's limitations and strengths" (p. 203). Besides involving parents in goal setting, they should also be involved in the treatment itself. In general, parents have more opportunities to interact with their child(ren) in different settings, enhancing the generalization of the adaptive skills (Matson et al., 2009; Siebes et al., 2006). In addition, parents are also able to successfully implement treatment packages for their child with ID to address adaptive behaviors and/or challenging behaviors (see Matson et al., 2009 for a review).

Several studies have assessed parental perspectives in AS. Parents of children with AS were interviewed on the challenging behaviors of their child (Clarke & Marston, 2000; Summers et al., 1995). Findings revealed elevated rates of eating problems, sleeping problems, and hyperactivity. Frequent episodes of laughter and fascination with water were also mentioned by parents. In a study by Leyser and Kirk (2011) parents of children with AS were asked about their attitudes towards schooling and inclusion. Results indicated that parents wanted their child to develop communication skills, life skills opposed to academic skills and skills concerning socialization. Parents also indicated concerns about staff training and knowledge of AS and stressed that more partnership and communication between themselves and the school/teachers was desired. Twenty-five percent of the parents pointed out that they were not satisfied with the IEP process, indicating that improvements can be made. Parental priorities in communication training were further studied by Calculator and Black (2010). Results showed that parents highlighted skills to express wants and needs and to share feelings and experiences. Parents also wanted their child to acquire functional skills, but it remained unclear which skills. Leyser and

Kirk (2011) and Calculator and Black (2010) signified that collaboration between parents and professionals concerning the care of a child with ID is strongly desired.

When parents determine which skill(s) to address in an IEP, the ability or intellectual level of their child might be of importance. In comparing the parental priorities of children with Prader-Willi syndrome (PWS; Pituch et al., 2010a) to those of children with Cri-du-Chat syndrome (CdC; Pituch et al., 2010b) the authors noted that parents of children with PWS primarily prioritized skills in which the children showed deficits; in CdC parents also prioritized skills in which the child showed emerging abilities. It was hypothesized that this difference stemmed from differences in the level of ID and that parents of children with more severe ID more often valued training in domains in which their child showed some abilities. This notion appears to be in line with the findings of King et al. (2006) who studied the belief systems in families of children with autism or Down syndrome. Parents adopted either a strength-based or a needs-based strategy: "They focused on what their children needed and could do, rather than on what their child 'wasn't' or couldn't accomplish" (p. 392). Focusing on strengths instead of deficits possibly gives parents a sense of control, in that their child can actually accomplish (small) steps in development. This strength-based focus might also be beneficial for parents of children with AS, as they often feel a loss of control (van den Borne et al., 1999). Adaptive behavior profiles in individuals with AS show relative strengths in socialization skills and relative deficits in motor skills (Peters et al., 2004; Gasca et al., 2010), but it is not yet clear how parental priorities relate to this behavioral profile.

The abovementioned studies clarify which behavioral problems are evident in AS as observed by parents and which broad-spectrum goals parents consider important in the lives of their children. We extent this line of research by assessing a wider range of adaptive behaviors.

We also included parents of adults with AS to explore if and how training priorities change throughout the lifespan. Parents were asked to prioritize skills for training and to rate the current ability of their child on those skills. By combining both skill level and training prioritization, it could be assessed if parents value the training of skills in which their child shows a major, minor or mediocre deficit. This allowed us to evaluate if parents adopted a deficit- or strength-based logic or if they prioritize the training of emerging skills. This type if information is important in the development of IEPs and gives future directions for staff training, targeted at the goals for children with AS as viewed by their parents.

3. Research questions and thesis outline

3.1. Research questions

In the present thesis, the following research questions will be addressed:

1. What are the functions of challenging behaviors in children with Angelman syndrome and does functional communication training reduce these behaviors?
2. To what extent is incontinence part of the behavioral phenotype of Angelman syndrome and which factors are associated to incontinence. Does a modified Response Restriction toilet training protocol result in continence? Does the uroflow show an abnormal pattern?
3. Which adaptive and maladaptive skills and behaviors value parents for training and treatment in the care for their child with Angelman syndrome?

3.2. Outline of this thesis

Chapter 2 and 3 answer the first research question. In both studies the function of challenging behavior in children with AS and the effects of FCT on challenging behavior were assessed. In *Chapter 2*, functional analysis and training sessions primarily took place in a therapy room, with researchers acting as therapists, whereas in *Chapter 3* natural settings and familiar therapists were used. In FCT, precursor based prompting was administered and functional equivalence between challenging behavior and the taught communicative behavior was assessed.

In *Chapter 4* incontinence was assessed by asking primary caretakers of individuals with AS. Associated factors, level of adaptive functioning and voiding characteristics were also explored. Data was compared to individuals with severe ID of other origin.

Chapter 5 answers research question number two. We adapted the Response Restriction training protocol and implemented the intervention in the natural environment. All protocols were tailor-made to do justice to each participant's individual characteristics, capabilities and deficits.

Voiding characteristics were further studied in *Chapter 6*. We used uroflowmetric analysis to assess the flow-curve and volume of urinary voids in six individuals with AS. The flow-curves were designated to be either "normal" or "pathological".

In *Chapter 7*, we asked parents to assess educational priorities with respect to their child's care. We asked them to prioritize which behavioral skills they wanted their child to learn. Skills from seven adaptive and maladaptive skill domains were questioned. We assessed if parents highlighted skills for training in which their child showed a minor, mediocre or major deficit.

In the general discussion, *Chapter 8*, the results of all six studies are discussed. Clinical implications are discussed and directions for further research are given.

4. References

Arron, K., Oliver, C., Hall, S., Sloneem, J., Forman, D., McClintock, K., & Bodfish, J. (2006). Effect of social context on social interaction and self-injurious behavior in Cornelia de Lange syndrome. *American Journal on Mental Retardation, 111*, 184-192.

Arron, K., Oliver, C., Moss, J., Berg, K., & Burbidge, C. (2011). The prevalence and phenomenology of self-injurious and aggressive behavior in genetic syndromes. *Journal of Intellectual Disability Research, 55*, 109-120.

Azrin, N. H., & Foxx, R. M. (1971). A rapid method of toilet training the institutionalized retarded. *Journal of Applied Behavior Analysis, 42*, 89-99.

Borrero, C. S. W., & Borrero, J. C. (2008). Descriptive and experimental analyses of potential precursors to problem behavior. *Journal of Applied Behavior Analysis, 41,* 83-96.

Braam, W., Didden, R., Smits, M. G., & Curfs, L. M. G. (2008). Melatonine for chronic insomnia in Angelman syndrome: A randomized placebo-controlled trial. *Journal of Child Neurology, 23*, 649-654.

Buntinx, I. M., Hennekam, R. C. M., Brouwer, O. F., Stroink, H., Beuten, J., Mangelschots, K., & Fryns, J. P. (1995). Clinical profile of Angelman syndrome at different ages. *American Journal of Medical Genetics, 56*, 176-183.

Buntinx, W., Herps, M., & de Ruiter, M. (2013). *Handreiking Ondersteuningsplannen (Advice report Individual Education Plans)*. Utrecht: Kennisplein Gehandicaptensector.

Calculator, S. N., & Black, T. (2010). Parent's priorities for AAC and related instruction for their

children with Angelman syndrome. *Augmentative and Alternative Communication, 26,* 30-40.

Carr, E. G., & Durand, M. V. (1985). Reducing behavior problems through functional communication training. *Journal of Applied Behavior Analysis, 18*, 111-126.

Carr, E. G., Robinson, S., Taylor, J. C., & Carlson, J. I. (1990). Positive approaches to the treatment of severe behavior problems in persons with developmental disabilities: A review and analysis of reinforcement and stimulus-based procedures. *Monograph of the Association for Persons with Severe Handicaps, 4*, 1-40.

Cicero, F. R., & Pfadt, A. (2002). Investigation of a reinforcement-based toilet training procedure for children with autism. *Research in Developmental Disabilities, 23*, 319-331.

Clarke, D., & Marston, G. (2000). Problem behaviors associated with 15q- Angelman syndrome. *American Journal on Mental Retardation, 105*, 25-31.

Clayton-Smith, J. (2001). Angelman syndrome: Evolution of phenotype in adolescents and adults. *Developmental Medicine & Child Neurology, 43,* 476-480.

Clayton-Smith, J., & Laan, L. (2003). Angelman syndrome: A review of the clinical and genetic aspects. *Journal of Medical Genetics, 40*, 87-95.

Didden, R., Duker, P. C., & Korzilius, H. (1997). A meta-analytic study on treatment effectiveness for problem behaviors with individuals who have mental retardation. *American Journal on Mental Retardation, 101*, 387-399.

Didden, R., Sigafoos, J., Korzilius, H., Baas, A., Lancioni, G. E., O'Reilly, M. F., & Curfs, L. M. G. (2009). Form and function of communicative behaviors in individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disability, 22,* 526-537.

Didden, R., Sikkema, P. E., Bosman, I. T. M., & Duker, P. C. (2001). Use of a modified Azrin-

Foxx toilet training procedure with individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 14*, 64-70.

Di Nuovo, S. & Buono, S. (2011). Behavioral phenotypes of genetic syndromes with intellectual disability: Comparison of adaptive profiles. *Psychiatry Research, 189*, 440-445.

Duker, P. C., Averink, M., & Melein, L. (2001). Response restriction as a method to establish diurnal bladder control. *American Journal on Mental Retardation, 3*, 209-215.

Duker, P., Didden, R., & Sigafoos, J. (2004). *One-to-one training: Instructional procedures for learners with developmental disabilities*. Austin, TX: Pro-Ed.

Dykens, E. M. (1995). Measuring behavioral phenotypes: Provocations from the ‘‘new genetics’’. *American Journal of Mental Retardation, 99*, 522-532.

Feldman, A. S., & Bauer, S. B. (2006). Diagnosis and management of dysfunctional voiding. *Current Opinion in Pediatrics, 18*, 139-147.

Foxman, B. (2002). Epidemiology of urinary tract infection: Incidence, morbidity, and economic costs. *American Journal of Medicine, 113*, 5-13.

Gasca, C. B., Obiols, J. E., Bonillo, A., Artigas, J., Lorente, I., Gabau, E., … Turk, J. (2010). Adaptive behavior in Angelman syndrome: Its profile and relationship to age. *Journal of Intellectual Disability Research, 54*, 1024-1029.

Hanley, G. P., Iwata, B. A., & McCord, B. E. (2003). Functional analysis of challenging behavior: A review. *Journal of Applied Behavior Analysis, 36,* 147-185.

Hannestad, Y. S., Rortveit, G., Daltveit, A. K., & Hunskaar, S. (2003). Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. *BJOG: An International Journal of Obstetrics & Gynaecology, 110*, 247-254.

Heald, M., Allen, D., Villa, D., & Oliver, C. (2013). Discrimination training reduces high rate social approach behaviors in Angelman syndrome: Proof of principle. *Research in Developmental Disabilities, 34*, 1797-1803.

Horsler, K., & Oliver, C. (2006). The behavioral phenotype of Angelman syndrome. *Journal of Intellectual Disability Research, 50*, 33-53.

Horsler, K., Oliver, C., & Dykens, E. (2006). Environmental influences on the behavioral phenotype of Angelman syndrome. *American Journal on Mental Retardation, 111*, 311-321.

King, G. A., Zwaigenbaum, L., King, S., Baxter, D., Rosenbaum, P., & Bates, A. (2006). A qualitative investigation of changes in the belief systems of families of children with autism or Down syndrome. *Child: Care, Health and Development, 32*, 353-369.

Kennisplein Gehandicaptensector (2013). *Handreiking ondersteuningsplannen*. Utrecht: VGN.

Kroeger, K. A., & Sorensen-Burnworth, R. (2009). Toilet training individuals with autism and other developmental disabilities. *Research in Autism Spectrum Disorders, 3,* 607-618.

Kurtz, P. F., Chin, M. C., Huete, J. M., Tarbox, S. F., O'Connor, J. T., Paclawskyj, T.R., & Rush, K. S. (2003). Functional analysis and treatment of self-injurious behavior in young children: A summary of 30 cases. *Journal of Applied Behavior Analysis, 36*, 205-219.

Laan, L. , den Boer, A. Th., Hennekam, R., Renier, W. O., & Brouwer, O. F. (1996). Angelman syndrome in adulthood. *American Journal of Medical Genetics*, *66,* 356-360.

Lang, R., O'Reilly, M., Machalicek, W., Lancioni, G., Rispoli, M., & Chan, J. (2008). Preliminary comparison of functional analysis results when conducted in contrived versus natural settings. *Journal of Applied Behavior Analysis, 41*, 441-445.

Langdon, N. A., Carr, E. G., & Owen-deSchryver, J. S. (2008). Functional analysis of precursors

for serious problem behavior and related intervention. *Behavior Modification, 32*, 804-827.

Leyser, Y., & Kirk, R. (2011). Parents' perspectives on inclusion and schooling of students with Angelman syndrome: Suggestions for educators. *International Journal of Special Education, 26,* 1-14.

Lydon, S., Healy, O., O'Reilly, M. F., & Lang, R. (2012). Variations in functional analysis methodology: A systematic review. *Journal of Physical and Developmental Disability, 24,* 301-326.

Maglieri, K. A., DeLeon, I. G., Rodriguez-Catter, V., & Sevin, B. M. (2000). Treatment of covert food stealing in an individual with Prader-Willi syndrome. *Journal of Applied Behavior Analysis, 33*, 615-618.

Matson, J., Mahan, S., & LoVullo, S. V. (2009). Parent training: A review of methods for children with developmental disabilities. *Research in Developmental Disabilities, 30*, 961-968.

McClintock, K., Hall, S., & Oliver, C. (2003). Risk markers associated with challenging behaviors in people with intellectual disabilities: a meta-analytic study. *Journal of Intellectual Disability Research, 47*, 405-416.

Ministerie van Volksgezondheid, Welzijn en Sport (Ministry of Public Health, Welfare and Sports) (2009). *Besluit Zorgplanbespreking AWBZ-zorg (Decree care plan meetings for individuals with special needs)*. Retrieved November 20, 2013 from http://wetten.overheid.nl/BWBR0025521/geldigheidsdatum_20-11-2013.

Nevéus, T., von Gontard, A., Hoebeke, P., Hjälmas, K., Bauer, S., Bower, W., … Djurhuus, J. C. (2006). The standardization of terminology of lower urinary tract function in children and

adolescents: Report from the Standardization Committee of the International Children's Continence Society (ICCS). *The Journal of Urology, 176*, 314-243.

Oliver, C., Demetriades, L., & Hall, S. (2002). Effects of environmental events on smiling and laughing behavior in Angelman syndrome. *American Journal on Mental Retardation, 107*, 197-200.

Ouslander, J. G., Palmer, M. H., Rovner, B. W., & German, P. S. (1993). Urinary incontinence in nursing homes: incidence, remission and associated factors. *Journal of the American Geriatric Society, 41*, 1083-1089.

Pat, M. (1997). Supporting individuals with challenging behavior through functional communication training and AAC: Research review. *Augmentative and Alternative Communication, 13*, 207-225.

Pelc, K., Cheron, G., & Dan, B. (2008). Behavior and neuropsychiatric manifestations in Angelman syndrome. *Neuropyschiatric Disease and Treatment, 4*, 577-584.

Peters, S. U., Goddard-Finegold, J., Beaudet, A. L., Madduri, N., Turcich, M., & Bacino, C. A. (2004). Cognitive and adaptive behavior profiles of children with Angelman syndrome. *American Journal of Medical Genetics, 128A*, 110-113.

Petty, J., Allen, D., & Oliver, C. (2009). Relationship among challenging, repetitive, and communicative behaviors in children with severe intellectual disabilities. *American Journal on Intellectual and Developmental Disabilities, 114*, 356-368.

Pituch, K. A., Green, V. A., Didden, R., Lang, R., O'Reilly, M., Lancioni, G., et al. (2010a). Rehabilitation priorities for individuals with Prader-Willi syndrome. *Disability and Rehabilitation, 32*, 2009-2018.

Pituch, K. A., Green, V. A., Didden, R., Whittle, L., O'Reilly, M., Lancioni, G., & Sigafoos, J.

(2010b). Educational priorities for children with Cri-du-Chat syndrome. *Journal of Developmental and Physical Disabilities, 22*, 65-81.

Radstaake, M., Didden, R., Bolio, M., Lang, R., Lancioni, G., & Curfs, L. M. G. (2011). Functional assessment en behavioral treatment of skin picking in a teenage girl with Prader Willi syndrome. *Clinical Case Studies, 10*, 67-78.

Reichle, J., & Johnston, S. S. (1993). Replacing challenging behavior. The role of communication intervention. *Topics in Language Disorders, 13*, 61-76.

Ringdahl, J. E., & Sellers, J. A. (2000). The effects of different adults as teachers during functional analysis. *Journal of Applied Behavior Analysis, 33*, 247-250.

Schalock, R. L., & Verdugo, M. A. (2002). *Handbook on quality of life for human service practitioners*. Washington, DC: American Association on Mental Retardation.

Siebes, R. C., Wijnroks, L., Ketelaar, M., van Schie, P. E. M., Gorter, J. W. & Vermeer, A. (2006). Parent participation in paediatric rehabilitation treatment centers in the Netherlands: A parent's viewpoint. *Child: Care, Health and Development, 33,* 196-205.

Steffenburg, S., Gillberg, C. L., Steffenburg, U., & Kyllerman, M. (1996). Autism in Angelman syndrome: a population-based study. *Pediatric Neurology, 14*, 131-136.

Stokes, T., & Baer, D. M. (1977). An implicit technology of generalization. *Journal of Applied Behavior of Analysis, 10,* 349-367.

Strachan, R., Shaw, R., Burrow, C., Horsler, K., Allen, D., & Oliver, C. (2009). Experimental functional analysis of aggression in children with Angelman Syndrome. *Research in Developmental Disabilities, 30,* 1095-1106.

Sturmey, P., & Didden, R. (Eds). (2014). *Evidence Based Practice and Intellectual Disabilities.* Chichester: Wiley Blackwell.

Summers, J., Allison, J., Lynch, P., & Sandler, L. (1995). Behavior problems in Angelman syndrome. *Journal of Intellectual Disability Research, 3,* 97-106.

Taylor, L., & Oliver, C. (2008). The behavioral phenotype of Smith-Magenis syndrome: evidence for a gene-environment interaction. *Journal of Intellectual Disability Research, 52*, 830-841.

Thompson, A. K., Glasson, E. J., & Bittles, A. H. (2006). A long-term population-based clinical And morbidity profile of Angelman syndrome in Western Australia: 1953-2003. *Disability and Rehabilitation, 28*, 299-305.

Tunnicliffe, P., & Oliver, C. (2011). Phenotype-environment interactions in genetic syndromes Associated with severe or profound intellectual disability. *Research in Developmental Disabilities, 32*, 404-418.

Van den Borne, H. W., van Hooren, R. H., van Gestel, M., Rienmeijer, P., Fryns, J. P., & Curfs, L. M. G. (1999). Psychosocial problems, coping strategies, and the need for information of parents of children with Prader-Willi syndrome and Angelman syndrome. *Patient Education and Counseling, 38*, 205-216.

Van Laecke, E., Hoebeke, P., Raes, A., & Vande Walle, J. (2010). Urinary incontinence in physically and/or intellectually disabled children: A multifactorial problem. *Journal of Pediatric Urology, 6*, S67.

Van Laecke, E. V., Golinveaus, L., Goossens, L., Raes, A., Hoebeke, P., & Vande Walle, J. (2001). Voiding disorders in severely mentally and motor disabled children. *The Journal of Urology, 166*, 2404–2406.

Vereniging Gehandicaptenzorg Nederland (2013a). *Kwaliteitskader Gehandicaptenzorg. Visiedocument –2.0.* Utrecht: VGN.

Von Gontard, A., & Neveus, T. (2006). *Management of disorders of bladder and bowel control in childhood.* London: MacKeith Press.

Williams, C. A. (2010). The behavioral phenotype of Angelman syndrome. *American Journal of Medical Genetics, 154C*, 432-437.

Williams, C. A., Driscoll, D. J., & Dagli, A. I. (2010). Clinical and genetic aspects of Angelman syndrome. *Genetics in Medicine, 12*, 385-395.

Yang, P., Meng, N., & Chou, E. C. (2010). Voiding dysfunctions in children with mental retardation. *Neurology and Urodynamics, 29,* 1272-1275.

Chapter 2

Functional analysis and functional communication training in individuals with Angelman syndrome

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Abstract

Objective: To assess the functions of challenging behavior in four children with Angelman syndrome (AS) and to study the effects of functional communication training (FCT) with precursor based prompting. This study builds on and extends the study of Allen et al. (2010).

Method: Experimental functional analysis assessed behavioral functions. FCT was implemented within an ABAB design and effect sizes were calculated. Burst analyzes depict tendencies in (precursor) behaviors surrounding target behaviors.

Results: Results show challenging behavior to be aimed at receiving attention, tangibles or escape. Burst analysis designated physical and eye contact and reaching for tangibles as precursors. Effects of FCT ranged from small to large.

Conclusion: Behavioral functions for challenging behavior were found and FCT was effective in reducing its frequency, when precursors were used as the onset of prompting. Functional equivalence between challenging and communicative behavior was found. Implementing treatment for challenging behavior based on precursors is advised.

1. Introduction

Angelman syndrome (AS) is a neurodevelopmental disorder caused by the absence of expression of maternally imprinted genes in the critical region at 15q11-13 (Lalande & Calciano, 2007). Clinical features consist of severe intellectual disability (ID), absence of speech, ataxic, jerky and tremulous movements and distinctive behaviors such as hand flapping and frequent smiling (Williams, 2010). Smiling behavior occurs more often when social interaction is in effect than when social interaction is not in effect (Oliver et al., 2007), indicating that adult attention may be a source of positive reinforcement for individuals with AS. Due to speech and motor deficits, their ability to request attention or to maintain interaction with others is limited (Williams, 2010).

Challenging behavior may arise when communication is limited and such behavior is relatively common in individuals with AS (see e.g. (Clayton-Smith & Laan, 2003; Strachan et al., 2009). Functional behavior analysis (FBA) is a validated methodology to assess the function of challenging behavior (Hanley, Iwata, & McCord, 2003). FBA uses an experimental approach for determining its discriminative and maintaining variables (Steege & Watson, 2009). Numerous studies in individuals with severe ID have shown that challenging behavior may be maintained by access to adult attention and preferred objects/activities and/or by escaping from a task demand (Hanley et al., 2003). That challenging behavior also may be maintained by positive and/or negative social reinforcement in individuals with AS, was suggested by (Clayton-Smith & Laan, 2003) and demonstrated by Strachan et al. (2009) and Allen et al. (2010). The latter two studies used FBA in the form of analogue baselines and observed the children while under several conditions that differed according to level of attention, availability of preferred activities

and demand. The frequency of challenging behavior varied across sessions, indicating that the children's challenging behaviors were maintained by environmental variables.

Challenging behavior is often preceded by other behaviors that are called precursors. When a precursor is not reinforced, challenging behavior may emerge, ultimately leading to reinforcement (Borrero & Borrero, 2008). Precursors and challenging behaviors are thus regarded as part of the same response class, presuming to be preceded and followed by the same maintaining variables or events, making them functionally equivalent (Carr & Durand, 1985; Petty, Allen, & Oliver, 2009). Interventions aimed at precursor behaviors have been shown to be effective in reducing challenging behaviors in individuals with ID (Borrero & Borrero, 2008; Langdon, Carr, & Owen-deSchryver, 2008). For example, Langdon et al. (2008) taught three children with severe to mild ID to replace their precursor behaviors for a communicative response. When their challenging behavior consistently followed within 30 sec of a certain behavior, this behavior was assumed to be a precursor. FBA revealed that the children's challenging behavior was escape-motivated. Upon exhibiting a precursor, they were prompted to exchange or touch a symbol for "stop", and this intervention resulted in a decrease in challenging behavior. Prompting individuals with ID upon the onset of a precursors, comprises a couple of advantages; the child is not disturbed by the (consequences) of his or hers challenging behavior (e.g. pain, discomfort) and it prevents the individual from chaining communicative behavior to challenging behavior (Reichle & Johnston, 1993).

The procedure whereby a type of challenging behavior is treated by teaching a functionally equivalent communicative response is also known as functional communication training (FCT; Carr & Durand, 1985; Langdon, Carr, & Owen-deSchryver, 2008). FCT has been shown to be highly effective in the treatment of challenging behavior and can be even more

successful when combined with extinction (Buckley & Newchok, 2005; Didden, Duker, & Korzilius, 1997; Kurtz et al., 2003). Studies on FBA and effectiveness of FCT on challenging behaviors in individuals with AS are scarce. Allen et al. (2010) taught five children with AS to press the button of a voice output device to make their request which led to a significant decline in challenging behavior in four children. In their research communicative behavior was prompted upon the onset of challenging behavior, not upon the possible precursor as was done in the current study. Strachan et al. (2009) used FBA, but did not assess the effectiveness of FCT on the challenging behavior of children with AS. Summers and Szatmari (2009) used FCT to teach three children with AS to request preferred items by exchanging an icon. Although these studies showed positive outcomes of FCT in individuals with AS, none of them used precursor as the onset of prompting communicative behavior. It remains to be assessed if such an intervention leads to a reduction in challenging behavior.

The aim of the current study, therefore, was fourfold: (a) to assess the function of challenging behavior in four children with AS using FBA, (b) to determine if precursor behaviors can be identified, (c) to assess whether FCT is effective in reducing challenging behavior, when prompting is based on precursors and (d) to assess if the communicative response is indeed functionally equivalent to the challenging behavior(s).

2. Methods

2.1. Participants

Participants were four children with AS who were between 5 and 18 years old (mean age in years;months: 8;6) and who showed challenging behavior at least once a day. According to results of Vineland-Z (de Bildt & Kraijer, 2003) all children had severe ID. The Vineland-Z

assesses the communicative and social capabilities and the capabilities regarding activities of daily living in individuals with ID. None of the children used words to communicate; they mainly reached for the desired item or pointed towards it for the purpose of requesting. Child C was able to exchange pictures for requesting desired activities. Three children lived at home with their parents and visited a day-care facility for children with ID. Child D lived in a sheltered facility for individuals with ID and joined a group for daytime activities during working hours. The diagnosis of AS was confirmed in each child by chromosomal testing. Only one child (i.e. child B) had epilepsy and she showed short absences which did not interfere with the study.

Throughout all phases of the study, the well-being of the children was closely monitored and sessions were terminated if the child appeared upset or too tired to cooperate. Parents were informed that their child's challenging behaviors could (temporarily) increase. All parents gave their informed consent.

Table 1. Characteristics of the children.

Child	Age (years)	Gender	Genetic subtype	Adaptive behavior[1]	Communicative ability[2]	Epilepsy
A	6	M	Deletion	61; 1;0-1;2	18 1;2-1;4	No
B	5	F	UBE3A-mutation	73, 1;2-1;4	26 1;6-1;8	Yes
C	5	M	UBE3A-mutation	80, 1;2-1;4	26 1;6-1;8	No
D	18	M	Deletion	70, 1;2-1;4	21 1;4-1;6	No

[1]Adaptive score derived from the Vineland-Z (de Bildt & Kraijer, 2003), age-equivalent in years;months.
[2]Communicative ability score derived from the Vineland-Z (de Bildt & Kraijer), age equivalent in years;months.

2.2. Setting

The study was conducted at the centre that the children visited at daytime, in a room with as little distraction as possible. Sessions primarily took place during the morning; some were carried out in the afternoon. Child C's FBA and FCT sessions were carried out during the regular break, during lunch and during a one-on-one play session in his classroom.

2.3. Procedure

2.3.1. Functional behavioral analysis

To assess the function of challenging behavior, an experimental functional analysis was conducted according to the format developed by Iwata, Dorsey, Slifer, Bauman and Richman (1994a). All sessions lasted for two-and-a-half (participant A, C and D) or five minutes (participant B). During the sessions, two to four adults were present, including the first author. One of these adults functioned as the therapist. To prevent sequence effects, the sessions were carried out in a random order for child A, B and D. As child C responded heavily on the unfamiliar room and adults, sessions were videotaped during the scheduled lunch in his classroom and his caretaker carried out the sessions, taking the role of the therapist. The following analogue conditions were in effect.

During the *control condition* the child received attention from the therapist who sang songs, played interaction games (e.g. peek-a-boo) and made eye contact to the child. No toys or other objects were used during this condition and the child was regularly praised for playing along. No consequences were scheduled for challenging behavior. This condition served as a control condition.

At the beginning of the *attention condition* the child was told that the therapist would talk to the other adult and that she would come back to the child in a minute. This was used to create a more natural situation. The therapist moved away from the child, but stayed within arm-reach. No physical, verbal or eye contact was made with the child. When the child displayed challenging behavior, eye contact was established and the child was told to stop after which the therapist withdrew herself from the child. This condition was used to assess if the child displayed challenging behavior to receive attention.

In the *tangible-edibles condition* the child received a piece of food instead of attention contingent upon an instance of challenging behavior, despite not having finished or swallowed the previous piece. All other behaviors of the child were ignored. This condition was only used for children A and C who often showed challenging behavior during mealtime.

The *tangible-toys condition* was identical to the previous condition, except that instead of food, a favorite toy was given to the child to play with for 20 sec contingent upon challenging behavior. At the beginning of every session, the child was allowed 10 sec of play with the toy.

Both tangible conditions were used to assess if the function of the challenging behavior was to request food or a toy and were only used when parents stated that challenging behavior was seen when the children wanted to receive such item. When challenging behavior occurred, the child was told s/he could play with the tangibles or have a piece of food. In child A and C, the tangible-edibles condition was performed with and without attention. In the first instance, the child received attention continuously. During the second condition the therapist withdrew herself from the child after she gave the child a piece of food. This was done to investigate if the availability of tangibles interacted with the level of attention. If the child was highly motivated to obtain food, the level of attention was hypothesized not to influence the frequency of challenging behavior (Iwata et al., 1994b).

In the *demand condition* the child was requested to put a small object in a box. Prompts were increased if the child did not comply following the least-to-most format (Duker, Didden, & Sigafoos, 2004). After finishing the task, regardless of the prompt, the child was shortly praised and the task was represented. When challenging behavior occurred, the task was withdrawn from the child and s/he was given a break. After 20 sec the task was offered again. When the child sought attention, the therapist shortly gave attention, said “hello” and looked at the child. If the

child showed challenging behavior directed at the task or the therapist during the time-out interval, a new 20 sec interval was started. This condition was used to assess if the child showed escape-motivated challenging behavior.

A small break was offered after one, two or three sessions, depending on the distractibility of the child. Four researchers randomly worked with the child as the therapist, to ensure the child showed the challenging behavior independent from researcher characteristics. Functional analysis ended when a stable pattern in the occurrence of challenging behavior became apparent, which yielded different numbers of sessions due to differences in number of conditions and child characteristics. In total, the time spent on functional analysis ranged from two to eight hours.

2.3.2. Functional communication training

Functional communication training (FCT) was carried out in the same condition in which challenging behavior was seen most often during FBA. The child was taught to exchange a referent object or picture to request for the objective that formerly maintained challenging behavior (as evinced during FBA), using the exchange phase of the Picture Exchange Communication System (PECS) (Bondy & Frost, 2001), which has been found to be very effective in teaching communicative behavior to individuals with ID (Lancioni et al., 2005). Requesting to escape from a demand was not taught, as the other behavioral functions were more prominent as indicated by results from FBA.

If the child showed a precursor (see Data Analysis) or reached for the referent the child was prompted to exchange the referent to the therapist. The intrusiveness of the prompt was reduced (prompt fading) until independent exchange was facilitated. Prompting ceased when the

child independently exchanged a referent or object at least 80% of trials during two consecutive sessions. No consequences were scheduled for challenging behaviors, thereby constituting an extinction condition. In the beginning of FCT for child A-edibles and B, challenging behavior was also followed by prompting. After session 24 (child A) and 42 (child B) extinction was implemented as their training did not progress. The choice of the referent picture or object depended on the capabilities of the child and was discussed with his or her caretakers. Except for child C, the FCT was administered by two to four adults, of whom one functioned as the therapist. The adults changed roles during training to prevent the child to depend on adult characteristics and to enhance generalization. As in FBA, the caretaker of child C carried out the FCT sessions. FCT sessions lasted for two-and-a-half minutes in all participants.

2.3.3. Design

Data were collected in an ABAB with follow-up design, whereby baseline sessions preceded FCT. After the FCT sessions, baseline sessions were repeated. The study ended with a few FCT sessions, in which prompting was withheld. A follow-up was conducted three to five months after training; these sessions equaled the procedure during the last training sessions wherein no prompting was administered.

Table 2. Definitions of coded behaviors

Behavior	Definition	Child
Hitting a person	Intentionally slapping the therapist with a flat hand.	A, B, C
Pinching a person	Pinching the therapist by squeezing its skin with two or more fingers.	A, B, C, D
Hair pulling	Pulling the hair of the therapist with one or both hands. Excludes holding on to the hair.	A, C, D
Back arching	When the child stretches its back, holds it stiff.	B
Throwing away items	Non-accidental throwing of an item	B, D
Pulling cloths	When the child pulls the cloths of the therapist.	B
Pulling diaper	Ripping small pieces from the diaper can include throwing these pieces away.	D
Throwing saliva	Throwing saliva from the mouth to the therapist.	D
Disruptive vocalisations	Verbal indications displayed by the child, indicating that he or she is feeling uncomfortable or in denial, including cries.	A, B, C
Laughter	Positive affect shown as a laughing vocalisation or a clear smile on the child's face.	
Physical contact	When the child makes physical contact with the therapist. Only when the physical contact is initiated or actively maintained by the child. For example, cuddling, grabbing and touching the therapist.	
Eye contact	When the child actively seeks eye contact with the therapist, by aimed looking or turning their heads to see the eyes of the therapist.	
Reaching	When the child extends his or her hand to the preferred tangible.	
Demand	When the child is in demand. Usually starts with an instruction; 'put the block in the box', or when the child is shown the materials. It ends after the onset of the time out or when the task is finished completely and the child receives praise.	
Reprimand	Any verbal request to stop the child from engaging in challenging behavior, or to tell the child that that was not good.	
Attention	When the therapist turns toward and gives positive attention to the child, for instance, praising the child, talking to child or singing a song.	
Time out from demand	Child is given a time out from his/her task. Starts usually with the phrase; 'Ok you can stop, go and play'	

2.3.4. Data collection

All sessions were videotaped and analyzed using *OBSWIN* software (Martin, Oliver, & Hall, 2001). Child and adult behaviors were coded (see Table 2 for the full list of codes). Different challenging behaviors were seen in the children, some of which occurred in low frequencies. As challenging behavior appeared during comparable situations and led to equal consequences, all separate challenging behaviors were combined into one variable to benefit

analysis, unless otherwise specified. When different functions were apparent, challenging behaviors were not combined.

2.3.5. Data analyzes

Experimental functional analyzes

Cohen's *d* was calculated to verify in which experimental condition most challenging behavior occurred compared to the frequency of challenging behavior during the control condition. Values above 0.2 indicated a small effect, above 0.6 a medium effect and values higher than 0.8 designated a large effect to the manipulated variable. Burst analyzes were also conducted (Oliver, Hall, & Murphy, 2005) in which tendencies in the probabilities of attention, demand and acquisition of tangibles surrounding challenging behavior were analyzed as to determine the function of the challenging behaviors. In burst analysis, all occurrences of the target behavior (challenging behavior or independent referent exchange) are pooled together ("the burst"), intervals between target behaviors are normalized and divided into percentiles. This analysis produces a graph, which consists of three different lines: the probability of a certain behavior occurring before, during and after the target behavior. The probabilities are depicted on the *y*-axis, the percentiles on the *x*-axis. For example, when the child was hypothesized to display challenging behavior to obtain attention, the probability of attention before the challenging behavior was expected to be very low and to rise afterwards, indicating that low levels of attention motivated the child to gain. This type of analysis goes beyond assigning a function to the challenging behavior solely based on the frequencies of challenging behaviors in several conditions. The level of laughter surrounding challenging behavior or independent referent exchange was also analyzed using the burst analysis. To benefit analysis, graphs for all children

were combined only when separate analyzes revealed comparable results. As differences between the tangible-edibles condition with or without attention were not clear, the data from both conditions were combined when using the burst analysis to enhance these results.

Precursor analysis

Two datasets were constructed; baseline and return to baseline data were combined as "baseline sessions", FCT session with and without prompting were combined as "training sessions". Tendencies in presumed precursors (eye-contact, looking at tangible, physical contact and reaching for tangible) surrounding challenging behavior in baseline sessions were compared using burst analysis, to determine if these behaviors were in fact precursors. When the probability of a certain behavior rose before the onset of challenging behavior, this was considered to be a precursor.

Functional communication training

Cohen's *d* was used to analyze the effectiveness of FCT, by comparing baseline session levels of challenging behavior with the levels in the last eight training sessions. When baseline session lasted for five minutes, the challenging behavior during the first two-and-a-half minutes was counted and this frequency was used in analyzes. Results from the follow-up sessions were not used in the calculation of the effect size.

Functional equivalence

To find evidence for functional equivalence between challenging behavior and independent referent exchange, burst analysis were used. The probabilities of the maintaining

variable (attention or acquisition of tangibles) surrounding challenging behavior during baseline sessions were compared with these probabilities surrounding independent referent exchange during training sessions. When functional equivalence was in effect, tendencies in both burst analyzes ought to be alike. To find further proof of functional equivalence, burst analysis were also used to compare tendencies in precursors and laughter surrounding both challenging behavior in baseline sessions and independent referent exchange in training sessions.

Reliability

Interobserver agreement was analyzed by calculating the kappa value. Twenty percent of the FBA and FCT sessions were coded by a second observer. Agreement was calculated on the presence of a variable within a 10 sec interval. The mean kappa of all kappa indices was 0.78 (0.39-1.0), indicating that the data could reliably be used for analysis.

3. Results

3.1. Functional analysis

The results from FBA are depicted in Figure 1A-D, Table 3 gives corresponding statistics. *Child A* showed challenging behavior in all conditions, even during the control condition and outliers were found in all conditions. His challenging behavior was highest during the attention condition (d = 1.19), followed by the tangible-edibles conditions (with attention: d = 0.63, without attention: d = 0.79) and the demand condition (d = 0.57). During the edibles conditions he showed disruptive vocalizations, in the attention condition he showed disruptive vocalizations, hair pulling, hitting and pinching of the therapist.

Compared to the control condition high levels of challenging behavior were shown by *child B* during the attention condition (d = 2.57) and in the demand condition (d = 1.7). Cohen's d indicated a stronger effect (d = 2.33) in the latter condition when disruptive vocalizations were not included as challenging behavior. Figure 2B shows that when the probability of a demand was high (left), child B indulged in challenging behavior (hair pulling, throwing away items and hitting the therapist). The graph depicting the probability of disruptive vocalizations surrounding challenging behavior (right) is mirrored, indicating that the disruptive vocalizations mainly occurred in periods wherein the level of demand was low (e.g. the time-out interval).

Child C showed a differentiated pattern in the level of challenging behavior across conditions. His challenging behavior consisted of hair pulling, pinching and hitting the therapist. Challenging behavior occurred during tangible-edibles with and without attention, with higher levels of challenging behavior in the tangible edibles condition without attention (d = 1.48) compared to when he did receive attention (d = 0.91).

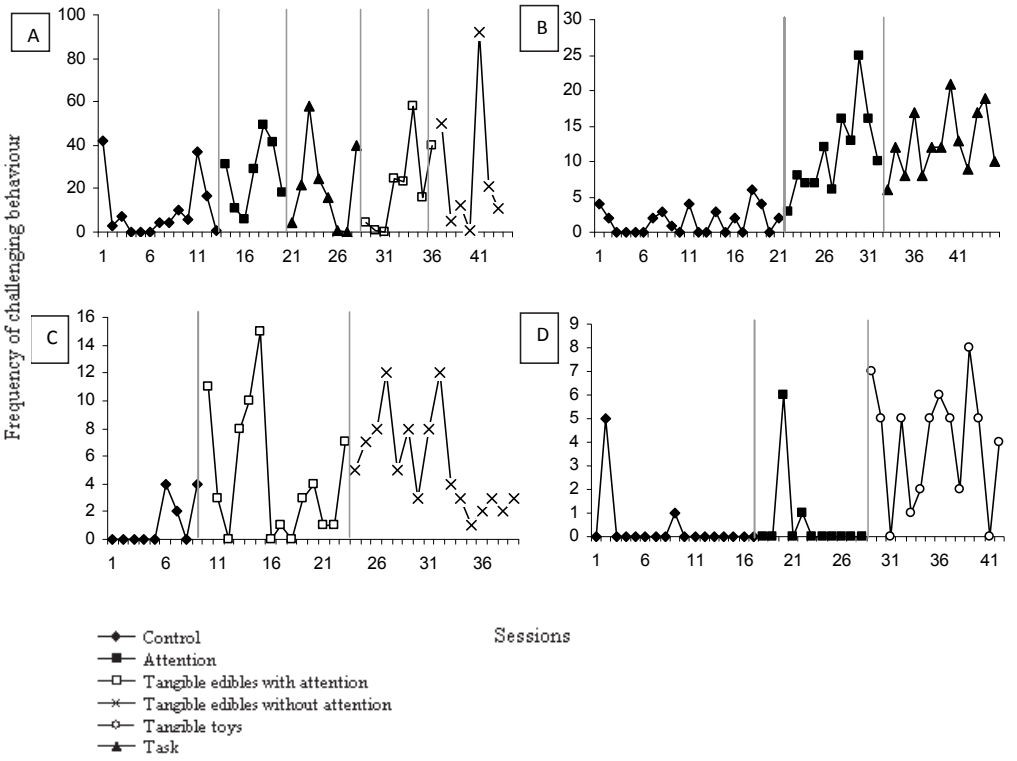
Child D showed most challenging behavior during the tangible-toys (reading a magazine) condition (d = 2.65). A small effect was found in the attention condition (d = 0.21). He showed hair pulling, pinching the therapist, pulling his diaper and throwing saliva at the therapist.

Table 3. Statistics for analogue conditions per child.

Child/ Condition	A mean (range)	B mean (range)	C mean (range)	D mean (range)
Control	10.1 SD 13,9 (0-42)	1.57 SD 1.83 (0-6)	1.11 SD 1.76 (0-4)	0.35 SD 1.22 (0-5)
Attention	26,43 SD 15.68 (6-49)	11.18 SD 6.18 (3-25)		0.64 SD 1.8 (0-6)
Tangibles A[1]	20.88 SD 20.73		5.38 SD 3.44	
B	(0-58)		(1-12)	
C	27.43 SD 32.74 (1-92)		4.57 SD 4.83 (0-15)	3.93 SD 2.53 (0-8)
Escape	19.22 SD 20.64 (0-51)	12.62 SD 4.83 (6-12)		

[1] A=edibles with attention, B=edibles without attention, C=toys

Figure 1A-D. Frequency of challenging behavior during baseline sessions of participant A, B, C and D.



To further analyze the behavioral function, the probabilities of the assumed maintaining variables occurring before, during and after the occurrence of challenging behavior were assessed using burst analysis (see Figure 2A). Child A, C and D (left) displayed challenging behavior when the probability of access to a preferred tangible was very low. In child A and B (right), the probability of attention was on its lowest before the onset of challenging behavior. Figure 3 shows a decline in laughter before the onset of challenging behavior and independent referent exchange and a rise afterwards. Due to low levels of laughter for child A-edibles, C and D, no graphs could be depicted.

Figure 2. (a) Probability of a receiving a tangible before, during and after the burst of challenging behavior in analogue baseline sessions combined for child A, C and D (left). Probability of attention before, during and after the burst of challenging behavior in analogue baseline sessions, combined for child A and B (right). (b) Probability of a demand before, during and the burst of challenging behavior (left) and disruptive vocalisations (right) in analogue baseline sessions for child B.

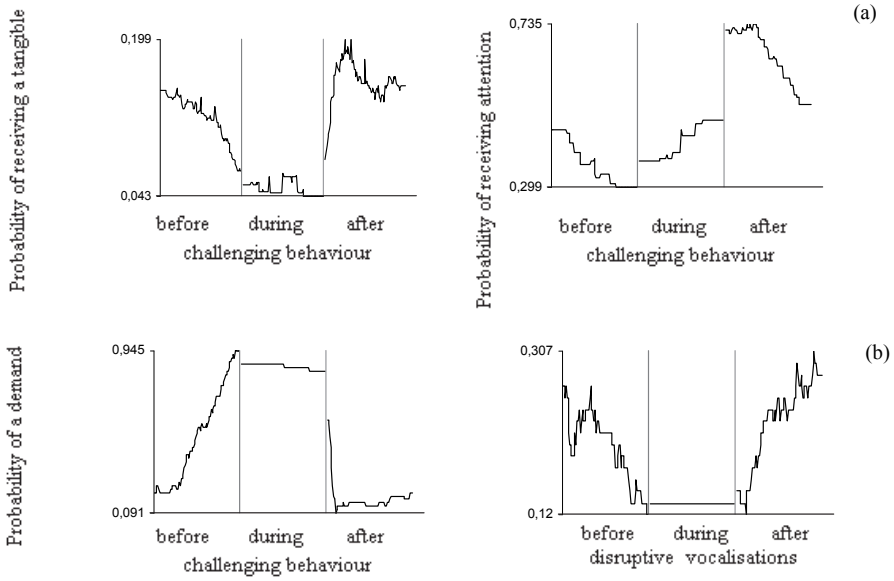
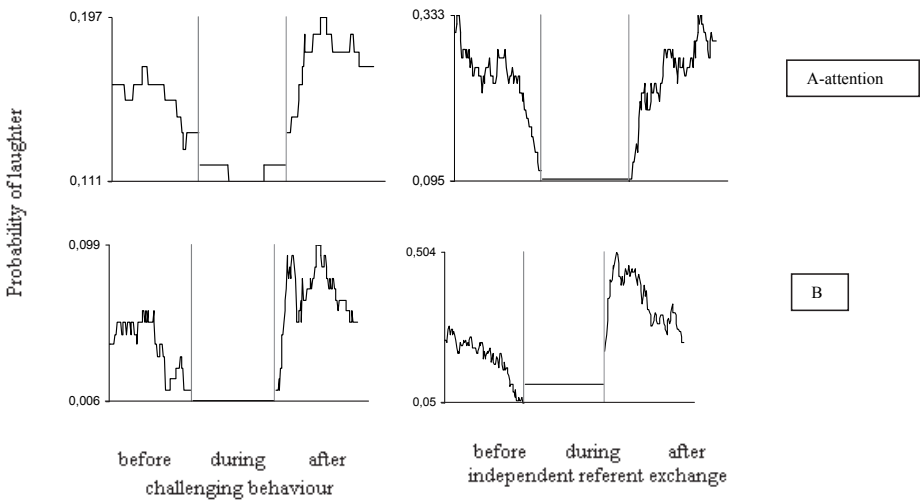


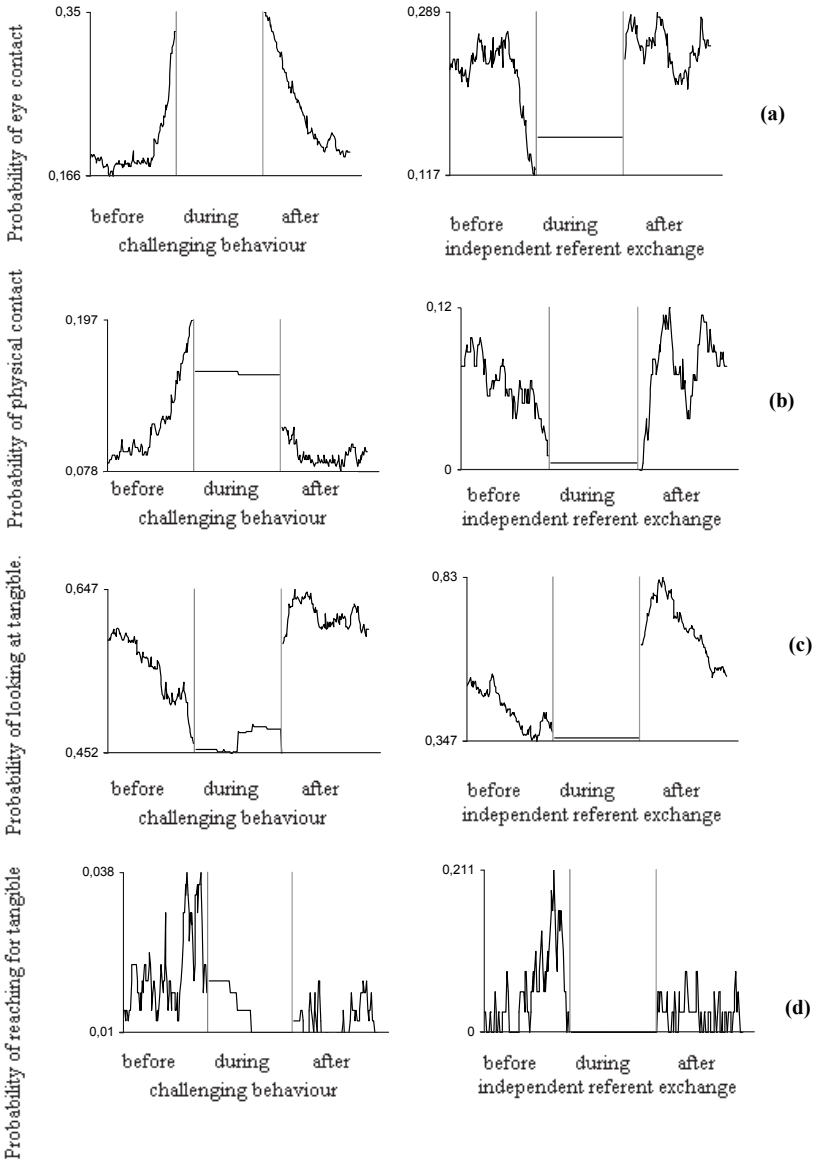
Figure 3. Probability of laughter before, during and after the burst of challenging behavior during baseline sessions (left) and the burst of independent referent exchange in training sessions (right) in child A-attention and B.



3.2. Precursor analysis

Figure 4a indicates that all children showed an increase in *eye-contact* prior to challenging behavior during baseline sessions. When the probabilities of eye contact prior to challenging behavior were analyzed for every child separately, the probabilities were higher for children who showed this behavior during attention condition than during the tangible conditions. During training sessions, the probability of eye contact in child A, B and C declined prior to the independent referent exchange and was higher afterwards. The level of eye contact for child D was very low and showed a constant pattern throughout the training sessions. Except for child A-edibles, who showed very little physical contact, all children showed an increase in *physical contact* prior to the display of challenging behavior in the baseline sessions (see Figure 4b). An opposite tendency was found during the training sessions, as physical contact decreased before and increased after the independent exchange of the referent. The graphs for *looking at tangible* both show a decline in this behavior before the onset of challenging behavior and independent referent exchange, with a small increase before engaging in challenging behavior or exchanging the referent (see Figure 4c). After the occurrence of both behaviors, looking at the tangible increased. The probabilities of *reaching for tangible* strongly increased before the onset of challenging behavior and independent exchange of the referent (see Figure 4d). Child A-edibles and C did not show reaching for the tangible during training sessions.

Figure 4. **(a)** Probability of eye-contact before, during and after the burst of challenging behavior in baseline sessions of all children (left) and before of the independent referent exchange in training sessions for child A, B and C (right). **(b)** Probability of physical contact before, during and after the burst of challenging behavior during baseline sessions (left) and of the independent exchange of the referent (right), graphs combined for child A-attention, B, C and D. **(c)** Probability of looking at tangible before, during and after the burst of challenging behavior during baseline sessions (left) and of independent referent exchange training sessions (right) combined for child A, C and D. **(d)** Probability of reaching for the tangible before, during and after the burst of challenging behavior during baseline sessions for child A-eating, C and D (left) and of independent referent exchange during training sessions (right) for child D.



3.3. Functional communication training

Figures 5a, b, c and d show the effectiveness of FCT on the frequency of challenging behavior. *Child A and B* were taught to request for attention. *Child A and C* were taught to request for food, and child D to request for a magazine. Figure 5a-I (tangible-edibles) shows that when the frequency of challenging behavior for *child A* during baseline sessions is compared with its frequency during the last eight training sessions, a small effect was found (d = -0.21). Figure 5a-II (attention) shows the results of the FCT to request for attention in *child A*, FCT had a large effect (d = -1.27). Only hair pulling and pinching were incorporated as challenging behaviors, as these behaviors were only apparent during the attention conditions and disruptive vocalizations appeared in all conditions, indicating that hair pulling and pinching presumably functioned to receive attention. For *child B*, FCT had a large effect (d = -1.44, see Figure 5b). The graphs for *child C and child D* show that FCT was highly effective in reducing their challenging behavior, showing large effect sizes (d = -1.49, d = -2.06, see Figure 5c and 5d).

During follow-up*, child A, B and C* independently exchanged their referent. Only child A was prompted in the second, third and fourth follow-up session during the attention condition. At follow-up, *child A* showed high levels of disruptive vocalizations during the tangible-edibles condition. *Child D* showed challenging behavior at baseline levels during follow-up sessions. He only exchanged the referent independently during follow-up session four, five and seven. During this last session, no challenging behavior was seen.

Figure 5a-I, 5a-II, b, c and d. Frequency of challenging behavior during baseline, training, return to baseline and follow up sessions for all participants.

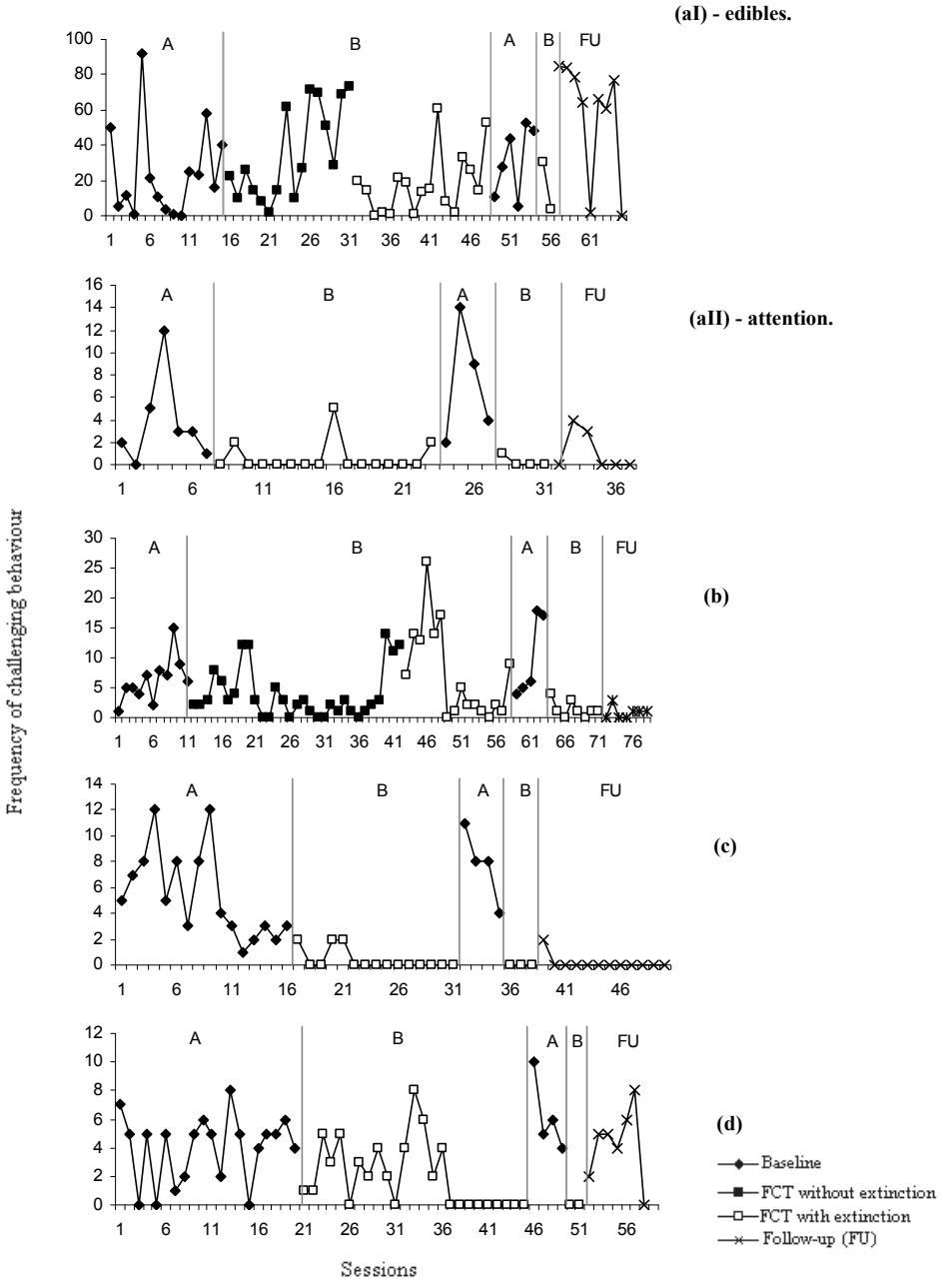
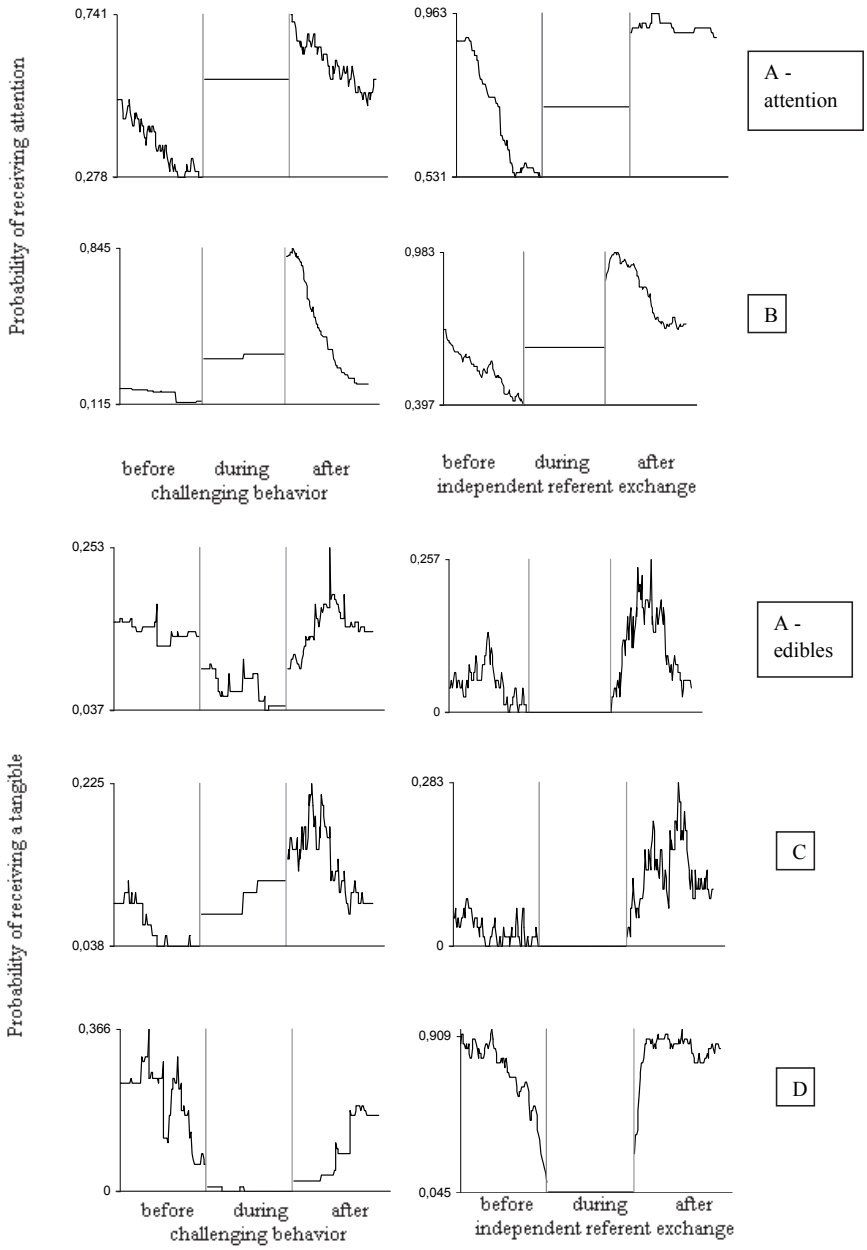


Figure 6. Probability of receiving attention (child A-attention and B) or having access to the preferred tangible (child A-eating, C and D) before, during and after the burst of challenging behavior during baseline sessions (left) and of independent referent exchange in training sessions (right).



3.4. Functional equivalence

Figure 6 shows similar tendencies in probabilities of having access to a preferred tangible or to attention surrounding bursts of challenging behavior (left) or independent referent exchange (right). Probabilities of the reinforcing variables are on their lowest, before challenging behavior or independent referent exchange is initiated.

4. Discussion

In this study, functional analysis identified a behavioral function for challenging behavior in four children with Angelman syndrome. All children learned to independently exchange a referent picture or object, which resulted in a decrease in challenging behavior. They showed skill maintenance over a period of three to five months. This study expands the one by Allen et al. (2010) by prompting communicative behavior upon the onset of the precursor instead of the challenging behavior and by using referent pictures and objects instead of a voice output communication aid.

4.1. Functional analysis

Results of FBA indicated that the frequency of the children's challenging behavior was influenced by the level of attention, access to tangibles and to a lesser extent by demand. FBA yielded differentiated patterns of responding across conditions suggesting that their challenging behaviors served one or more operant functions.

When the challenging behavior was maintained by adult attention, the probability of laughter declined before the onset of both challenging behavior and independent referent exchange and rose when the therapist turned towards and gave attention to the child. This

tendency was not seen when challenging behavior functioned to receive a preferred tangible. As in the tangible condition the children focused their eye gaze on the preferred tangible, less eye-contact was made with the adult, which could be an explanation for the lower probability of laughter during these sessions. This corroborates the finding that environmental variables influence the levels of challenging behavior and laughter in individuals with AS (Allen et al., 2010; Oliver et al., 2007; Strachan et al., 2009). FBA can reliably be used in individuals with AS and should be the starting point of treatment for their challenging behavior (Hanley, Iwata, & McCord, 2003).

4.2. Precursor behavior

In all children, precursor behaviors were identified; eye and physical contact and reaching for the preferred tangible were found to precede challenging behavior. The probability of looking at the preferred tangible rose directly after the display of challenging behavior, instead of before the occurrence of this behavior. This may suggests that the children were very interested in their reïnforcers (Saunders et al., 2005), thereby supporting the results of the FBA that their challenging behavior functioned to receive tangibles. Making eye-contact and looking at the tangible cannot be done simultaneously; explaining why looking at tangible did not show to be a clear precursor. The precursor analyzes give strong implications that challenging behavior was preceded by other behaviors. This is in accordance with previous research, which found that proto-imperatives such as hand-gestures and vocalizations reliably precede challenging behavior in individuals with AS and other ID (Langdon et al., 2008; Petty et al., 2009). Attention seeking behaviors are common in AS, but should not merely be seen as part of their behavioral phenotype, especially when challenging behavior is at hand. As was shown in this research,

attention seeking behaviors as eye contact and physical contact may be conceptualized as precursors and should be targeted for treatment for challenging behavior. Consequences or prompting for communicative behavior should be administered upon the onset of a precursor, thereby preventing and eliminating challenging behavior, which builds on previous findings (Borrero & Borrero, 2002; Langdon et al; 2008; Reichle & Johnston, 1993).

4.3. Functional communication training

A large effect of FCT on the levels of challenging behaviors was found for all children. The effect sizes in child A-tangible-edibles and B were low compared to the other children. In these children disruptive vocalizations were considered as challenging behaviors. Exchanging a referent is not incompatible with vocalizing, indicating that both behaviors could occur simultaneously, thereby explaining why disruptive vocalizations did not fully decrease as a function of the new communicative response as every act of communicative behavior was responded to in this research. The taught communication skill was maintained over a period of three to five months even without frequent one-on-one FCT, a result not found in earlier research on FCT in AS. This implicates that FCT, with the onset of the precursor as the starting point for training, is an effective method to decrease challenging and increase communicative behavior in individuals with AS. The latter being an important educational goal in itself.

4.4. Functional equivalence

In all children, challenging behavior and independent exchange of the referent both occurred when probabilities of reinforcements were low, establishing the presumed functional equivalence of both behaviors. When precursors and laughter surrounding challenging behavior

during baseline sessions and independent referent exchange during training sessions were compared, tendencies in reaching for and looking at the preferred tangible and laughter were similar, favoring the functional equivalence hypothesis. An opposite tendency was seen for eye and physical contact (see Figure 4a and 4b). Eye contact and physical contact increased before the onset of challenging behavior, but decreased before independent referent exchange. An explanation is that during training, children were very interested in the referent and looked at and touched it before exchanging it and could not simultaneously look at or touch the therapist (Saunders et al., 2005). The probabilities of eye contact, physical contact and looking at the tangible were higher before the onset of challenging behavior than before the onset of independent referent exchange (see Figure 4a, 4b and 4c), which also strengthens the functional equivalence hypothesis. As the children were taught to request for the tangible or attention, they did not need to try and communicate this in any other way. This study not only shows that challenging behavior decreases as a function of FCT, but burst analysis also shows that challenging behavior is employed at the same level of reinforcement as the newly taught communicative behavior. This adds to the literature in that functional equivalence is not only assumed through indirect measures (e.g. decreases in challenging behavior), but is made visible in a direct way. Results from this study give further evidence for the influence of environmental factors on challenging, precursor and/or communicative behaviors in individuals with AS.

4.5. Limitations and implications for further research

The outcomes of this study combined with those of the study of Allen et al. (2010) show that FBA and FCT can successfully be used to treat challenging behavior in individuals with AS. But as only four individuals participated in this research, caution should be taken when

generalizing the results of this research to other individuals with AS. Precursors were identified, but the nature of the precursor can differ per individual.

Not all experimental conditions were used according to the format of Iwata et al. (1994a) and not all behavioral functions were analyzed in every child in this research. The main reason for this was that experimental functional analyzes was reduced to a minimal time span to enhance efficiency and effectiveness, as individuals with AS are known to have a short concentration span (Clayton-Smith & Laan, 2003) and could not partake in the sessions for longer periods of time. Non-social behavioral functions (e.g. automatic reinforcement or arousal reduction) were not included as parents did not provide the researches with clear evidence that their child's challenging behavior functioned to alleviate physical discomfort and as individuals with AS show pleasure in interacting with others (Oliver et al., 2007), automatic reinforcement was not considered a highly likely function for their challenging behavior. In the contrary, challenging behavior was seen during multiple social conditions during experimental functional analysis, indicating that more non-social functions could have been at hand (Iwata et al., 1994b). Future studies should focus on functional assessment and communication training in more natural settings opposed to clinical settings. As researchers and conditions do not completely mimic every day life situations, this may cause differences in responding and difficulties in generalizing the results (Huete & Kurtz, 27; Matson & Mishawi, 2007). This may especially be the case in AS, as autism spectrum disorder (ASD) has been linked with AS (Trillingsgaard & Østergaard, 2004). Individuals with ASD are especially sensitive to changes in their environment and may react to these, thereby altering their way of responding. This was seen in child C in the research. Further, Clayton-Smith (2001) named that challenging behavior in AS was often seen when a change in routine or caretakers emerged. Training in natural settings can also be advised

as children with AS showed more social approach towards mothers than towards strangers (Mount, Oliver, Berg, & Horsler, 2011). Finally, in this research, children were only taught to exchange one referent thereby limiting their communication possibilities. Research on correct use of multiple referents when offered simultaneously determines if individuals with AS syndrome can make correct choices, providing them with more independence and thereby increasing their quality of life.

5. Acknowledgements

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6. Declaration of interest

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7. References

Allen, D., Oliver, C., Webster, P., Reid, D., Villa, D., Beaumont, S., … Radstaake, M. (2010). Behavioral intervention for challenging behavior in children with Angelman syndrome.

Journal of Intellectual Disability Research, 54, 885.

Buckley, S. D., & Newchok, D. K. (2005). Differential impact of response effort within a response chain on use of mands in a student with autism. *Research in Developmental Disabilities, 26,* 77-85.

Bondy, A., & Frost, L. (2001). The Picture Exchange Communication System. *Behavior Modification,* 25, 725-744.

Borrero, C. S. W., & Borrero, J. C. (2002). Descriptive and experimental analyzes of potential precursors to problem behavior. *Journal of Applied Behavior Analysis, 41*, 83-96.

Carr, E. G., & Durand, M. V. (1985). Reducing challenging behaviors through functional communication training. *Journal of Applied Behavior Analysis, 18,* 111-125.

Clayton-Smith, J. (2001). Angelman syndrome: Evolution of the phenotype in adolescents and adults. *Developmental Medicine & Child Neurology, 43*, 476–480.

Clayton-Smith, J., & Laan, L. (2003). Angelman syndrome: A review of the clinical and genetic aspects. *Journal of Medical Genetics, 40*, 87-95.

De Bildt, A.A., & Kraijer, D. W. (2003). *Vineland-Z: Sociale zelfredzaamheidschaal voor kinderen en jeugdigen met een verstandelijke beperking.* [Vineland Adaptive Behavioral Scales, Survey Form]. Leiden: PITS.

Didden, R., Duker, P., & Korzilius, H. (1997). Meta-analytic study on treatment effectiveness of problem behavior with individuals who have mental retardation. *American Journal of Mental Retardation, 101,* 387–399.

Duker, P. C., Didden, R., & Sigafoos, J. (2004). *One-to-One training: Instructional procedures for learners with developmental disabilities.* Austin, TX: Pro-ED. p 8-11.

Hanley, G. P., Iwata, B. A., & McCord, B. E. (2003). Functional analysis of challenging

behavior: A review. *Journal of Applied Behavior Analysis, 36*, 147-185.

Huete, J. M., & Kurtz, P.F. (2010). Therapist effects on functional analysis outcomes with young children. *Research in Developmental Disabilities, 31*, 804-810.

Iwata, B. A., Dorsey, M. F., Slifer, K. J., Bauman, K. E., & Richman, G. S. (1994a). Towards a functional analysis of self-injury. *Journal of Applied Behavior Analysis, 27*, 197-209.

Iwata, B. A., Pace, G. M., Dorsey, M. F., Zarcone, J. R., Vollmer, T. R., Smith, R. G., … Willis, K. D. (1994b). The functions of self-injurious behavior: An experimental-epidemiological analysis. *Journal of Applied Behavior Analysis, 27*, 215-240.

Kurtz, P. F., Chin, M. C., Huete, J. M., Tarbox, S. F., O'Connor, J. T., Paclawskyj, T.R., & Rush K. S. (2003). Functional analysis and treatment of self-injurious behavior in young children: A summary of 30 cases. *Journal of Applied Behavior Analysis, 36*, 205–219.

Lalande, M., & Calciano, M. A. (2007). Molecular epigenetics of Angelman syndrome. *Cellular and Molecular Life Sciences, 6,* 947-960.

Lancioni, G. E., O'Reilly, M. F., Cuvo, A. J., Singh, N. N., Sigafoos, J., & Didden, R. (2005). PECS and VOCAs to enable students with developmental disabilities to make requests: An overview of the literature. *Research in Developmental Disabilities, 2*, 468–488.

Langdon, N. A., Carr, E. G, & Owen-DeSchryver, J. S. (2008). Functional analysis of precursors for serious problem behavior and related intervention. *Behavior Modification, 32*, 804-827.

Martin, N., Oliver, C., & Hall, S. (2001*). Obswin: software for the collection and analysis of observational data.* Birmingham, UK: University of Birmingham.

Matson, J. L., & Minshawi, N. F. (2007). Functional assessment of challenging behavior:

Toward a strategy for applied settings. *Research in Developmental Disabilities, 28*, 353-361.

Mount, R., Oliver, C., Berg, K., & Horsler, K. (2011). Effects of adult familiarity on social behaviors in Angelman syndrome. *Journal of Intellectual Disability Research, 55,* 339-350.

Oliver, C., Hall, S., & Murphy, G. (2005). The early development of self-injurious behavior: evaluating the role of social reinforcement. *Journal of Intellectual Disability Research, 49,* 591-599.

Oliver, C., Horsler, K., Berg, K., Bellamy, G., Dick, K., & Griffiths, E. (2007). Genomic imprinting and the expression of affect in Angelman syndrome: What's in the smile? *Journal of Child Psychiatry, 48*, 571-579.

Petty, J., Allen, D., & Oliver, C. (2009). Relationship among challenging, repetitive, and communicative behaviors in children with severe intellectual disabilities. *American Journal on Intellectual and Developmental Disabilities, 14,* 356-368.

Reichle, J., & Johnston, S. S. (1993). Replacing challenging behavior. The role of communication intervention. *Topics in Language Disorders, 13,* 61-76.

Saunders, M. D., Saunders, R. R., Mulugeta, A., Henderson, K., Kedziorski, T., Hekker, B., & Wilson, S. (2005). A novel method for testing learning and preferences in people with minimal motor movement. *Research in Developmental Disabilities, 26,* 255-266.

Steege, M. W., & Watson, S. T. (2009). *Conducting school-based functional behavioral assessments: A practitioner's guide. 2nd ed*. New York, NY: Guilford Press, p16.

Strachan, R., Shaw, R., Burrow, C., Horsler, K., Allen, D., & Oliver, C. (2009). Experimental functional analysis of agression in children with Angelman Syndrome. *Research in*

Developmental Disabilities, 30, 1095-1106.

Summers, J. A., & Szatsmari, P. (2009). Using discrete trial instruction to teach children with Angelman. *Focus on Autism and Other Developmental Disabilities, 24,* 216-226.

Trillingsgaard, A., & Østergaard, J. R. (2004). Autism in Angelman syndrome. *Autism, 8*, 163-174.

Williams, C. A. (2010). The behavioral phenotype of the Angelman Syndrome. *American Journal of Medical Genetics, 154C,* 432-437.

Chapter 3

Functional analysis and functional communication training in the classroom for three children with Angelman syndrome

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Abstract

Effectiveness of functional analysis (FA) and functional communication training (FCT) on challenging behavior was assessed in three children with Angelman syndrome (AS). Analogue FA conditions were used to assess the behavioral function of the challenging behavior. FA and FCT protocols were administered in the children's classroom and were performed by their teachers. Replacement behavior was prompted upon the onset of precursor behavior. One or more function(s) of their challenging behavior were identified and challenging behavior appeared to be escape or tangibly motivated. Making physical contact with the teacher was found to be a precursor of challenging behavior in one child. In all children, challenging behavior decreased as a function of FCT. Functional equivalence of both challenging and replacement behavior was evinced. Clinical and research implications are discussed.

1. Introduction

Angelman syndrome (AS) is a rare genetic disorder caused by the absence or malfunctioning of chromosome 15q11-13 (Lalande & Cacliano, 2007). Individuals with AS have severe intellectual disability (ID) and many suffer from epilepsy. The behavioral phenotype consists of an easy evocable laughter, absence of speech, and a tremulous and ataxic gait. They are often known for their apparent happiness and positive social disposition (Williams, 2010).

Individuals with AS also present with challenging behaviors (e.g., self-injury, aggression, and property destruction) that may serve a communicative function (Didden et al., 2009; Strachan et al., 2009). For example, Radstaake, Didden, Oliver, Allen, and Curfs (2012) conducted a functional analysis of the challenging behaviors of four children with AS and identified access to attention and tangibles and escape from demands to be maintaining events. Challenging behavior was reduced following functional communication training (FCT; Tiger, Hanley, & Bruzek, 2008). FCT involves teaching a communicative response functionally equivalent to challenging behavior (Carr & Durand, 1985). In the Radstaake et al. (2012) study, participants were taught to use pictures and small objects as a means to request attention, tangibles, and breaks from work.

Challenging behavior frequently involves a precursor, that is, a relatively benign behavior that reliably precedes and serves the same function as the challenging behavior (Borrero & Borrero, 2008). Implementing FCT contingent upon the occurrence of a precursor behavior may facilitate the acquisition of the communicative behavior by ensuring that the discriminative stimuli and motivating operations that should evoke this behavior are in place (Langdon, Carr, & Owen-deSchryver, 2008). Radstaake et al. (2012) demonstrated the decline in challenging behavior after implementing FCT contingent upon precursor behavior for children with AS in a

barren contrived setting and a classroom. Behavioral changes achieved in contrived environments may fail to generalize to more natural environments (e.g., homes and schools) unless strategies to promote generalization are included in intervention (Stokes & Baer, 1977). One strategy to prevent resurgence of challenging behavior is to conduct FCT in the natural environment and involve caregivers present in those environments in the implementation of the functional analysis (FA) and intervention (Lang, Sigafoos, Lancioni, Didden, & Rispoli, 2010; Ringdahl & Sellers, 2000; Stokes & Baer, 1977; Wood, Cho-Blair, & Ferro, 2009). For individuals with developmental and intellectual disabilities other than AS, FA and FCT has been effectively administered by caregivers (e.g., parents and teachers) in homes, schools, and community settings (Lydon, Healy, O'Reilly, & Lang, 2012; Ringdahl & Sellers, 2000; Tait et al., 2004; Tiger et al., 2008). However, there is a paucity of research involving caregivers of children with AS in their child's education and care (Leyser & Kirk, 2011).

This study replicates and extends previous research by Allen et al. (2010) and Radstaake et al. (2012) by training teachers to conduct a FA and implement FCT for three children with AS in their classroom. Specifically, this study aims to: (a) identify behavioral functions of challenging behavior with a FA, (b) identify precursor behaviors, (c) assess if challenging behavior decreases as a function of FCT and (d) determine if challenging behavior and communicative behavior are functionally equivalent.

2. Materials and methods

2.1. Participants

Participants were three children diagnosed with AS, which was confirmed by chromosomal testing conducted prior to this study. All three participants had severe ID and no

functional speech. They lived at home with their parents and attended a specialized daycare center. Prior to the study, Amy and Cody communicated occasionally with simple points and gestures. Bob reached for desired objects. Bob and Cody had epilepsy that was controlled by medication. Parents gave their informed consent. Table 1 provides participant characteristics.

Table 1 Characteristics of participants

	Child		
	Amy	Bob	Cody
Gender	Female	Male	Male
Age/Developmental Age	7 / 1;6 years [a]	15 / 0;6-1;0 years[b]	6 / 1;5-2;5[b]
Subtype	Imprinting error	Deletion	Mutation
Epilepsy	No	Yes	Yes
Main behavioral function	Escape from task	Receiving tangibles	Escape from task
Precursor(s)	Not Identified	Making physical contact with teacher	Not identified
Replacement behavior	Referent object	Speech-generating device	Speech-generating device

[a]Developmental age in years;months, score derived from the Bayley Scale of Infant Development (BSID-II-NL, Van der Meulen, Ruiter, Lutje Spelberg and Smrkovsky 2002).
[b]Developmental age in years;months, scores derived from Vineland Adaptive Behavior Scales (VABS, De Bildt and Kraijer 2003). F=female, M = male

2.2. Setting

FA and FCT sessions were conducted in the participants' typical classroom at the daycare center. This classroom initially contained other students with moderate to severe ID and up to three teachers. FA in the classroom in which peers were present did not lead to conclusive results in all three participants and assessment was continued in a classroom without peers, to minimize distraction. This was the case for all sessions of Bob and the demand-escape sessions of Amy and Cody.

2.3. Procedure

2.3.1. Teacher training

In a meeting prior to the FA and the FCT sessions, the aims of the study were explained to the teachers. They were given verbal and written instructions as to how and when to administer the prompts and consequences during the sessions. The first author was present during all FA and FCT sessions.

2.3.2. Functional analysis

Analogue FA conditions were used to assess the behavioral function of the children's challenging behaviors (Iwata et al. 1982; 1994). A teacher and one or two researchers (first and fifth author) were present during all sessions. The FA conditions were individualized for each participant based upon information obtained by interviewing parents and teachers. The tangible-edibles and demand-escape sessions were performed sequentially; other sessions were implemented in a random order to minimize sequence effects. Tangible-edibles sessions were performed during lunchtime as it was considered unnatural to allow a child to eat for 2.5 minutes, and to continue with the other FA conditions consecutively. The initial FA for Amy and Cody did not produce conclusive results. Therefore, the demand-escape condition was added to the analysis even though that function was not hypothesized by parent and teacher interviews. Due to the teachers' time limitations and in order to minimize strain on the participants, all FA conditions were based on 2.5-min sessions, no more than three conditions were run consecutively without a break, and the demand-escape sessions were performed sequentially as the other FA sessions were already done. For Cody, two demand-escape sessions were followed by a play condition. Three or more of the following conditions were used in a manner similar to that described by Iwata et al. (1982; 1994).

Play condition (Amy and Cody). During the high attention condition the child received continuous attention from the teacher. For instance, playing peek a boo games or singing songs. No consequences were scheduled for challenging behavior. This condition served as the control condition.

Attention condition (Amy and Cody). In this condition, the teacher told the child that she would talk to another adult in the room and would return to the child soon. Contingent upon challenging behavior, the teacher returned to the child and said, "Stop doing that" while physically interrupting or blocking the challenging behavior. The teacher then moved away from the child and turned to talk to the other adult.

Tangible-edibles condition (Bob). The child was given a piece of bread. Once the child consumed the bread, additional bread was only given contingent upon challenging behavior.

Tangible-toys condition (Amy, Bob and Cody). Prior to this condition the child was given brief access to a preferred toy. A session began when the toy was taken away. The toy was returned to the child for 20-s contingent upon challenging behavior.

Demand-escape (Amy and Cody). Task demands typically implemented in school were selected for Cody. Amy's task demand was to finish her drink. The child was prompted to complete a task. When the child did not comply with the teacher's request, s/he was prompted with a more intrusive prompt to perform the task following a least-to-most prompting procedure. After completion of each task, another task was presented. Contingent upon challenging behavior the task materials were removed and a 20-s time-out was given in which the child was allowed to leave his or her seat. Following the time-out interval the task was reinstated. Challenging behavior during the time-out interval did not prolong this interval.

Demand-drink (Amy). This condition was the same as the demand-work condition, except Amy was not allowed to leave her seat after the drink was taken away following challenging behavior. This individualized condition was only used with Amy, because teachers stated that challenging behavior was often seen during drink situations in the classroom.

Alone (Bob). During this condition no attention or toys were given to the child, and no consequences were programmed for challenging behavior. This condition was used to assess if automatic reinforcement maintained challenging behavior and was used for Bob as the control condition, because during the play condition Bob consistently moved away from his teacher and was disinterested in play making the play condition unsuitable as a control condition.

2.3.3. Functional communication training

FCT was conducted in the participants' classroom. Replacement behaviors for each participant can be found in Table 1. Previous research supports the use of picture exchange and speech-generating device as replacement behaviors in FCT (see e.g., Lancioni, O'Reilly, Cuvo, Singh, & Didden, 2007; Rispoli, Franco, van der Meer, Lang, & Camargo, 2010). The Picture Exchange Communication System training protocol was used to teach PECS to Amy (Bondy & Frost, 2001), using a small object instead of a picture. Prompts were given on the onset of the potential precursors (see *2.6.2.* Precursor analysis) and no consequences were scheduled for challenging behavior. A precursor behavior was not identified for Cody. Cody was prompted to press the single-button speech-generating device (BIGmack®) on the onset of challenging behavior. In Amy, initial FCT sessions were done in the demand-drink situation, but she did not respond to prompting, appeared not to be interested in the reinforcer and threw away the referent object throughout the sessions. It was decided to repeat baseline sessions and she was now

allowed to leave her table after challenging behavior, thereby constituting the demand-escape condition and this condition was used during FCT.

When the child communicated that he or she wanted a time out from task during a time-out interval, the child was told that s/he already had a time-out from task. This did not prolong the time-out interval. When challenging or replacement behavior would have been reinforced, chances were relatively high that the entire session would become a time-out interval, as sessions lasted only 2.5 min. In this way, the child would not experience the contingencies of the escape hypothesis (i.e. escape from task contingent upon target behavior). When the child requested a piece of food while eating a piece of food, s/he was offered another piece. The communication aids or objects were available to the children throughout all training sessions.

2.4. Design

FA results were evaluated in a multielement design. The effects of FCT were evaluated in an ABAB design in which "A" represented baseline and "B" represented FCT. No prompts to engage in the replacement behavior were delivered during the final FCT phase to measure the occurrence of unprompted replacement behavior.

2.5. Data collection and dependent variables

All sessions were recorded on camera and OBSWIN software was used to code and analyze the data (Martin, Oliver, & Hall, 2001). The behaviors of the children and teachers were coded. Operational definitions of the precursor, challenging and replacement behaviors and reinforcements are given in Table 2. Different topographies of challenging behavior were collapsed and coded only as challenging behavior.

The fifth author coded all sessions. Twenty percent of all baseline, training and training evaluation sessions were randomly selected and coded independently by a second observer (first author). The variables have been used in other studies (Allen et al. 2010; Radstaake et al. 2012) and were found to be reliable. The kappa value was calculated on the presence of the variable within a10-s interval. Mean kappa was 0.78 (0.36-1), indicating reliable and accurate coding.

Table 2. Codes and definitions per child

Behavior	*Definition*	*Child*
Head banging	Banging the head towards an object or the ground.	Bob
Hitting a person	Intentionally slapping the teacher with a flat hand.	Bob, Cody
Kicking a person	Intentionally kicking the teacher with his or her foot.	Cody
Hitting him or herself	Slapping him or herself with a flat hand.	Bob
Pinching a person	Pinching the teacher by squeezing its skin with two or more fingers.	Amy, Bob,Cody
Hair pulling	Pulling the hair of the teacher with one or both hands. Excludes holding on to the hair without downward pull.	Bob
Pulling clothes	When the child pulls the cloths of the teacher.	Bob
Biting a person	Closing the jar on a body part or in the clothing of the teacher.	Cody
Biting him or herself	Closing of the jar on a body part of the child his- or her selves.	Amy, Bob,Cody
Throwing materials	Non-accidental throwing of a task-related item.	Amy, Cody
Demand	When a demand was placed on the Boby showing the materials, verbal, model or physical prompting.	Amy, Cody
Time-out	When the child received a time out from task in which no demands were placed upon the child.	Amy, Cody
Receiving a piece of food	When the child was given a piece of food or was enabled and took it himself.	Bob
Receiving a toy	When the child was given a toy to play with.	Amy, Cody
Pushing away task materials (precursor)	Pushing away materials associated with the task with their hands.	Amy, Cody
Looking at food (precursor)	Focussing the eye gaze on the food	Bob
Reaching for food (precursor)	Holding the hand in the direction of the food, includes grasping for food.	Bob
Making physical contact with the teacher (precursor)	When the child made self-initiated physical contact with the teacher.	Bob
Unprompted replacement behavior	When the child made use of the replacement behavior without prompting.	Amy, Bob,Cody

2.6. Data analyses

Functional analysis

Frequencies of challenging behavior were graphically shown. The condition in which most challenging behavior was found was considered to comprise the primary behavioral function. To verify the effect of the manipulated variable in this condition, burst analyses were conducted (Oliver, Hall, & Murphy, 2005). In this analysis, periods between two target behaviors (challenging behavior or unprompted replacement behavior) are normalized and divided into percentiles. It produces a graph consisting of three different lines, the first showing the probability (*p*) of a certain variable before the target behavior, the second and third showing the probability of this variable during and after the target behavior, respectively. This graph shows the pattern of the variable surrounding the target behavior and enables analysis of tendencies in behaviors. For example, when the probability of attention was low or the probability of a demand placed on the child was high before challenging behavior occurred, receiving attention or escaping the task were considered to be the behavioral functions.

Precursor analysis

To analyze the precursor behavior of challenging behavior, data from baseline sessions before and after the FCT were combined. Potential precursors were analyzed using burst analysis (Oliver et al., 2005). A behavior was considered to be a precursor when it showed a peak in probability before the onset of challenging behavior and when the probability of the precursor preceding the challenging behavior was above 0.4. Based on visual inspection during the baseline sessions, the variables ‘reaching for food’, ‘making physical contact with the teacher’,

'looking at food' and 'pushing away the object' were considered to be potential precursors, as the children showed these behaviors prior to the challenging behavior during baseline.

Functional communication training

The effect of FCT on the frequency of challenging behavior was analyzed using Cohen's *d.* (Cohen, 1988). Effect sizes were calculated by comparing the mean frequency of challenging behavior of all baseline sessions with the mean frequency of challenging behavior during all FCT sessions without prompting per child. This was done as prompting was no longer in effect during these sessions and prompts were mainly administered before the occurrence of challenging behavior, thereby influencing the (frequency of) unprompted replacement and challenging behavior of the children. When reliable precursors were found, the effect size was calculated to analyze if the precursor had declined in FCT sessions (with and without prompting) compared to baseline levels, as a function of acquiring the replacement behavior.

Functional equivalence

To assess functional equivalence, burst analyses of the maintaining variable preceding and following challenging behavior during baseline sessions and preceding and following unprompted replacement behavior during training sessions (with and without prompting) were compared (Oliver et al., 2005). Functional equivalence can be presumed when comparable tendencies are seen in the burst analysis graphs. For example, if the probability of maintaining variable (e.g. attention) is relatively low before both challenging behavior in baseline sessions and unprompted replacement behavior in FCT sessions and declines afterwards, functional equivalence can be assumed as the child showed both behaviors under the same environmental

conditions. If graphs are comparable, this gives qualitative support that the replacement behavior does indeed replace the challenging behavior, in addition to quantitative data showing reduced frequencies of challenging behavior after the implementation of FCT.

3. Results

3.1. Functional behavioral analysis

Figure 1 shows the results of the functional analysis for Amy, Bob and Cody. For Amy and Bob, the majority of challenging behavior occurred during the demand-escape condition. Cody primarily engaged in challenging behavior when he wanted a piece of food during the tangible-edibles condition, but challenging behavior also occurred during the tangible-toys condition. No challenging behavior was observed during the alone condition, which functioned as the control condition.

Figure 2a shows that Amy and Cody's probability of a demand rose before they engaged in challenging behavior. The probability of a piece of food was very low before the onset of challenging behavior in Bob.

Figure 1. The frequency of challenging behavior during functional analysis conditions in Amy, Bob and Cody

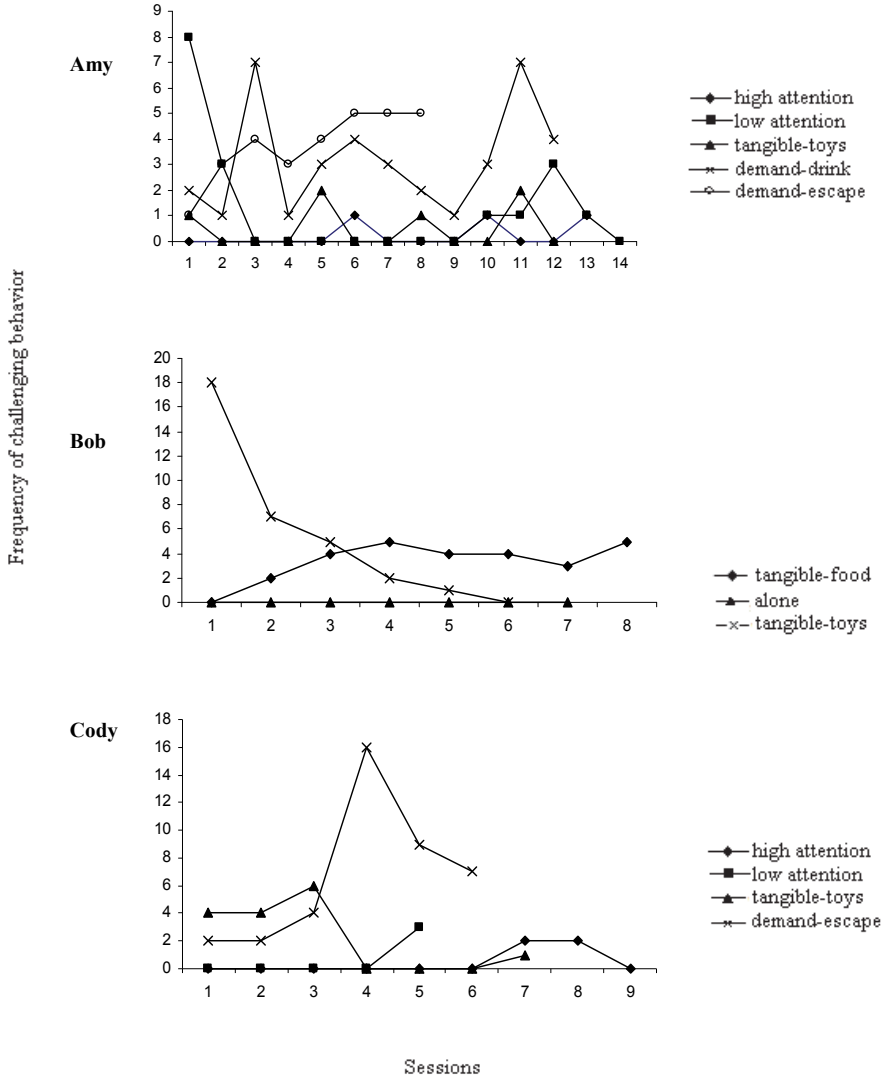
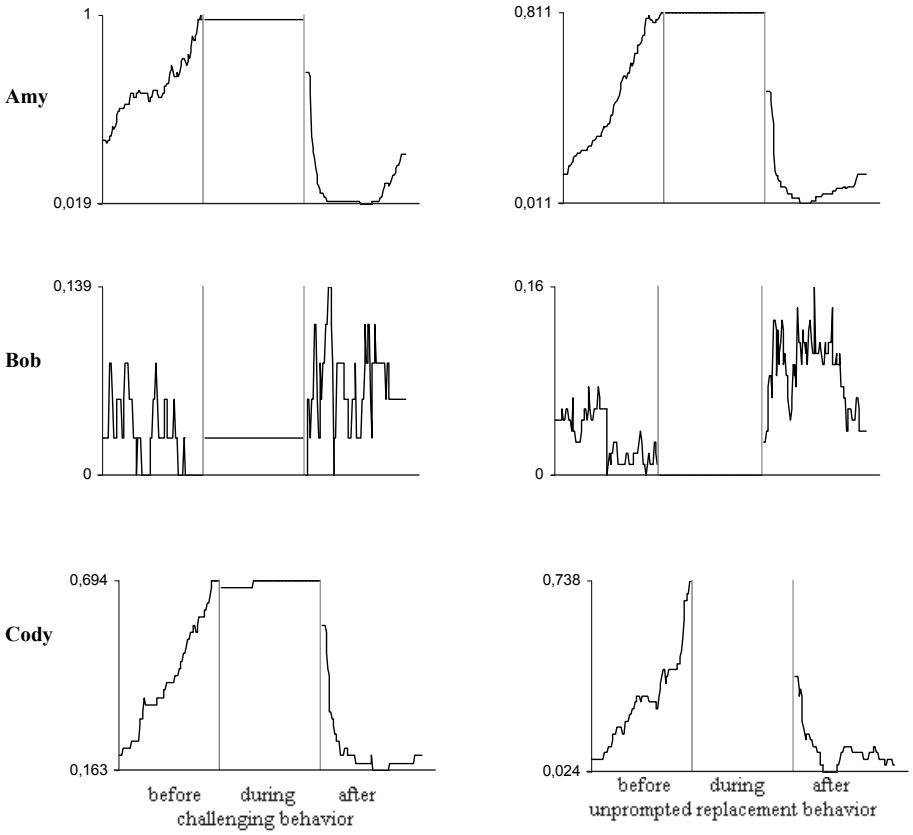


Figure 2a (left row). The probability of a demand in Amy and Cody and of receiving a piece of food in Bob before, during and after the onset of challenging behavior during baseline sessions

Figure 2b (right row). The probability of a demand in Amy and Cody and a piece of food in Bob before, during and after the onset of unprompted replacement behavior during training sessions

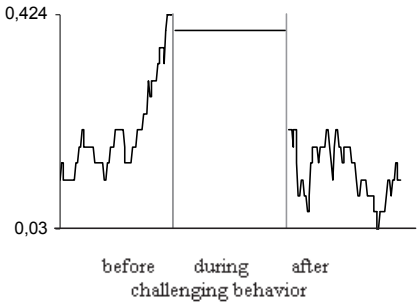


3.2. Precursor analyses

Amy frequently threw away the cup immediately, pushing away the cup only occasionally preceded the throwing away and other challenging behavior ($p = 0.07$). In Bob, challenging behavior was often preceded by making physical contact with the teacher ($p = 0.424$, see Figure 3), making this behavior a reliable precursor. No clear pattern was identified for

looking at (p = 0.176) or reaching for food (p = 0.09) in Bob. No precursor behaviors were identified for Cody. After he was given a demand, Cody immediately engaged in challenging behavior.

Figure 3. The probability of making physical contact before, during and after challenging behavior in baseline sessions in Bob

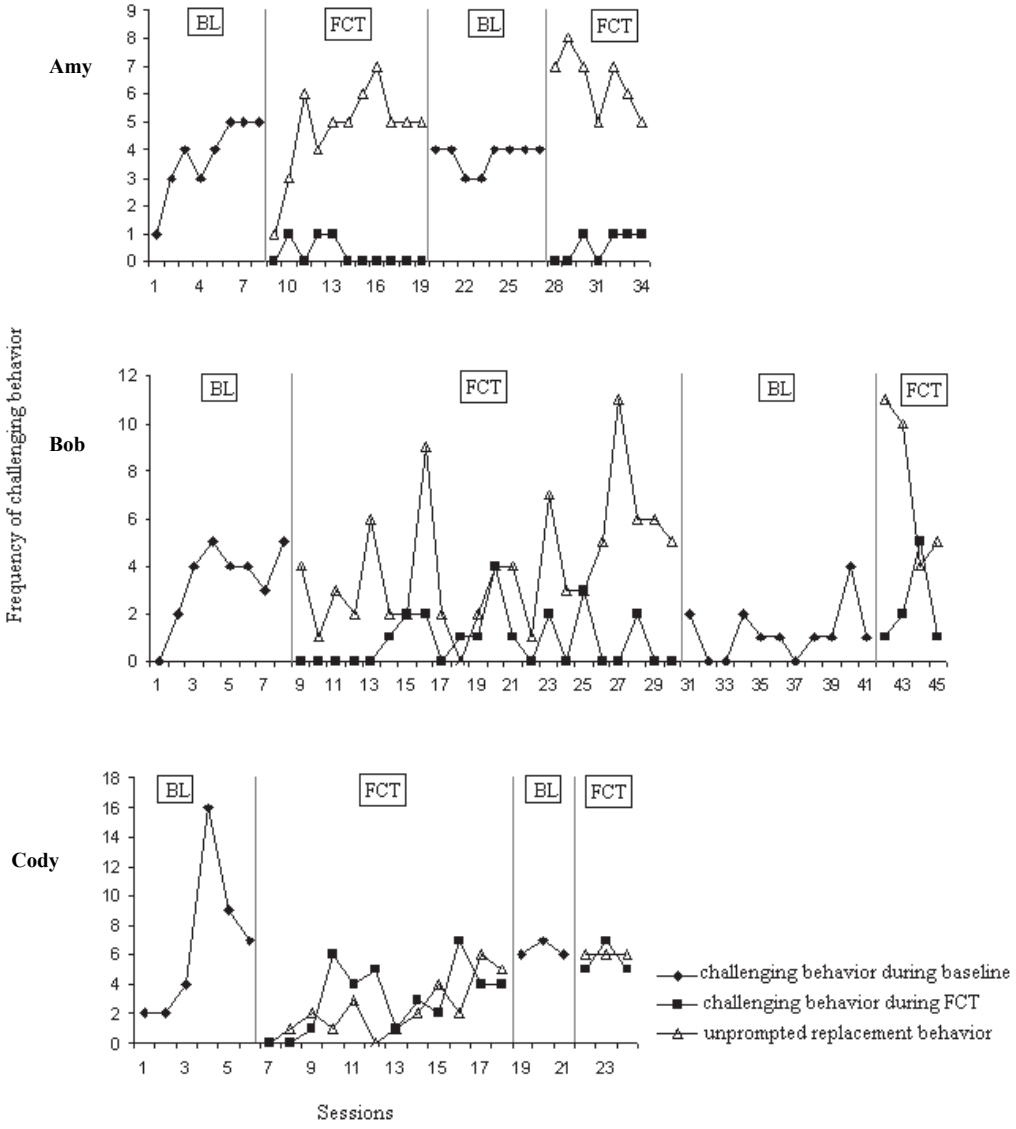


3.3. Functional communication training

Figure 4 shows the results of FCT. A large effect of FCT on challenging behavior was found for Amy (d = -4.5), whereas a medium effect was found for Bob (d = -0.6) and Cody (d = -0.5). The graph for Bob shows a diffuse pattern of challenging behavior in baseline and training sessions, a more stable pattern was found with Amy and Cody. For Bob, the precursor "making physical contact with teacher" showed a strong decline (large effect) as a function of the FCT (d = -1.25). During the training sessions carried out with Cody, it became apparent that throwing away task materials continued to persist through time-out, but aggression directed at the teacher declined. When aggression directed at the teacher (biting, kicking and hitting) was analyzed, FCT showed a large effect (d = -1.1). No clear pattern emerged for the unprompted replacement

behavior compared to challenging behavior (see Figure 4): the challenging does not clearly show a decrease when the frequency of unprompted replacement behavior rises or vice versa.

Figure 4. The frequency of challenging and unprompted replacement behavior in Amy, Bob and Cody during baseline (BL) and training (FCT) sessions



3.4. Functional equivalence

In Tables 2a and 2b, comparable patterns of responding can be seen. The probabilities of a demand were raised before challenging (left row) or unprompted replacement behavior (right row) for Amy and Cody. For Bob, the probability of receiving a piece of food was relatively low before compared to after he indulged in challenging or unprompted replacement behavior.

4. Discussion

In the present study, classroom teachers used functional analysis procedures to identify the communicative functions of challenging behavior in three children with AS. Teachers then implemented FCT and the frequency of challenging behavior for all three participants was diminished, particularly for Amy. For Bob, a reliable precursor was found and across all children challenging and replacement behavior were functionally equivalent. These results replicate previous research that found FCT to be an effective intervention for people with AS and extend previous research by demonstrating that these procedures can be used effectively by teachers of students with AS in a school context.

The functional analysis findings support those of Strachan et al. (2009), Allen et al. (2010) and Radstaake et al. (2012). These studies suggest that the challenging behavior of children with AS may be reinforced by attention, but in this study attention was not found to be the primary maintaining consequence for challenging behavior The conditions were filmed in naturally occurring circumstances and stimulation (in the form of other children's or teacher's play or visual stimuli) was provided in the classroom, presumably leading to satiation of attention, reducing the motivational threshold for showing challenging behavior to receive attention.

A reliable precursor behavior was identified for only one participant. Compared to the study of Radstaake et al. (2012), in which more precursors were found, these findings were somewhat surprising. An explanation might be that some sessions were performed sequentially, and as reinforcement was only given upon the onset of challenging behavior, precursors might have been omitted by the children in following sessions as these did not lead to reinforcement. Precursors might not have been identified as a result of associations between teacher, challenging behavior and consequences (Ringdahl & Sellers 2000). Nonetheless, this study shows the potential of using precursors as the onset of prompting in FCT in the classroom, thereby preventing challenging behavior.

During FCT, all children learned to independently use their replacement behavior, which was associated with a large effect on challenging behavior in one child (Amy) and with a medium effect in the other two children (Bob and Cody). Bob showed a decline in precursor and challenging behavior, suggesting that he no longer communicated his desire by showing precursor or challenging behavior, but by using his speech-generating device. Cody's aggression toward the researcher showed a stronger decrease than challenging behavior directed at task materials. Other behavioral functions might have influenced the results for Bob and Cody, as their challenging behavior (although less frequent) was still observed while they received reinforcement. Different topographies (and even similar topographies) of challenging behavior may be maintained by multiple functions (Derby et al., 2000; Sigafoos & Meikle, 1996). However, in this current study only one behavioral function was targeted with FCT. An explanation for the medium effect sizes may be that strong associations were already made between the teacher, the child and the challenging behavior and more FCT sessions would have been necessary to establish new associations.

As in the study by Radstaake et al. (2012) challenging and replacement behaviors appeared to be functionally equivalent in all children. The communication object or aid was not only a new and hypothetically interesting object for them, the children made use of it in the absence of their motivational variable. In future research, functional equivalence should be given more attention, because when equivalence is in effect, the results can be expected to be maintained over time (Derby et al., 1997) and is not expected to decrease as the communicative object or aid becomes more familiar and less interesting to the child.

Several limitations to the current study should be noted. The small number of participants hinders generalization of the results. As relatively low levels of challenging behaviors were observed, the challenging behaviors were combined into one variable. In some sessions, the peers had to be asked to play elsewhere as they caused too much distraction for the children or vice versa; this hampers generalization as this situation was not completely comparable with the typical classroom situation. In line with this, peer presence was not kept constant between the conditions and this may have influenced our results; for instance, the reinforcer magnitude of adult attention may depend on peer presence and future research should focus on this. Further, prompting was administered upon the onset of the precursors based on visual inspection during baseline sessions, but only "making physical contact with the teacher" was found to be a reliable precursor after analysis. It was decided to prompt upon all potential precursors to increase learning opportunities as the precursors that were prompted upon were all directed at the maintaining variable (e.g., reaching for the object or pushing the non-desired object away). If prompting based on these potential precursors would not have been done, more precursor and challenging behaviors may have shown during FCT. Another limitation is that the communicative objects and aids were not available to the children during the baseline sessions,

as the children did not possess the appropriate skills to operate them. When available, they might have used the object and aids as play materials and not for communicative purposes.

Future research should focus on analyzing differences in generalization and maintenance between FA and FCT conducted in the natural and contrived environments. As discriminative and evocative stimuli are different or absent in the contrived environments, generalization and maintenance is expected to be fostered FCT in the natural environment (see Lang et al., 2008). Research should also focus on using communicative aids, before challenging behavior becomes part of their behavioral pattern. When FCT is given at a young age, challenging behavior may be prevented (Reeve & Carr, 2000). Interventions based on applied behavior analysis principles showed to have some positive developmental outcomes for children with AS, regardless of age or genetic subtype (Summers, 2012).

Challenging behavior may occur in AS, but can be successfully addressed by FCT, despite the challenges posed by their genotype and behavioral phenotype. But to take these challenges into account, adjustments in FA antecedents, consequences and design may be needed to find a reliable behavioral function in individuals with AS, as research has shown these changes to be successful in identifying behavioral functions (Hagopian, Rooker, Jessel., & DeLeon, 2013). In this study, the inclusion of peers was seized as they caused too much distraction, new conditions were added, divided attention was used and consequence magnitude was altered. Efforts were made to make these changes as small as possible and familiar teachers and classrooms were used throughout as to enhance generalization of the replacement behavior.

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6. Declaration of interest

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7. References

Allen, D., Oliver, C., Webster, P., Reid, D., Villa, D., Beaumont, S., et al. (2010). Behavioral intervention for challenging behavior in children with Angelman syndrome. *Journal of Intellectual Disability Research, 54,* 885.

Bondy, A., & Frost, L. (2001). The Picture Exchange Communication System. *Behavior Modification, 25*, 725-744.

Borrero, C. S. W., & Borrero, J. C. (2008). Descriptive and experimental analyses of potential precursors to problem behavior. *Journal of Applied Behavior Analysis, 41*, 83-96.

Carr, E. G., & Durand, M. V. (1985). Reducing behavior problems through functional communication training. *Journal of Applied Behavior Analysis, 18*, 111-126.

Cohen, J. (1988). *Statistical Power Analysis for the Behavioral Sciences*. Hillsdale, New York: Lawrence Erlbaum Associates.

De Bildt, A. A., & Kraijer, D. W. (2003). *Vineland-Z: Sociale zelfredzaamheidschaal voor kinderen en jeugdigen met een verstandelijke beperking.* [Vineland Adaptive Behavioral

Scales, Survey Form]. Leiden, The Netherlands: PITS.

Derby, M., Hagopian, L., Fisher, W. W., Richman, D., Augustine, M., Fahs, A., & Thompson, R. (2000). Functional analysis of aberrant behavior through measurement of separate response topographies. *Journal of Applied Behavior Analysis, 33*, 113-117.

Derby, K. M., Wacker, D. P., Berg, W., DeRaad, A., Ulrich, S., Asmus, et al. (1997). The long-term effects of functional communication training in home settings. *Journal of Applied Behavior Analysis, 30*, 507-531.

Didden, R., Sigafoos, J., Korzilius, H., Baas, A., Lancioni, G. E., O'Reilly, M. F., & Curfs, L. M. G. (2009). Form and function of communicative behaviors in individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disability, 22,* 526-537.

Hagopian, L. P., Rooker, W. G., Jessel, J., & DeLeon, I. G. (2013). Initial functional analysis outcomes and modification in pursuit of differentiation: A summary of 176 inpatient cases. *Journal of Applied Behavior Analysis, 46*, 88-100.

Iwata, B., Dorsey, M., Slifer, K., Bauman, K., & Richman, G. (1994). Toward a functional analysis of self-injury. *Journal of Applied Behavior Analysis, 27*, 197-209. Reprinted from *Analysis and Intervention in Developmental Disabilities, 1982, 2,* 3-20.

Lalande, M., & Calciano, M. A. (2007). Molecular epigenetics of Angelman syndrome. *Cellular and Molecular Life Sciences, 65,* 947-960.

Lancioni, G. E., O'Reilly, M. F., Cuvo, A. J., Singh, N. N., & Didden, R. (2007). PECS and VOCAs to enable students with developmental disabilities to make requests: An overview of the literature. *Research in Developmental Disabilities, 2,* 468-488.

Lang, R., Sigafoos, J., Lancioni, G., Didden, R., & Rispoli, M. J. (2010). Influence of assessment

setting on the results of functional analyses of problem behavior. *Journal of Applied Behavior Analysis, 43*, 565-568.

Lang, R., O'Reilly, M., Machalicek, W., Lancioni, G., Rispoli, M., & Chan, J. M. A. (2008). Preliminary comparison of functional analysis results when conducted in contrived versus natural settings. *Journal of Applied Behavior Analysis, 41*, 441-445.

Langdon, N. A., Carr, E. G., & Owen-DeSchryver, J. S. (2008). Functional analysis of precursors for serious problem behavior and related intervention. *Behavior Modification, 32,* 804-827.

Leyser, Y., & Kirk, R. (2011). Parent's perspectives on inclusion and schooling of students with Angelman syndrome: Suggestions for educators. *International Journal of Special Education, 26,* 1-14.

Lydon, S., Healy, O., O'Reilly, M. F., & Lang, R. (2012). Variations in functional analysis methodology: A systematic review. *Journal of Physical and Developmental Disability, 24,* 301-326.

Martin, N., Oliver, C., & Hall, S. (2001). *Obswin: software for the collection and analysis of observational data*. Birmingham, UK: University of Birmingham.

Oliver, C., Hall, S., & Murphy, G. (2005). The early development of self-injurious behavior: Evaluating the role of social reinforcement. *Journal of Intellectual Disability Research, 49,* 591-599.

Petty, J., Allen, D., & Oliver, C. (2009). Relationship among challenging, repetitive, and communicative behaviors in children with severe intellectual disabilities. *American Journal on Intellectual and Developmental Disabilities, 114*, 356-368.

Radstaake, M., Didden, R., Oliver, C., Allen, D., & Curfs, L. M. G. (2012). Functional analysis

and functional communication training in individuals with Angelman syndrome. *Developmental Neurorehabilitation, 15*, 91-104.

Reeve, C. E., & Carr, E. G. (2000). Prevention of severe problem behavior in children with developmental disorders. *Journal of Positive Behavior Interventions, 2,* 144-160.

Ringdahl, J. E., & Sellers, J. A. (2000). The effects of different adults as teachers during functional analysis. *Journal of Applied Behavior Analysis, 33*, 247-250.

Rispoli, M. J., Franco, J. H., Van der Meer, L., Lang, R., & Camargo, S. P. H. (2010). The use of speech generating devices in communication interventions for individuals with developmental disabilities: A review of the literature. *Developmental Neurorehabilitation, 13*, 276-293.

Sigafoos, J., & Meikle, B. (1996). Functional communication training for the treatment of multiply determined challenging behavior in two boys with autism. *Behavior Modification, 20,* 60-84.

Strachan, R., Shaw, R., Burrow, C., Horsler, K., Allen, D., & Oliver, C. (2009). Experimental functional analysis of aggression in children with Angelman Syndrome. *Research in Developmental Disabilities, 30,* 1095-1106.

Stokes, T., & Baer, D. M. (1977). An implicit technology of generalization. *Journal of Applied Behavior of Analysis, 10,* 349-367.

Summers, J. (2012). Neurodevelopmental outcomes in children with Angelman syndrome after 1 year of behavioral intervention. *Developmental Neurorehabilitation*, 15, 239-252.

Tait, K., Sigafoos, J., Woodyatt, G., O'Reily, M. F., & Lancioni, G. E. (2004). Evaluating parent use of functional communication training to replace and enhance prelinguistic behaviors in six children with developmental and physical disabilities. *Disability and Rehabilitation,*

26, 1241-1254.

Tiger, J. H., Hanley, G. P., & Bruzek, J. (2008). Functional Communication Training: A Review and Practical Guide. *Behavior Analysis in Practice, 1*, 16-23.

Van der Meulen, B. F., Ruiter, S. A. J., Lutje Spelberg, H. C., & Smrkovsky, M. (2002). *Bayley Scales of Infant Development – Second Edition – Dutch Version (BSID-II-NL)*. Lisse, the Netherlands: Swets & Zeitlinger.

Williams, C. A. (2010). The behavioral phenotype of the Angelman Syndrome. *American Journal of Medical Genetics, 154C*, 432-437.

Wood, B. K., Cho-Blair, K., & Ferro, J. B. (2009). Young children with challenging behavior function-based assessment and intervention. *Topics in Early Childhood Special Education, 2*, 68-78.

Chapter 4

Incontinence in individuals with Angelman syndrome:

A comparative study

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Abstract

Frequency and type of incontinence and variables associated with incontinence were assessed in individuals with Angelman syndrome (AS; *n* = 71) and in a matched control group (*n* = 69) consisting of individuals with non-specific intellectual disability (ID). A Dutch version of the "Parental Questionnaire: Enuresis/Urinary Incontinence" (Beetz, von Gontard, & Lettgen, 1994) was administered and information on primary caretakers' perspectives regarding each individual's incontinence was gathered. Results show that diurnal incontinence during the day more frequently occurred in the control group than in the AS group. In both groups, nocturnal enuresis was the most common form of incontinence. More incontinence was seen in individuals with AS who were younger, had a lower level of adaptive functioning and/or had epilepsy. Individuals with AS were able to stay dry for longer periods of time than the controls and often showed both in-toilet urination and urinary accidents during the day, whereas accidents and correct voids during the day were more set apart in the control group. Also, persons with AS had a lower micturition frequency implying possible voiding postponement. Both groups showed high rates of LUTS (lower urinary tract symptoms) possibly indicative of functional bladder disorders such as voiding postponement, dysfunctional voiding, or even an underactive bladder. In general, most primary caretakers reported severe intellectual disability as the main cause for urinary incontinence. Based on these results incontinence does not appear to be part of the behavioral phenotype of Angelman syndrome. Therefore, paediatric or urologic diagnostics and treatment are recommended for all persons with incontinence and intellectual disability. Further implications for practice and research are given.

1. Introduction

Angelman syndrome (AS) is a neurodevelopmental disorder caused by the absence or malfunctioning of expression of maternally imprinted genes in the region at 15q11-13 (Lalande & Calciano, 2007). Individuals with AS often suffer from epilepsy and their behavioral phenotype includes severe intellectual disability (ID), motor and speech deficits, easy evocable and sometimes inappropriate laughter, and sleep disturbances (Clayton-Smith & Laan, 2003; Didden, Korzilius, Smits, & Curfs, 2004; Williams, 2010). The developmental age of individuals with AS rarely exceeds two years (Peters et al., 2004) suggesting that development of continence may be severely delayed, as continence in typically developing children is often achieved at the age of three years (Schum, Kolb, McAuliff, Simms, & Underhill, 2002).

Incontinence can be defined as uncontrollable leakage of urine in individuals older than five years, for 2 or more episodes per week (DSM-IV; American Psychiatric Association, 2000). It can be further classified as continuous and intermittent incontinence during the day (diurnal incontinence; DI) and/or during sleep (enuresis of nocturnal enuresis; NE). DI comprised a heterogeneous groups of disorders, including overactive bladder, voiding postponement, dysfunctional voiding and underactive bladder. When an individual is continent, but relapses for a period of six months or longer, this is called secondary incontinence, if the longest interval is less than 6 months, incontinence is termed primary. If lower urinary tract symptoms (LUTS) are present, the term non-monosymptomatic NE is chosen – without LUTS it is termed monosymptomatic NE. Fecal incontinence (FI) is defined as voluntary and involuntary defecation in inappropriate places occurring at least once per month for three consecutive months (according to DSM-IV). FI can occur with functional constipation or as non-retentive fecal incontinence.

Incontinence may result in social stigmatization, anxiety, physical discomfort, and urinary tract infections, which may lead to dependency of caregivers, exclusion from peer groups and certain activities (Cicero & Pfadt, 2002; Kroeger & Sorenson-Burnworth, 2009; Mehta et al., 2003). In addition to adverse effects for the individuals themselves, incontinence can place a burden on the lives of family members (Gotoh et al., 2009) and costs for diapers and medical treatments are often considerable (Borrie & Davidson, 1992; Landefeld et al., 2008).

Prevalence studies of incontinence in AS are scarce and have yielded inconsistent outcomes. For example, Buntinx et al. (1995) showed that 14 (63%) of the children and youngsters aged 2-16 years with AS suffered from DI, whereas two (12.5%) of the individuals with AS aged 16 and older were incontinent. A study on adults with AS aged 20 to 53 years (N = 28) showed that 43% of the individuals were incontinent when they were sent to the toilet at regular scheduled times during the day (Laan, den Boer, Hennekam, Renier, & Brouwer, 1996). Didden et al. (2004) found that 93% out 133 of individuals with AS between five and 44 years old suffered from NE and FI; however, DI was not studied.

The previous research on incontinence in people with AS has several limitations. Specifically, none of the studies included a control group, nor did they address all types of incontinence, and sample sizes were relatively small. Further, detailed information about incontinence was not given and relationships between incontinence and associated variables were not explored. The aim of this current study is to gain more insight regarding the nature and prevalence of incontinence in AS by increasing the sample size, including all types of incontinence, and comparisons with a control group. Further, the inclusion of a matched control group allows this study to test the hypothesis that incontinence may be part of the behavioral

phenotype of AS (Dykens, 1995). Finally, the present study extends our knowledge on AS as it also explores associations between incontinence and other variables in individuals with AS.

2. Materials and methods

2.1. Participants

Participants in the AS group (N = 71; 36 male) had a mean age of 20.5 years (SD = 9.8; range 6.8-45.8), a mean developmental age of 1.4 years (SD = 0.10; range 0.4-2.9) and their motor abilities reached a mean age of 1.8 years (SD = 0.9; range 0.4-3.2). Most participants had the deletion subtype (n = 45, 63%), followed by mutation (n = 6, 9%) and uniparental disomy (n = 5, 7%); in the remaining participants the cause of AS was unknown or not reported (n = 15, 21%). The majority (n = 59, 83%) of participants also suffered from epilepsy of whom 43 (61%) successfully used anticonvulsive medication to control seizures. Eleven (16%) participants were wheelchair bound and 24 (36%) participants lived in a facility.

Participants in the control group (N = 69; 37 male) had a mean age of 22.9 years (SD = 12.6; range 5.3-48.11), a mean developmental age of 1.3 years (SD = 1.2, range 0.2-3.7) and their motor abilities reached a mean age of 1.3 years (SD = 1.3, range 0.0-4.5). In 21 individuals (34%) the cause of the ID was known, 13 causes were mentioned including (Down syndrome (n = 3) and oxygen deficiency at birth (n = 2). The larger part (n = 44, 64%) of participants suffered from epilepsy of whom 10 (27%) successfully used anticonvulsive medication to control seizures. Thirty-three (50%) participants were wheelchair bound and 42 (68%) participants lived in a facility.

Individuals' characteristics were compared between the two groups. Differences in gender distribution ($\chi^2(1) = 0.12$, $p = .73$), age ($t(128.72) = 1.21$, $p = .23$), level of adaptive functioning ($t(114.15) = 0.58$, $p = .56$), motor abilities ($t(107.81) = 1.70$, $p = .09$), and presence

of urinary tract infections ($\chi^2(1) = 0.01$, $p = .95$) were not statistically significant. However, more participants from the CG lived in a facility ($\chi^2(1) = 12.07$, $p < .01$) and were wheelchair bound ($\chi^2(1) = 18.68$, $p < .01$). Fewer participants suffered from epilepsy ($\chi^2(1) = 6.73$, $p = .01$) as compared to the AS group.

2.2. Materials

The "Parental questionnaire: Enuresis/Urinary Incontinence" (Beetz et al., 1994), a clinical, non-validated questionnaire, was translated into Dutch and adapted for use in AS. The adapted version questioned background variables (e.g. age, genetic subtype of AS, presence of epilepsy) and entailed 43 questions concerning urinary and fecal incontinence during the day- and nighttime (e.g., 'How many times a day does your child/client urinate on the toilet?') and assesses toileting habits (e.g., 'Does your child/client show signs of straining during the urination?'), behavioral reactions concerning wetting and toileting (e.g., 'Does your child/client sense a urinary accident?'), urinary tract infections and general behaviors such as fears and distractibility. Further, caretakers were asked about their perception on causes of incontinence, the influence of the child's incontinence on everyday life and about the results of former attempts at toileting training. Most questions followed a yes/no format and in several items frequencies or qualitative information were asked.

The original questionnaire is suitable for use in individuals who are at least five years old and has been used in children with spinal muscular atrophy (von Gontard, Laufersweiler-Plass, Backes, Zerres, & Rudnik-Schöneborn, 2001) and in individuals with Prader-Willi syndrome (von Gontard, Didden, Sinnema, & Curfs, 2010). A slightly adapted version has been used in individuals with Rett syndrome (Giesbers et al., 2012).

The Dutch version of the Vineland-Screener 0-6 years was used to determine the level of adaptive functioning. It is a psychometrically validated questionnaire that measures adaptive behavior in individuals with an adaptive level to 6 years across four domains. It consists of 72 items assessing the child's communicative, social, daily living and motor abilities (e.g., "Does he or she listen to a story for at least 5 minutes?") on a Likert-type 3-point scale ranging from 0 (no, never) to 2 (yes, usually). The scores can be converted into a mean adaptive developmental age for the total scale or domains separately. The questionnaire has good internal consistency (i.e., Cronbach's alpha is .80 or higher for the four developmental domains), good inter-rater reliability ($r > .7$) and a good test-retest reliability ($r > .8$; Scholte et al., 2008). It also has a good construct validity (i.e. factor loadings of subscales on "Adaptive Behavior" factor were .95 or higher, strong correlation between Total Adaptive Behavior score and age; $r = .94$, $p < .01$), the questions represent the adaptive behaviors and the scores significantly predict the criterion group ($p < .01$; Scholte et al.).

2.3. Procedure

The questionnaires (see Materials) were sent to primary caregivers of individuals aged five to 55 years, as incontinence cannot be diagnosed before the age of five and incontinence can be influenced by factors as dementia in elderly people (Moss & Patel, 1997; Nevéus et al., 2006). A total of 129 questionnaires were sent to members of the Dutch Prader Willi Angelman Association, of which 74 were returned (response rate: 58%). After four weeks, non-respondents were sent a reminder. Two participants with AS were excluded because of missing date of birth and one participant was excluded due to uncertainty of the diagnosis of AS (as indicated by the primary caregiver).

Three facilities participated to meet the requirements of the control group (CG) which was matched on age and ID (IQ < 35, level of adaptive functioning < 48 months) to the AS group. A total of 142 questionnaires and accompanying letters were sent to the primary caregivers (parents or professional caretakers, depending on living facility) of individuals with mixed etiology with a severe to profound ID (response rate: 69%). Eight participants of the control group (CG) were excluded because they were too old (> 55 years), six were excluded due to a too high level of adaptive functioning (> 48 months), two because of a missing date of birth, and one because of presence of a bladder catheter. Of the remaining participants in the control group ($N = 81$), the mean level of adaptive functioning of individuals with Down syndrome ($n = 15$) was significantly higher than that of the other participants in this group ($t(80) = 4.3$, $p < .01$). Therefore, participants with Down syndrome were excluded sequentially from the CG starting with the individual with the highest level of adaptive functioning until there was no significant difference in level of adaptive functioning between individuals with and without Down syndrome within the CG. In total, 12 participants with Down syndrome were excluded from the control group.

2.4. Data analysis

Data were analyzed using the SPSS statistical package V15.0. Chi-square analyses were used to test associations between incontinence and categorical variables within AS. Independent samples *t*-tests were used to test associations between incontinence and metric variables within AS. Variables related to incontinence were separated in background variables (e.g., age, gender, and level of adaptive functioning) and behavioral variables (lower urinary tract symptoms (LUTS), solid stool, medical conditions, nighttime behavior, and hyperactivity). When

associations were found between background variables and incontinence, these variables were entered in a logistic regression analysis model to assess whether these variables independently contributed to the variance in incontinence.

Chi-square analyses and independent sample *t*-tests were done to explore differences in frequency of voiding, defecation and incontinence between AS and the CG. As lower urinary tract symptoms can only be observed during urination, only participants who showed in-toilet voiding were used when these symptoms were assessed throughout this study. As significant differences between AS and the CG were found in wheelchair dependency, living facilities, and presence of epilepsy, these variables were controlled for by entering these variables in a logistic regression analysis model, together with participant group to assess the unique contribution of each variable to the presence of incontinence. Table 1 shows the definitions of types of incontinence.

Table 1. Definitions of types of incontinence.

Type of incontinence	Definition
Diurnal urinary incontinence (DI)	When an individual had two or more urinary accidents per week during the day.
Nocturna enuresis (NE)	When an individual had two or more urinary accidents per week during the night.
Fecal incontinence during the day (FI-day)	When an individual had two or more fecal accidents per month during daytime.
Fecal incontinence at night (FI-night)	When an individual had two or more fecal accidents per month during the night.
Secondary continence	When an individual was continent for at least six months, followed by a period of incontinence.

3. Results

3.1. Descriptive statistics

Angelman syndrome

Out of the respondents, 43 indicated to be the parent and four to be the professional caretaker of the child or client. In 24 cases the relationship between the child/client and the

respondent remains unknown. Table 2 shows the percentages and frequencies of the four types of incontinence in AS. In Table 3, frequencies are broken down for each age group. Highest rates were found for NE, lowest for fecal incontinence during the day. A differentiated pattern in urinations was seen in DI; not all incontinent individuals had daily urinary accidents. Fecal accidents occurred in wide ranges, with an average of nearly 5 times a week. During the night, incontinent individuals were wet nearly every night. Secondary DI was found in one individual with AS, he was continent for 12 months at the age of 3.6 years (Table 1).

The percentages of LUTS are shown in Table 4. Relatively high levels of "interrupted stream", "takes too little time to void", and "hesitancy" were found within the AS group compared to the other LUTS. Individuals with AS could stay dry for a mean of five hours and 25 minutes (*SD* = 3.59 hours, range = 1-22 hours).

Two individuals (3%) had a medical malfunction on the urinary tract; one with reflux and the other is unknown. Urinary tract infections (UTI) were present in 18 participants (25%), with a mean of 9.12 UTIs (*SD* = 21.44). Fourteen individuals (78%) received antibiotics for their UTI.

Table 2. Frequencies and percentages of incontinence in AS and the CG, χ^2, *t,* and *p* values.

	Incidence of incontinence			Frequency of accidents		Statistics
	Group	*n* (%)		Frequency	(*SD*; range)	
DI	AS	38 (54)	$\chi^2(1) = 9.05$, *p*	6.42 days/week	(1.57; 2-7)	*t* (37) = 2.27,
	CG	54 (78)	< .01	7.00 days/week	(0; 7-7)	*p* < .05
NE	AS	62 (89)	$\chi^2(1) = 6.00$, *p*	6.58 nights/week	(1.17; 2-7)	*t* (111.55) = 1.21,
	CG	58 (84)	= .39	6.81 nights/week	(0.85; 2-7)	*p* = .23
FI-day	AS	43 (61)	$\chi^2(1) = 3.31$, *p*	4.51 times/week	(4.51; 0.25-14)	*t* (76.49) = 3.78,
	CG	51 (75)	= .07	8.27 times/week	(6.11; 1-32)	*p* < .01
FI-night	AS	38 (57)	$\chi^2(1) = 0.06$, *p*	10.47 nights/month	(9.12; 1-31)	*t* (70) = .98,
	CG	35 (54)	= .82	9.12 nights/month	(6.81; 1-32)	*p* = .33
Solid stool	AS	38 (54)	$\chi^2(1) = 11.82$,			
	CG	17 (25)	*p* < .01			

Note. DI = Diurnal urinary incontinence; NE = Nocturnal enuresis; FI-day = Fecal incontinence during the day; FI-night = Fecal incontinence at night; AS = Angelman syndrome; CG = Control group.

Table 3. Frequencies and percentages of incontinence for age groups in AS and the CG.

Age Group	Type of incontinence	AS (%)	CG (%)
5-12		*n* = 20	*n* = 15
	DI	90%	87%
	NE	95%	93%
	FI-day	90%	86%
	FI-night	61%	50%
13-18		*n* = 21	*n* = 16
	DI	43%	75%
	NE	81%	69%
	FI-day	52%	69%
	FI-night	43%	50%
19-30		*n* = 18	*n* = 19
	DI	50%	68%
	NE	94%	84%
	FI-day	50%	63%
	FI-night	77%	53%
31-55		*n* = 12	*n* = 19
	DI	17%	84%
	NE	75%	90%
	FI-day	42%	84%
	FI-night	36%	65%

Note. DI = Diurnal urinary incontinence; NE = Nocturnal enuresis; FI-day = Fecal incontinence during the day; FI-night = Fecal incontinence at night; AS = Angelman syndrome; CG = Control group.

Table 4. Percentage of LUTS in individuals who show in-toilet urination in AS and the CG.

	AS *n* (%), n = 45	CG *n* (%), n = 23
Mean duration of dryness	*m* = 5;30 hours (*SD* = 3;59 hours, range = 1-22 hours)	*m* = 2;44 hours (*SD* = 2;15 hours, range = 5 minutes – 10 hours)
Goes to toilet independently or indicates need to void.	29 (64)	13 (57)
Straining	12 (27)	3 (14)
Interrupted stream	18 (31)	4 (20)
Weak stream	1 (2)	4 (19)
Post-micturition dribble	6 (13)	6 (29)
Takes too little time to void	24 (55)	8 (38)
Hesitancy	17 (38)	6 (29)
Urgency	13 (31)	5 (23)
Holding maneuvers	5 (11)	5 (23)

Note. LUTS = lower urinary tract symptoms; AS = Angelman syndrome; CG = Control group.

Control Group

Out of the respondents, 21 indicated to be the parent and 37 to be the professional caretaker of the child or client. In 11 cases the relationship between the child/client and the respondent remains unknown. Table 2 shows the percentages and frequencies of the four types of incontinence in the CG. In Table 3, frequencies are broken down for each age group. Secondary DI, NE and FI were found in three individuals in the CG, which had a mean duration of continence of 2;6 years (*SD* = 2;2 years, range 1-5 years), on a mean age of 10;6 years (*SD* = 12;7 years, range 3-25 years). Individuals could stay dry for a mean of two hours and 44 minutes (*SD* = 2.15 hours, range = 5 minutes – 10 hours; Table 4).

Six individuals (9%) suffered from medical malfunction on the urinary tract, for which they were treated. Seventeen individuals had had at least one UTI (26%), with a mean of three UTIs (*SD* = 1.70). Fifteen individuals (94%) received treatment for their UTI; fourteen used antibiotics of whom one as a prophylaxis. One individual was given additional bladder flushes.

3.2. Within Group analysis – Angelman syndrome

3.2.1. Background variables

Incontinence during the day (DI and FI-day) was positively associated with a lower chronological age, lower level of adaptive functioning, and a lower level of motor abilities (see Table 5). More DI and FI-day were found in wheelchair bound individuals compared to ambulant individuals and in individuals living at home, compared to individuals living in a facility. Individuals who were incontinent at night (NE and FI-night) had a lower level of adaptive functioning and lower level of motor abilities than individuals who were continent. More NE and FI-day was found in individuals with epilepsy, compared to individuals without

epilepsy. No statistically significant differences in all types of incontinence were found for gender, AS subtype and urinary tract infections.

Logistic regression analysis showed that age and level of adaptive functioning significantly predicted DI and FI-day, that having epilepsy significantly predicted NE and that no variables showed to have a unique contribution to FI-night.

For DI, logistic regression analysis revealed that the model with age, level of adaptive functioning, motor abilities, wheelchair dependency, and living facility was significant ($\chi^2(4) = 55.96$, $p < .01$), but only age and level of adaptive functioning significantly predicted DI. An extra month in age made the odds on being continent 1.02 times more likely, and one extra point on the level of adaptive functioning made the odds 1.34 times more likely.

In NE, the model with the significant variables was significant ($\chi^2(3) = 19.26$, $p < .01$). Only epilepsy had a unique contribution to the variance in incontinence; having epilepsy made the odds of having NE 13.52 times more likely.

For FI-day, logistic regression analysis revealed the model with the significant variables to be significant ($\chi^2(6) = 41.21$, $p < .01$), but no variables had a significant influence on the variance in continence. Living facility almost reached significance ($p = 0.05$). Living in a facility instead of at home made the odds of being continent 8.89 times more likely.

For FI-night, both age and level of adaptive functioning did not have a unique contribution to the variance in continence, but the model was significant ($\chi^2(2) = 8.25$, $p < .05$).

Table 5. Background variables associated with incontinence in AS, χ^2 , *t* and *p*-values.

	Age, *t*	Level of adaptive functioning, *t*	Motor abilities, *t*	Wheelchair dependency, χ^2	Epilepsy, χ^2	Living facility, χ^2
DI	4.05**	5.28**	5.29**	7.30**	Ns	9.3*
NE	ns	4.23**	3.88**	ns	13.08**	ns
FI-day	2.81**	5.82**	5.25**	8.48**	4.48*	12.79**
FI-night	ns	2.90**	2.80**	ns	Ns	ns

Note. DI = Diurnal urinary incontinence; NE = Nocturnal enuresis; FI-day = Fecal incontinence during the day; FI-night = Fecal incontinence at night; * p < .05; ** p < .01; ns = non-significant.

3.2.2. Behavioral variables related to incontinence in AS

Diurnal incontinence

Less DI ($\chi^2(1) = 16.30$, $p < .01$), more in-toilet voiding ($t(43) = 2.56$, $p < .05$) and less days with accidents (($t(18) = 4.07$, $p < .01$) were found in individuals who went to the toilet independently or communicated their need to void to caregivers. The frequency of in-toilet voiding was lower when there were difficulties when starting to void ($t(43) = 2.64$, $p < .05$). The other LUTS did not relate to DI, in-toilet voiding, or number of accidents.

Dripping urine and voiding after a visit to the toilet occurred in low frequencies and were therefore not analyzed (see Table 6 for statistic measures on all behavioral variables). Individuals who noticed a urinary accident, less often suffered from DI ($\chi^2(1) = 23.50$, $p < .01$). Hyperactivity did not relate to DI ($\chi^2(1) = 2.22$, $p = .14$), but high levels of hyperactivity were reported throughout. Due to low numbers of occurrence, the associations between medical malfunctions and incontinence could not be tested. Solid stool was not found to be related to DI ($\chi^2(1) = 0.41$, $p = .52$).

Table 6. Frequency and percentage of behavioral variables related to incontinence in AS ($N = 71$).

	n (%)
Large urinary accident at night	61 (95)
Hyperactive	57 (80)
Solid stool	38 (54)
Noticing urinary accident	38 (54)
Independent toileting visit after waking up	6 (40)
Medicine(s) for solid stool	24 (34)
Waking up after voiding when nocturnal enuresis is present	8 (14)
Deep sleep when nocturnal enuresis is present	8 (13)
Voiding after toileting visit	7 (13)
Waking up when need to void (nocturnia) when nocturnal enuresis is present	4 (7)
Dripping urine	3 (5)
Medical malfunctions on urinary tract	2 (3)

Nocturnal enuresis

More NE was found in individuals who did not wake up before voiding ($\chi^2(1) = 33.45$, $p < .01$), who did not wake up after a urinary accident ($\chi^2(1) = 9.98$, $p < .05$), and in individuals with a solid stool ($\chi^2(1) = 4.02$, $p < .05$). Deep sleep ($\chi^2(1) = 0.01$, $p = .93$) and hyperactivity ($\chi^2(1) = 2.06$, $p = .15$) did not relate to NE. Because most caretakers indicated participants voided large amounts of urine during their sleep, no analysis could be done for this variable and as only eight individuals were continent for urine during the night, these results have to be interpreted with caution.

Fecal incontinence

Individuals with a solid stool less often suffered from FI-night ($\chi^2(1) = 7.6$, $p < .01$), no association was found for FI-day ($\chi^2(1) = .24$, $p = .62$). Using medications for a solid stool was not significantly related to both forms of FI (FI-day: $\chi^2(1) = .04$, $p = .84$; FI-night: $\chi^2(1) = .06$, $p = .82$). Neither hyperactivity (FI-day: $\chi^2(1) = .09$, $p = .77$; FI-night: $\chi^2(1) = .01$, $p = .93$) nor deep sleep (FI-day: $\chi^2(1) = .17$, $p = .68$; FI-night: $\chi^2(1) = 3.38$, $p = .07$) were significantly related to FI.

3.2.3 Primary caretakers' perspectives on incontinence and training

Primary caretakers whose child or client with AS was incontinent for urine during the day ($n = 38$) were asked about their perspectives on incontinence and toilet training (see Table 7). The most common toilet training components identified by primary caretakers were bringing their child or client to the toilet at regular scheduled times ($n = 20$), reinforcing in-toilet voiding ($n = 3$), and not wearing the diaper during waking hours ($n = 2$). Ten primary caretakers

indicated that the training had not been effective, three stated that training was initially successful, but relapse occurred. The other toilet training protocols were partially successful; their children or clients voided on the toilet but still had accidents.

Table 7. Parent's perspectives on incontinence and toileting training in AS (n = 38)

		n (%)
Behavior of the child	Anxious - general	9 (24)
	Anxious - toilet	2 (7)
Impact incontinence	Burden	10 (28)
	Activities cannot be done	7 (18)
Toilet training	Efforts made in the past	24 (63)
	Efforts still made	13 (34)
Reasons for incontinence	Intellectual disability	35 (92)
	No access to toilet	5 (1)
	Never received training	5 (1)
	Physical disabilities	3 (1)
	Medical reasons	2 (1)
	Communication deficits	1 (<1)
	Fear	1 (<1)

Note. AS = Angelman syndrome.

3.3. Between-group analyses

3.3.1. Differences in incontinence

Between-group analysis revealed significant differences in incontinence between both groups (see Table 2). Significantly more DI was seen in the CG, compared to individuals with AS. No differences between groups appeared for NE and FI-day and FI-night.

Significant differences were found between the CG and AS group in wheelchair dependency, living facility, and epilepsy. Participant group, wheelchair dependency, living facility, and epilepsy were entered as independent variables in a logistic regression analysis, with DI as the dependent variable. Results revealed that this model was significant ($\chi^2(4) = 28.49$, $p < .01$). For DI, participant group, living facility, and wheelchair dependency had a significant influence on incontinence. Being part of the CG made the odds on having DI 3.93 times more likely, compared to being part of the AS group. Living at home made the odds on being

incontinent 3.13 times more likely, compared to living in a facility and being wheelchair dependent made the odds 3.88 times more likely, compared to being ambulant.

Table 8. Mean frequency of urination and defecation, *SD* and range in AS and CG.

		n	M	SD (range)	df	T	P
In toilet urinations per day when continent for urine during the day	AS	33	3.82	1.55 (1-7)	46	3.61	< .01
	CG	15	5.67	1.84 (3-10)			
Defecations per week	AS	71	5.78	2.50 (2-14)	91.58	3.51	=.001
	CG	67	8.36	5.49 (2-35)			

Note. AS = Angelman syndrome; CG = Control group.

3.3.2. Differences in urination and defecation

When DI was present, more days with accidents were found in the CG compared to the AS group (see Table 2 and 8). No interaction effect was found for participant group * wheelchair dependency ($F(1, 85) = 0.05$, $p = .83$), participant group * living facility ($F(1, 79) = 3.46$, $p = .06$) or participant group * epilepsy ($F(1, 88) = 1.49$, $p = .23$).

When individuals were continent for urine during the day, individuals with AS showed less in-toilet urination compared to the CG. No interaction effect was found for participant group * wheelchair dependency ($F(1, 44) = 1.33$, $p = .26$), participant group * living facility ($F(1, 40) = 0.43$, $p = .52$), or participant group * epilepsy ($F(1, 40) = 0.06$, $p = .81$).

Individuals with AS could stay dry for significantly longer periods than individuals in the CG ($t(53) = 2.68$, $p = .01$). Again, no interaction effect was found for participant group * living facility ($F(1, 49) = 0.37$, $p = .55$), participant group * wheelchair dependency ($F(1, 50) = 0.00$, $p = .99$) or participant group * epilepsy ($F(1, 51) = 0.13$, $p = .72$).

More defecations were seen within the CG (see Table 8), no interaction effect was found for participant group * living facility ($F(1, 119) = 0.01$, $p = .94$), participant group * wheelchair dependency ($F(1, 129) = 1.44$, $p = 0.23$) or participant group * epilepsy ($F(1, 132) = 0.04$, $p =$

0.85). More fecal accidents were found in the CG when the individual was incontinent for feces during the day (see Table 2), no interaction effect was found for participant group * living facility ($F(1, 67) = 0.02$, $p = .89$), participant group * wheelchair dependency ($F(1, 74) = 1.44$, $p = .23$) or participant group * epilepsy ($F(1, 76) = 1.08$, $p = .30$). Differences in nighttime fecal or urinary accidents were not found (see Table 2).

Logistic regression analysis revealed that the model with participant group, living facility, wheelchair dependency, and epilepsy as independent variables and solid stools as the dependent variable was significant ($\chi^2(4) = 17.52$, $p < .01$). Participant group was found to be the only predictor for solid stools; the odds of having a solid stool were 2.84 times more likely for individuals with AS, as compared to the CG.

4. Discussion

This is the first study to compare the frequencies and types of incontinence between a relatively large group of individuals with AS and a matched control group with non-specific ID. Results reveal that less DI was found within the AS group compared to the CG.

Within AS, the most common form of incontinence was NE. This was also found in the CG of the present study, in Prader-Willi syndrome (von Gontard et al., 2010) and in Rett syndrome (Giesbers et al., 2012) Out of the individuals with AS who had NE, 63% also had DI, indicating that most individuals had non-monosymptomatic NE (Nevéus et al., 2006). In addition, one or more LUTS were present in the majority of individuals with AS. Specifically, there were signs indicative of possible overactive bladder (urgency) voiding postponement (long micturition intervals, holding manoeuvers) and dysfunctional voiding (hesitancy, straining, interrupted stream). The relative high frequency of NE might be associated with the sleep problems and symptoms of circadian rhythm disorder, reported in AS (Didden et al., 2004).

Braam, Didden, Smits, and Curfs (2008) found that melatonin supplementation improved quantity and quality of sleep in AS, but also led to high salivary melatonin levels, suggesting that there might be a disturbed melatonin metabolism. A disturbed melatonin metabolism and a possible decreased melatonin level might be related to nighttime voiding, since melatonin supplementation was found to decrease nighttime voiding (Sugaya, Nishijima, Miyazato, Kadekawa, & Ogawa, 2007) in elderly people. In addition, Matsuta et al. (2010) found that melatonin increases the capacity of the bladder and decreases the urine quantity through the GABAergic system in rats. It remains to be assessed what the impact of a possible disturbed melatonin metabolism and/or sleep problems is on NE in AS and if melatonin supplementation decreases NE.

Another explanation for the high frequency of NE might be that individuals with AS possibly retain their urine until their pelvic-floor muscles relax at night, whereas hyperactive movements during the day common in AS (Williams, 2010) might impede this relaxation necessary for voiding. Also, because they are hyperactive, persons with AS might simply avoid going to the toilet and postpone micturition. However, our analyses showed that hyperactivity and deep sleep were not significantly related to any form of incontinence. This may be due to low frequencies of deep sleep and high frequencies of hyperactivity in our study, resulting in imbalanced groups which impeded statistical analysis.

Within-group analysis further revealed that a higher age and level of adaptive functioning were negatively related to DI in AS, whereas the presence of epilepsy was positively related to NE. This is in accordance with studies showing that a more severe level of ID is associated with higher rates of incontinence (Von Wendt, Simila, Niskanen, & Jarvelin, 1990) and that individuals with epilepsy more often have NE than individuals without epilepsy (Brylewski &

Wiggs, 1998). Differences in living facility, gender, wheelchair dependency, and UTIs were not associated with incontinence in AS. An explanation for the positive effect of aging on continence might be the decrease in hyperactive movements as individuals with AS mature (Clarke & Marston, 2000). However, in our data most primary caretakers indicated that their child or client was hyperactive and our data does not support the hypothesis that hyperactivity and incontinence are related. We did not qualify the severity of hyperactivity, which would have enabled us to more precisely assess the effect of hyperactivity on incontinence.

Although DI is positively influenced by age and level of adaptive functioning, in many children incontinence persists into adulthood. Research has shown that specialized training protocols can lead to continence in children and adults with AS (Didden, Sikkema, Bosman, & Duker, 2001; Radstaake, Didden, Moore, Anderson, & Curfs, 2013). Our findings suggest that: a) some primary caretakers may not deem their child or client ready for training, and b) that toilet training might not be seen as a priority. In typically developing children signs of readiness for toilet training (i.e. staying dry for two hours, showing interest in the toilet, and indicating a need to go) are seen between 24 and 29 months of age and daytime urinary continence is acquired around three years of age (Schum et al. 2002). This developmental age is rarely or never reached in this study (highest age equivalent 2:9 years), or in the study by Peters et al. (2004; highest age equivalent 1;4 years) and accordingly primary caretakers may believe that their child or client is too young for training, resulting in continuing incontinence. This manner of reasoning is supported by the finding that most primary caretakers named the ID of their child or client to be causing the incontinence. Only a few primary caretakers indicated that the incontinence of their child or client negatively impacted their lives, opposed to parents of typically developing children. In the study of De Bruyne et al. (2009), parents of children aged five to 13 years with

enuresis reported to experience more stress than children without. Primary caretakers of children or clients with AS might not see incontinence as an "extra burden", given the other developmental challenges inherent to individuals with AS, resulting in a decreased prioritization for toilet training. The same reasoning was suggested by Giesbers et al. (2012) in their study on incontinence in Rett syndrome. Nonetheless, many (63%) primary caretakers of individuals with DI reported that their child or client had undergone some sort of toilet training, mostly consisting of bringing the individual to the toilet at regular scheduled times. Although many primary caretakers indicated that their child or client was continent when they were sent to the toilet on regular times, the majority of the individuals were not continent, indicating that a more specific toilet training is required. Most importantly, persons with AS have not received standard, state-of-the-art paediatric or urologic assessment and treatment. Many signs are indicative of functional lower urinary tract disorders. Specific treatment options such as anticholinergics (in overactive bladder) have probably not been offered.

Outcomes of this study suggest that the following variables should be considered during toilet training in AS. First, communication training should be included as data suggests that when individuals can communicate their need to void, fewer accidents and more in-toilet voids occur. Research has shown that communicative behaviors can be taught to individuals with AS (Allen et al., 2010; Radstaake, Didden, Oliver, Allen, & Curfs, 2012). Second, during training the diaper should be exchanged for regular undergarments to foster continence (Tarbox, Williams, & Friman, 2004; Simon & Thompson, 2006), as less incontinence was found in the participants who noticed a urinary accident. Third, regular toileting times should be scheduled and fluid and fiber intake should be stimulated to foster continence (Anti et al., 1998; van Laecke, Raes, vande Walle, & Hoebeke, 2009; von Gontard & Nevéus, 2006, Kroeger & Sorensen-Burnworth, 2009),

as relative low frequencies of urination and defecations and high frequencies of hard stools were found in AS compared to the CG group. As this could be a sign of constipation, assessment and treatment with laxatives (such as PEG) and scheduled toilet sittings would be recommended.

Alongside these practical implications, further research should focus on assessing bladder dysfunction in individuals with AS. The LUTS and the combination of both in-toilet urination and accidents found in AS might be explained by the presence of an underactive bladder and/or a dysfunction in sensing bladder satiation (Nevéus, et al., 2006). These urological conditions may also explain the lower voiding frequencies and longer intervals between voids found in AS, compared to the CG. Relatively low numbers of urinary accidents were also reported during the baseline phases in toilet training studies in AS (Didden et al., 2001; Radstaake et al., 2013), compared to the number of voids in individuals with severe ID of other origin (Averink, Melein, & Duker, 2005). To our knowledge, no research has assessed the functioning of the urinary tract system in individuals with AS. Uroflowmetry and ultra sounds could reveal the flow curve, volume and rapidity of the void as well as the residual volume in individuals with AS (Nevéus et al., 2006). Deviations in these variables could have implications for medical treatment or toilet training in AS (Chase, Austin, Hoebeke, & McKenna, 2010).

Some limitations of this study should be considered. First, the non-respondents were not analyzed. It is possible that certain factors were responsible for not responding, thereby jeopardizing the generalizability of the results. Second, our data are derived from primary caretakers' reports and based on a questionnaire that has only been used once in its current form (Giesbers et al., 2012). Further research should combine the information of primary caretakers' reports with data derived from urodynamic assessment, as to discover more qualitative

differences and dysfunctions in urine flow. Finally, research should focus on evidencing psychometric properties of this questionnaire, as these are unknown yet.

This study shows that despite the severe developmental challenges individuals with AS face, there is a lack of evidence regarding incontinence as part of their behavioral phenotype. The majority of the participants showed in-toilet urination and 46% were continent for urine during the day. The findings in this study suggest that a higher age, an increased level of adaptive functioning, and absence of epilepsy can positively influence continence and that some behavioral variables (e.g., communication, noticing a urinary accident) are associated with continence. Tailor made toilet training protocols for individuals with AS should take these variables into consideration.

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6. Declaration of interest

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7. References

Allen, D., Oliver, C., Webster, P., Reid, D., Villa, D., Beaumont, S., … Radstaake, M. (2010). Behavioral intervention for challenging behavior in children with Angelman syndrome. *Journal of Intellectual Disability Research, 54,* 885-885.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Anti, J., Pignataro, G., Armuzzi, A. Valenti, A., Iascone, E., Marmo, R., … Gasbarrini, G. (1998). Water supplementation enhances the effect of high- fiber diet on stool frequency and laxative consumption in adult patients with functional constipation. *Hepato-gastroenterology, 45,* 727-732.

Averink, M., Melein, L., & Duker, P. C. (2005). Establishing diurnal bladder control with the response restriction method: Extended study on its effectiveness. *Research in Developmental Disabilities, 26*, 143-151.

Beetz, R., von Gontard, A., & Lettgen, B. (1994). *Anamnese-Fragebogen: Einnässen/Harninkontinenz unt Erläuterungen zum Anamnese-Frageboden [Parental Questionnaire Enuresis/Urinary Incontinence and Explanatory notes"]*. Bad Homburg: Enuresis Informationszentrum.

Braam, W., Didden, R., Smits, M. G., & Curfs, L. M. G. (2008). Melatonin for chronic insomnia in Angelman syndrome: A randomized placebo-controlled trial. *Journal of Child Neurology, 23*, *649-654.*

Brylewski, J. E., & Wiggs, L. (1998). A questionnaire survey of sleep and night-time behavior in a community-based sample of adults with intellectual disability. *Journal of Intellectual Disability Research, 42,* 154-162.

Buntinx, I. M., Hennekam, R. C. M., Brouwer, O. F., Stroink, H., Beuten, J., Mangelschots, K., &, Fryns, J. P. (1995). Clinical profile of Angelman syndrome at different ages. ` *American Journal of Medical Genetics, 56*, 176-183.

Borrie, M. J., & Davidson, H. A. (1992). Incontinence in institutions: Costs and contributing

factors. *Canadian Medical Association Journal, 147*, 322-328.

Chase, J., Austin, P., Hoebeke, P., & McKenna, P. (2010). The management of dysfunctional voiding in children: A report from the standardization committee of the International Children's Continence Society. *Journal of Urology, 183,* 1296-1302.

Cicero, F. R., & Pfadt, A. (2002). Investigation of a reinforcement-based toilet training procedure for children with autism. *Research in Developmental Disabilities, 23*, 319-331.

Clarke, D. J., & Marston, G. (2000). Problem behaviors associated with 15q-Angelman syndrome. *American Journal of Mental Retardation, 105*, 25-31.

Clayton-Smith, J., & Laan, L. (2003). Angelman syndrome: A review of the clinical and genetic aspects. *Journal of Medical Genetics, 40*, 87–95.

De Bruyne, E., Van Hoecke, E., Van Gompel, K., Verbeken, S., Baeyens, D., Hoebeke, P., & Vande Walle, J. (2009). Problem behavior, parental stress and enuresis. *The Journal of Urology, 182,* 2015-2021.

Didden, R., Korzilius, H., Smits, M. G., & Curfs, L. M. G. (2004). Sleep problems in individuals with Angelman syndrome. *American Journal on Mental Retardation, 19,* 275-284.

Didden, R., Sikkema, P. E., Bosman, I. T. M., & Duker, P. C. (2001). Use of a modified Azrin-Foxx toilet training procedure with individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 14*, 64-70.

Dykens, E. M. (1995). Measuring behavioral phenotypes: Provocations from the "new genetics". *American Journal on Mental Retardation, 99,* 522-532.

Giesbers, S., Didden, R., Radstaake, M., Korzilius, H., von Gontard, A., Lang, R., … Curfs, L. M. G. (2012). Incontinence in individuals with Rett syndrome: A comparative study. *Journal of Developmental and Physical Disabilities, 24,* 287-300.

Gotoh, M., Matsukawa, Y., Yoshikawa, Y., Funahashi, Y., Kato, M., Hattori, R. (2009). Impact of urinary incontinence on the psychological burden of family caregivers. *Neurourology and Urodynamics, 28*, 492-496.

Kroeger, K. A., & Sorensen-Burnworth, R. (2009). Toilet training individuals with autism and other developmental disabilities. *Research in Autism Spectrum Disorders, 3,* 607-618.

Laan, L. A. E. M., den Boer, A. Th., Hennekam, R. C. M., Renier, W. O., & Brouwer, O. F. (1996). Angelman syndrome in adulthood. *American Journal of Medical Genetics*, *66,* 356-360.

Lalande, M., & Calciano, M. A. (2007). Molecular epigenetics of Angelman syndrome. *Cellular and Molecular Life Sciences, 64*, 947-960.

Landefeld, C. S., Bowers, B. J., Feld, A. D., Hartmann, K. E., Hoffman, E., Ingber, M. J., … Trock, B. J. (2008). National institutes of health state-of-the-science conference statement: Prevention of fecal and urinary incontinence in adults. *Annals of Internal Medicine, 148,* 449-460.

Matsuta, Y., Yusup, A., Tanase, K., Ishida, H., Akino, H., & Yokoyama, O. (2010). Melatonin increases bladder capacity via GABAergic system and decreases urine volume in rats. *The Journal of Urology, 184,* 386-391.

Mehta, K. M., Simonsick, E. M., Penninx, B. W., Schulz, R., Rubin, S. M., Satterfield, S., & Yaffe, K. (2003). Prevalence and correlates of anxiety symptoms in well-functioning older adults: Findings from the health aging and body composition study. *Journal of the American Geriatrics Society, 51*, 499-504.

Moss, S., & Patel, P. (1997). Dementia in older people with intellectual disability: Symptoms of physical and mental illness, and levels of adaptive behavior. *Journal of Intellectual*

Disability Research, 41, 60-69.

Nevéus, T., von Gontard, A., Hoebeke, P., Hjälmas, K., Bauer, S., Bower, W., … Djurhuus, J. C. (2006). The standardization of terminology of lower urinary tract function in children and adolescents: Report from the Standardization Committee of the International Children's Continence Society (ICCS). *The Journal of Urology, 176*, 314-243.

Peters, S. U., Goddard-Finegold, J., Beaudet, A. L., Madduri, N., Turcich, M, & Bacino, C. A. (2004). Cognitive and adaptive behavior profiles of children with Angelman syndrome. *American Journal of Medical Genetics Part A, 128A*, 110-113.

Radstaake, M., Didden, R., Oliver, C., Allen, D., & Curfs, L. M. G. (2012). Functional analysis and functional communication training in individuals with Angelman syndrome. *Developmental Neurorehabilitation, 15*, 91-104.

Radstaake, M., Didden, R., Peters-Scheffer, N., Moore, D., Anderson, A., & Curfs, L. M. G. (2014). Toilet training in participants with Angelman syndrome: A case series. *Developmental Neurorehabilitation, 17,* 243-250.

Scholte, E., van Duin, G., Dijkxhoorn, Y., Noens, I., & van Berckelaer-Onnes, I. (2008). *Handleiding Vineland Screener (Manual Vineland Screener-Dutch version)*. Leiden: PITS.

Schum, T. R., Kolb, T. M., McAuliffe, T. L. Simms, M. D., Underhill, R. L., & Lewis, M. (2002). Sequential acquisition of toilet training skills: A descriptive study of gender and age differences in normal children. *Pediatrics, 109*, e48.

Simon, J. L., & Thompson, R. H. (2006). The effects of undergarment type on the urinary continence of toddlers. *Journal of Applied Behavior Analysis, 38*, 363-368.

Sugaya, K., Nisijma, S., Miyazato, M., Kadekawa, K., & Ogawa, Y. (2007). Effects of melatonin

and rilmazafone on nocturia in the elderly. *The Journal of International Medical Research, 35*, 685-691.

Tarbox, R. S. F., Williams, W. L., & Friman, P. C. (2004). Extended diaper wearing: Effects on continence in and out of the diaper. *Journal of Applied Behavior Analysis, 37,* 97-100.

Van Laecke, E., Raes, A., vande Walle, J., & Hoebeke, P. (2009). Adequate fluid intake, urinary incontinence, and physical and/or intellectual disability. *Journal of Urology, 182*, 2079-2084.

Von Gontard, A., Didden, R., Sinnema, M., & Curfs, L. (2010). Urinary incontinence in persons with Prader-Willi syndrome. *British Journal of Urology, 106,* 1758-1762.

Von Gontard, A., Laufersweiler-Plass, C., Backes, M., Zerres, K., & Rudnik-Schöneborn, S. (2001). Enuresis and urinary incontinence in children and adolescents with spinal muscular atrophy. *British Journal of Urology, 88,* 409-413.

Von Gontard, A., & Nevéus, T. (2006). *Management of disorders of bladder and bowel control in childhood.* Londen: MacKeith Press.

Von Wendt, L., Simila, S., Niskanen, P., & Jarvelin, M. R. (1990). Development of bowel and bladder control in the mentally retarded. *Developmental Medicine and Child Neurology, 32,* 515–518.

Williams, C. A. (2010). The behavioral phenotype of the Angelman syndrome. *American Journal of Medical Genetics, 154C*, 432-437.

Chapter 5

Toilet training in individuals with Angelman syndrome:

A case series

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Abstract

Objective: To assess if adapted versions of the response restriction toilet training protocol, based on the behavioral phenotype of Angelman syndrome (AS), were successful in fostering urinary continence in seven individuals with AS.

Method: Data were collected in AB-designs during baseline, training, generalization and follow-up. The response restriction protocol was adapted: individuals were trained in their natural environment, were prompted to void and along with improving continence, the interval between voids was prolonged and time-on-toilet decreased.

Results: During generalization five individuals had less than two accidents and one to six correct voids per day; during baseline more accidents and/or less correct voids occurred. In two participants correct voids increased, but several accidents still occurred. Three participants maintained positive results after 3-18 months.

Conclusion: Despite their intellectual and behavioral challenges, urinary continence can be acquired in AS. Several indications of voiding dysfunctions were found; further research is indicated.

1. Introduction

Angelman syndrome (AS) is a neurodevelopmental disorder caused by the absence of expression of maternally imprinted genes in the region at 15q11-13 (Lalande & Calciano, 2007). Individuals with AS have severe intellectual disability (ID), motor and speech deficits, and epilepsy is often present (Williams, 2010). In addition, they show jerky, tremulous movements and generally have an easily excited, happy demeanor. Incontinence is also common with individuals with AS, although prevalence rates differ across studies. For example, Buntinx et al. (1995) found that 62.5% of a sample of children aged 2-16 years (n = 23) were incontinent for urine and feces during the day. Of individuals aged 16 and older (n = 18), 12.5% were incontinent. Another study found that, when sent to the toilet on a regular basis, 12 out of 28 adults (43%) with AS were incontinent for urine throughout the day (Laan, den Boer, Hennekam, Renier, & Brouwer, 1996).

Incontinence is associated with a range of adverse effects. Being incontinent may cause stigmatization, urinary tract infections, physical discomfort, and it may lead to dependency on caregivers and exclusion from certain activities or peer groups (see e.g., Cicero & Pfadt, 2002; Kroeger & Sorenson-Burnworth, 2009). Further, it can place a burden on caregivers. Costs of diapers and medical treatments, and wages for caretakers are also considerable (Landefeld et al., 2008).

Research on toilet training individuals with AS is needed to help address these issues. To our knowledge, the one published study addressing toilet training in AS used a modified Azrin-Foxx procedure to toilet train six individuals aged 6-19 years who were living in a residential facility (Didden, Sikkema, Bosma, & Duker, 2001). The training mainly took place in the bathroom and included increased fluid intake, scheduled toileting, rewards for correct voiding,

together with overcorrection and time out from reinforcement upon an incorrect void (i.e., accident). Positive practice was not used because of participants' motor limitations. Training resulted in increased correct voiding but, after training, accidents still occurred. Results were maintained over a period of two-and-a-half years for five out of six participants. The authors suggested that behaviors characteristic of individuals with AS (noncompliance, hyperactivity, and bursts of laughter) may have impacted the efficacy of this intervention procedure, lengthening the training time required. This suggests that future toilet training procedures should be adapted to the behavioral characteristics of individuals with AS.

Duker, Averink and Melein (2001) developed the response restriction (RR) method which differed from other procedures in that overcorrection was not used and bladder control was the aim of training, not self-initiated voiding. The RR procedure entails: a) increased fluid intake, b) a 10-min reinforcement interval in the bathroom with toys and praise upon correct voiding, c) positive practice upon a urinary accident, d) increasing the distance between participants and toilet seat following correct voids and e) stepwise generalization to the living/daycare group once the training phase is completed. Training principally occurs in the bathroom where the participant has to stand near the toilet. Any behavior other than correct toileting (e.g. flushing the toilet, stereotypic behaviors, sitting on the ground) is prevented (i.e., restricted) by the trainer. Verbal interactions and eye contact between trainer and participant are avoided as much as possible and prompting is withheld.

The RR procedure has been shown to be effective in individuals with severe ID, but the effects of this protocol (with adaptations) with individuals with AS are unknown. In the present study, seven individuals with AS were toilet trained using a RR procedure which was modified to accommodate the aforementioned characteristics of individuals with AS. The aim of this study

was to assess the effects of a modified RR procedure on urinary accidents and correct voids within a prompted toileting schedule.

2. Methods

2.1. Participants

Participants were recruited through the Dutch Angelman Foundation, an organization for parents who have a child with AS. Individuals were included if they were: (a) incontinent of urine throughout the day, (b) able to sit for 5 minutes, (c) showed regular voiding (wet diapers), (d) were able to walk independently, (e) followed simple instructions, and (f) had no seizure activity.

Seven participants with a mean age of 14 years (range: 6-25) were included (see Table 1). Five participants lived at home, while two lived in a residential facility. During daytime, all participants attended a daycare centre or school for individuals with ID. They were non-verbal and communicated through vocalizations and gestures. All parents gave their informed consent for their child's participation in this study.

Table 1**.** Participant characteristics.

	Sex (M/F)	Age (years)	Developmental age (years; months)	Subtype AS	Epilepsy
Mandy	F	6	1;6[2]	Imprinting error	No
Daniel	M	18	1;2-1;4[1]	Deletion	Yes
Ella	F	25	1;0-1;2[1]	Deletion	Yes
Nate	M	21	1;4[1]	Deletion	No
Alice	F	7	1;2-1;4[1]	Mutation	Yes
Jonah	M	8	1-1;2[1]	Deletion	No
Kevin	M	13	1;2[1]	Deletion	No

Note. [1] Score derived from the Vineland Adaptive Behavior Scales (VABS, [14]);
[2] Score derived from the Bayley Scale of Infant Development (BSID-II-NL, [15]); AS = Angelman syndrome.

2.2. Setting

Training was implemented in the setting where accidents most often occurred. Depending on the participant's voiding pattern, training took place in the bathroom of the participant's home or daycare center/school or home. Training occurred between 9 and 3 or 4 pm. The time the participant actually spent in the bathroom during the day, depended on the progress of the training (see Table 2). When the child was not in the bathroom, s/he followed the normal curriculum in the class/daycare room or home and the attendance of the trainer in this period was slowly faded out.

Bathrooms included a toilet and were between 2 and 10 m^2 in size. Distracting objects (e.g., toilet brush, diapers) were removed and a table and one or two chairs were placed in the bathroom to seat the trainer(s). Peers were brought to another bathroom or toileting visits of the participants and peers were coordinated such that the toilet was available for training.

2.3. Procedure

Each case study protocol in our training consisted of three consecutive phases: baseline, training and generalization. The baseline phase lasted four to five days, the training phase was completed when the participant had remained dry for 1.5 to 2 hours during two to three consecutive reinforcement intervals following a correct void, after which the generalization phase was initiated, which lasted four to five days.

Prior to baseline, caretakers changed participants' diapers in the bathroom to familiarize them with the setting. During baseline diapers were removed and hourly toileting visits to the bathroom were scheduled, lasting for five minutes or until voiding occurred. No consequences were scheduled for correct and incorrect voids (see Table 3). Also, parents and caretakers were

Table 2. Setting, training components, individual adaptations or additions and correct voids and accidents per participant.

Child	Setting	Used training components	Individual adaptations per training component or additions	Mean nr correct voids BS - GEN	Mean nr accidents BS – GEN
Mandy	School	Increased fluid intake Response restriction Toy play on toilet Most to least prompting and praise	150 ml/30 minutes	0 - 2.3	0.5 - 0
		Increasing the reinforcement interval Reinforcement interval in natural environment Decrease in time-on-toilet Remain seated on toilet following an accident	30, 60, 75, 90 to 120 minutes after every second reinforcement interval without an accident.		
Daniel	Living facility	Increased fluid intake Response restriction Most to least prompting and praise	150 ml/30 minutes	1.7 - 3.8	1 - 0.5
		Increasing the reinforcement interval Reinforcement interval in natural environment Decrease in time-on-toilet Remain seated on toilet following an accident	60, 75, 90 to 120 minutes after every second reinforcement interval without an accident.		
Alice	Day care centre	Response restriction Toy play on toilet Most to least prompting and praise	Was seated for 5 minutes or until voiding occurred.	0 - 3.6	1.8 - 0.2
		Increasing the reinforcement interval Reinforcement interval in natural environment Positive practice	60, 75, 90 to 120 minutes after every second reinforcement interval without an accident.		
Jonah – 1	Day care centre	Increased liquid intake Response restriction Toy play on toilet Most to least prompting and praise	100 ml/hour Was seated for 10 minutes or until voiding occurred.	0.2 -1.6	1.8 - 0.8
		Increasing the reinforcement interval Reinforcement interval in natural environment Positive practice	60, 75, 90 to 120 minutes after every second reinforcement interval without an accident.		

Kevin	Day care centre	Response restriction Increased fluid intake Verbal prompting and praise Reinforcement interval in natural environment Increasing the reinforcement interval Decrease in time-on-toilet Positive practice	Instead of response restriction, all his non-toileting behaviors were ignored. Kevin had to stand in front of the toilet, was only verbally prompted to urinate on the toilet. 30, 60, 75, 90 to 120 minutes after every second reinforcement interval without an accident.	0.2 - 2.6	1.6 - 0
Ella	Living facility	Increased fluid intake Response restriction Verbal prompting and praise Reinforcement interval in natural environment Increasing the reinforcement interval	200 ml/30 minutes, until she had drunk 2000 ml without urinating. Ella had to stand in front of the toilet seat, was only verbally prompted to urinate on the toilet. Distance to toilet seat was increased from 30cm, 50cm, 75cm, 100cm, 150cm, 200cm up to entire bathroom (8m2), after every consecutive correct void. Reinforcement intervals were increased from; 10, 15, 30, 45, 60, 90 up to 120 minutes, minutes after every second reinforcement interval without an accident. After an accident, Ella received a verbal reprimand and was taken to the toilet to see if she continued voiding.	0 - 1.5	0 - 0.3
Nate	Home	Increased fluid intake Response restriction Most to least prompting and praise Reinforcement interval in natural environment Increasing the reinforcement interval Decrease in time-on-toilet	400 ml/hour, until he had drunk 3000 ml. His mother, accompanied by a trainer, sat him down on the toilet seat for a maximum of 30 minutes or until voiding occurred. After three correct voids, time on toilet was decreased to 10 minutes. Nate often indicated when he needed to go to the toilet by taking his mother to the bathroom. Reinforcement intervals were given whether he had voided or not and were increased from 60, 75, 90 to 120 minutes when he stayed dry for three	0 - 1.3	0.5 - 0.3

			intervals. After an accident, Nate received a verbal reprimand and was taken to the toilet to see if he continued voiding.		
Jonah – 2	Day care centre	Increased liquid intake Response restriction Toy play on toilet Most to least prompting and praise Increasing the reinforcement interval Positive practice	150 ml fruit with soda in every reinforcement interval. Time between drinking and going to the toilet was prolonged from 0 to 30 minutes. Reinforcement intervals were increased from 10, 15, 20, 30, 45, 60, 75 up to 90 minutes after every third consecutive correct void, without accidents in the reinforcement interval. During reinforcement intervals he played in the hallway next to his group. During the 90 minute interval, he was brought to his own group.	0.2 – 2	1.8 - 1.8

asked which items their child or client preferred (following the preference assessment procedure by Sigafoos, Didden, & O'Reilly (2003) and these items were placed on a small table in the bathroom, in sight of the participant, but out of reach.

The RR training protocol was adapted on several components (see Table 4), Additional and background information on the training components may be found in Duker et al. (2001), Didden et al. (2001) and Kroeger and Sorensen-Burnworth (2009). In Table 2, the interventions per participant are outlined. Clarifications on the selection rationale for components per participant are available from the first author. Outlines for the baseline and generalization phase can be found in Table 3.

Table 3**.** General outlines for the baseline and generalization phase.

Baseline phase	Participants stayed at their group and followed their own curriculum. Normal fluid intake. Participants were brought to the toilet every hour and were required to stay on the toilet for 5 minutes or until voiding occurred. Least-to-most prompting was used to promote correct sitting. When accidents occurred, the trainer neutrally expressed that the participant had voided in her/his pants and changed the pants.
Generalization phase	Participants stayed at their group and followed their own curriculum. Normal fluid intake. Participants were brought to the toilet every one-and-a-half to two hours, trials lasted for a maximum of 5-10 minutes or until voiding occurred. Prompts and rewards were faded out Similar consequences for accidents during the training and generalization phase (see Table 2). Training was transferred to caregivers, teachers and/or parents; they received the training outline on paper and were coached throughout the generalization process. In consultation with all persons involved, the diaper was removed outside training hours.

Table 4. Treatment components, their description, and their application.

Treatment component	Description	Application
Increased liquid intake	At the onset of the training phase, liquid intake was increased. When training progressed, liquid intake was brought back to normal levels with a 50/100 ml decrease alongside every increase of the reinforcement interval.	Increases the need to void and creates more learning opportunities.
Diaper removal	The diaper was removed during training hours in the three phases of the study. The participant walked around in normal, but light clothes to easily spot accidents.	To directly see and act upon accidents, and to make the participants aware of accidents, which might be perceived as aversive.
Response restriction	To block or restrict all behavior other than standing in front of the toilet, lowering pants, sitting down on the toilet and voiding in the toilet. Motor limitations, distractibility and hyperactivity made standing impossible; participants were allowed to sit on the toilet during toileting visits.	To stimulate correct voiding, as it is the only behavior that is not restricted.
Toy play on toilet seat	Some participants were given a toy to play with while sitting on the toilet seat to prevent them from playing with the water in the toilet bowl.	To prevent overexcitement by playing with the water and to focus on voiding.
Most-to-least prompting strategy and praise	Participants were given verbal, model and physical prompts to stay seated on the toilet seat and to void in the toilet. Prompts were given approximately every 5 minutes. After correct voiding, participants were given a reinforcement interval in which they received praise and tangibles. Both were faded out when the number of correct voids increased.	To promote and reinforce correct sitting on toilet seat and voiding.
Reinforcement interval in the natural environment.	Following a correct void, the participant was rewarded and allowed to go back to his or her normal curriculum for a certain amount of time, depending on the training-progress. This period is called the “reinforcement interval”	To normalize the day, to foster generalization of training results and to prevent stress and frustration on part of the

Increasing the reinforcement interval	The reinforcement interval was increased when the participant had stayed dry for two or three reinforcement intervals.	participant.
Decrease in time-on-toilet	When a decrease in time-on-toilet before voiding was seen (usually after two or three voids in the training phase), toileting visits were ended after a correct void or after 10 minutes, unless clear signs of straining were seen. Irrespective of voiding, the participant was given a reinforcement interval, but only received praise and tangibles when voiding had occurred.	To prevent the undermining of the developed association of the toilet seat and voiding.
Similar consequences for accidents during the training and generalization phase.	The participants received the same consequences for accidents during both training and generalization phase.	Little accidents occurred throughout the study and with this intervention, learning opportunities were increased.
Remain seated on toilet following an accident	Participants had to stay on the toilet until they voided or clearly tried to void, which was followed by a reinforcement interval.	To strengthen the association between urinating in the toilet and reinforcement interval. Was used when caretakers and/or trainers expected or saw that positive practice was too frustrating for the participant, as this would counter training compliance.
Positive practice	Participants were prompted to go to the toilet, lower their pants, sit on the toilet for 1-3 seconds and pull up their pants. This sequence was repeated three times in different locations.	To train the entire toileting sequence and prevent more accidents. Was only used when application was not too frustrating (see "Remain seated on toilet following an accident").

This study focused on urinary continence. When participants showed signs of defecating, they were brought to the toilet and verbally prompted to defecate in the toilet. When defecation occurred in the toilet, reinforcement was given similar to when a correct urinary void occurred. When they voided instead of defecating during this extra-training opportunity, they were reinforced according to the outlines in Tables 2 and 3. When this opportunity was less than 30 minutes prior to the following scheduled toileting time, 30 minutes were added to the following toileting visit.

2.4. Design

Data were collected in a case series design, wherein some components of the training differed per participant (see Table 3). The number of correct voids and accidents during the baseline and generalization phases were individually assessed. During the training phase, all training components were implemented at once, while most training components were faded out in the generalization phase (see Table 4). For Jonah, a second training was initiated after the first generalization phase, as the first training did not lead to a reduction in accidents (see Table 3 and Figure 1).

2.5. Recording

Dependent measures were correct voids and accidents. A correct void was defined as a urinary stream in the toilet. A urinary void was labeled as an accident when the void occurred elsewhere and when the void went through the participants' underwear (e.g., drops of urine in the underwear was not considered an accident). During baseline and training, correct voids and accidents were recorded, including date and time of the void. Trainers also noted related behaviors during training, for instance straining (i.e. raising intra-abdominal pressure to void), holding maneuvers (i.e. behaviors indicative of a compelling need to void) and facial expression while voiding.

Maintenance data were collected through a questionnaire that was completed by the primary caretaker. The mean daily or weekly frequency of toileting visits, number of correct voids, defecations and accidents, and nighttime incontinence were recorded. Follow-up data were collected after 18 months for Mandy, Daniel and Ella, after 6-9 months for Nate, Alice and Jonah, and after 3 months for Kevin. Parents and caretakers were also asked about their perspective on

the training (e.g., if the training effect had maintained or diminished and which factors they considered to have contributed to the long-term outcome).

2.6. Reliability

Toilet training protocols were administered by trained master students. In 33% of training days (during baseline, training and generalization), a second observer (first author) was present to supervise the trainers and to record the number of correct voids and accidents. There was a 100% agreement between the trainer and the first author (correct voids and accidents).

3. Results

Figure 1 shows the daily frequency of correct voids and accidents during baseline, training and generalization phases. The mean frequency of correct voids and accidents during the baseline and generalization phase per participant can be found in table 3. Visual inspection shows that most children benefited from the toilet training. For Ella, Mandy, Nate, Alice and Kevin correct voids during the baseline phase did not occur with a single exception (M = 0.08 correct voids per day, SD = 0.09, range = 0-0.2), but higher number of correct voids occurred during the generalization phase (M = 2.32 correct voids per day, SD = 1.25, range = 1.3-3.6). In these children, apart from Ella, the number of accidents per day decreased (baseline: M = 1.22, SD = 0.94, range = 0.5-1.8; generalization: M = 0.13, SD = 0.15, range = 0-0.5). No difference in accidents between the baseline and generalization phase was seen in Ella as her only accident in the entire training occurred on the final day of the generalization phase.

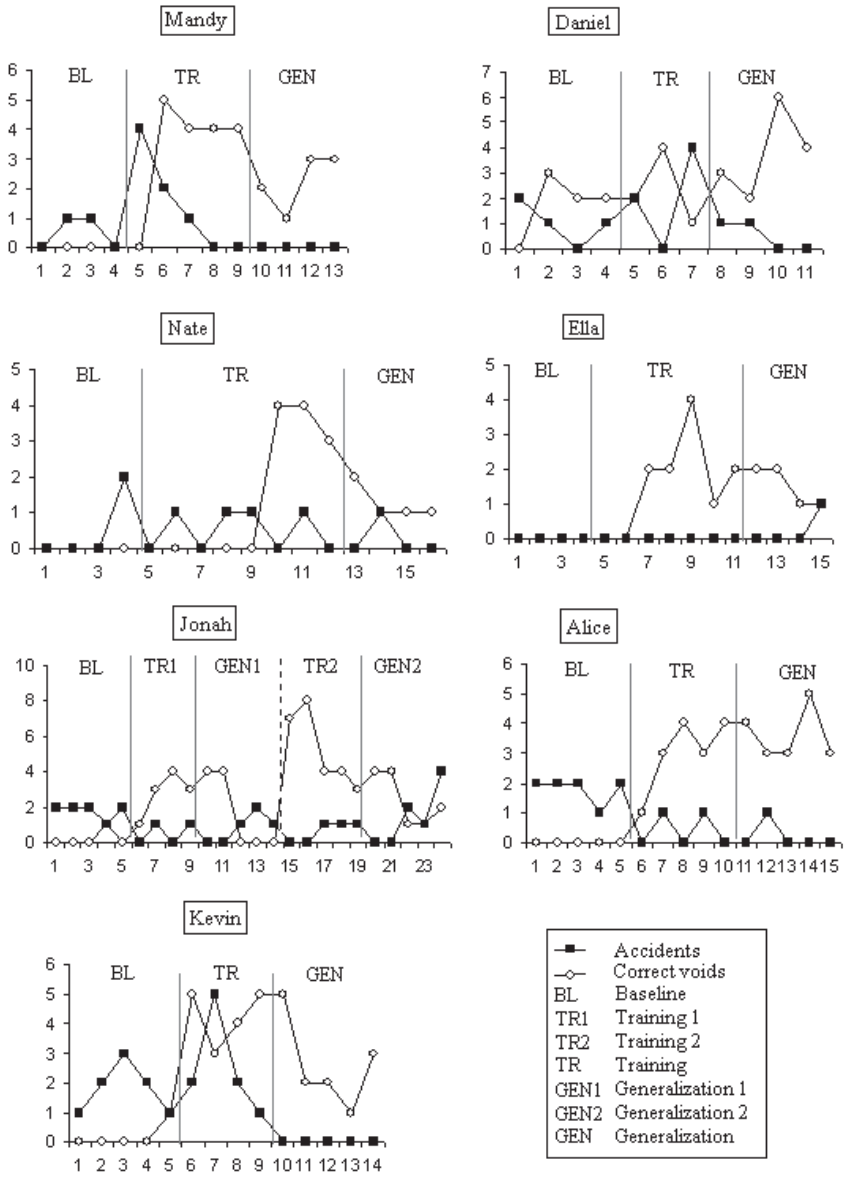
In Daniel's case, correct voids were seen during baseline. Daniel was ill during the third day of training (data point 7), probably explaining the absence of correct voids and his relative

high number of accidents on that day. During the generalization phase, a clear rise in correct voids and a decline in accidents were evident. Training for Jonah was only partially successful; his correct voids increased during both generalization phases compared to baseline (0.2 vs. 1.6-1.8 correct voids per day), but his number of accidents did not change (1.6 vs. 0.8-1.8 accidents per day).

Changes in the training protocols with four of the participants: Mandy (data point 6), Ella (data point 7), Nate (data point 11) and Jonah (initiation of TR2), were associated with increases in correct voids. At the start of these training days, Mandy and Jonah were required to remain seated until voiding occurred instead of leaving the toilet after 10 minutes and Jonah also received a further increase in fluid intake. In Nate and Ella, training was transferred from their day care center to their homes at this point in the intervention and, in Nate's case; his mother was introduced as the trainer.

The mean duration of the entire training protocol in days across all participants was 15.4 days (*SD* = 4.1, range 11-24 days).

Figure 1. Frequency of correct voids and accidents per participant.



3.1. Follow up

Information gathered at follow-up revealed that Ella, Alice and Kevin still voided on the toilet three to five times per day and urinary accidents did not occur. Response generalization was reported in Ella; her primary caretakers indicated that she became continent for feces during and following the toilet training and nighttime incontinence decreased. When her toileting visits occurred relatively late at night and early in the morning, she often stayed dry at night. Kevin showed self-initiated toileting during the day and could, according to his parents, appropriately answer questions about his needing to go to the toilet or not. Training results for Mandy, Daniel, Nate and Jonah were not maintained; they wore diapers during the day and of these four only Jonah occasionally voided or defecated on the toilet.

4. Discussion

In this study, modified RR training protocols were used to toilet train seven individuals with AS. Along with increases in correct voids and decreases in accidents, the reinforcement interval was prolonged, time-on-toilet was decreased and the liquid intake was returned to normal quantities. Individuals were trained in their natural environment and received prompts and consequences for correct voids and accidents to encourage correct voiding.

With all participants, correct voids were seen more frequently during the generalization phase as compared to the baseline phase. In four participants, a decrease in accidents between the baseline and generalization phase occurred, in association with the training. In the other three participants no differences in accidents were seen between both phases; accidents remained low (≤ 2) in Ella and Nate and high (≥ 6) in Jonah. Follow-up questionnaires indicate that positive

training results were maintained in three participants. In addition, in Ella continence had generalized to feces and nighttime continence.

Although the caregivers primarily attributed the observed relapses with Mandy, Daniel, Nate and Jonah to environmental factors such as too many changes in routines in daycare facilities, training factors could also have contributed to the relapses, as Didden et al. (2001) reported successful maintenance of training effects over time while using a modified Azrin-Foxx procedure. Differences in long term outcome between our and Didden et al. their study could be a function of differences between the two protocols, components present in their training, that were absent in ours (e.g., rewards for dry pants, restitutional overcorrection, 20 minute time-on-toilet during scheduled toileting visit) or vice versa (e.g., positive practice, decrease of fluid intake during training). Alternatively, differences in long-term training outcomes could be a function of the more extended post training phases included in Didden et al. their study during which participants were monitored and trained during waking hours for almost two months after the initial training phase with the training elements being faded more slowly. Overall, these differences may have resulted in more training opportunities for the participants in Didden et al. their study, possibly leading to a stronger discrimination between a correct void and an accident. Further research seeking to determine the additional benefits of each training component is clearly justified. Finally, our findings stress the need for continuing efforts and patience from the caretakers in all living and daytime environments to promote maintenance of continence (Averink, Melein, & Duker, 2005).

Other additional training components could also have been implemented during the training phase to foster maintenance. One of these components is a communication-mode with which children can indicate their need to void. Although the goal of the training was prompted

voiding, two participants (Nate and Kevin) showed self-initiated toileting during the training and generalization phase. They had started to imitate a gesture for toileting made by the trainer. Future research investigating the effect of communication training as an element of toilet training in AS is warranted. Second, as fecal incontinence is a risk factor for urinary incontinence (Kroeger & Sorenson-Burnworth, 2009) fecal continence should be trained alongside or following training for urinary continence. In the training and generalization phases, several participants defecated in the toilet but fecal accidents occurred as well, indicating that additional training for fecal continence is required (see e.g., Matson & LoVullo, 2009).

Besides these training components, medical factors should be taken into consideration. Lower baseline frequencies of accidents were found in individuals with AS when compared to frequencies of individuals with severe ID (Aveink et al., 2005; Duker, Averink, & Melein, 2001). This may be indicative of an underactive bladder (Nevéus et al., 2007). An underactive bladder is often accompanied by straining and an interrupted urinary flow pattern, which were also seen in the participants in our study. Further, during the training phase holding maneuvers were seen only once despite the increased liquid intake (up to 2000-3000 ml). This absence of holding maneuvers is a remarkable finding since most accidents consisted of large quantities of urine which could not be interrupted by the trainers, suggesting that the bladder was full enough to sense an urge to void. Future research should focus on abnormal voiding patterns and characteristics in individuals with AS.

Our results should be interpreted in the light of the following limitations. Because of the low number of participants and individualized training protocols, no firm statements can be made about the generalization of the results and about which training components were responsible for

the individual results. Another limitation is the use of AB designs. Due to practical constraints and time limitations we did not use a control group or multiple baseline design.

Despite obvious limitations, our study suggests that urinary continence is a feasible goal in the lives of individuals with AS. Further research is needed to evaluate procedures with which initial treatment effectiveness can be maintained long-term in natural environments. Also, qualitative (low voiding frequencies) and quantitative (e.g. straining, absence of holding maneuvers) voiding characteristics observed during training, suggest that individuals with AS may have voiding dysfunctions. Future studies should explore this, as this could impact toilet training protocols and medical treatments.

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6. Declaration of interest

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7. References

Averink, M., Melein, L., & Duker, P. C. (2001). Establishing diurnal bladder control with

the response restriction method: Extended study on its effectiveness. *Research in Developmental Disabilities, 26,* 143-151.

Buntinx, I. M., Hennekam, R. C. M., Brouwer, O. F. Stroink, H. Beuten, J., Mangelschots K., & Fryns, J. P. (1995). Clinical profile of Angelman syndrome at different ages. *American Journal of Medical Genetics, 56*, 176-183.

Cicero, F. R. & Pfadt, A. (2002). Investigation of a reinforcement-based toilet training procedure for children with autism. *Research in Developmental Disabilities, 23,* 319-331.

De Bildt, A. A., & Kraijer, D. W. (2002). *Vineland-Z: Sociale zelfredzaamheidschaal voor kinderen en jeugdigen met een verstandelijke beperking.* [Vineland Adaptive Behavioral Scales, Survey Form]. Leiden, The Netherlands: PITS.

Didden, R., Sikkema, P. E., Bosman, I. T. M., & Duker, P. C. (2001). Use of a modified Azrin-Foxx toilet training procedure with individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 14*, 64-70.

Duker, P. C., Averink, M., & Melein, L. (2001). Response restriction as a method to establish diurnal bladder control. *American Journal on Mental Retardation, 3*, 209-215.

Kroeger, K. A., & Sorensen-Burnworth, R (2009). Toilet training individuals with autism and other developmental disabilities. *Research in Autism Spectrum Disorders, 3*, 607-618.

Laan, L. A. E. M., den Boer, A. Th., Hennekam, R. C. M., Renier, W. O., & Brouwer, O. F. (1996). Angelman syndrome in adulthood. *American Journal of Medical Genetics, 66,* 356-360.

Lalande, M., & Calciano, M. A. (2007). Molecular epigenetics of Angelman syndrome. *Cellular and Molecular Life Sciences, 65*, 947-960.

Landefeld, C. S., Bowers, B. J., Feld, A. D., Hartmann, K. E., Hoffman, E., Hoffman, E., … Trock, B. J. (2008). National institutes of health state-of-the-science conference statement: Prevention of fecal and urinary incontinence in adults. *Annals of Internal Medicine, 148*, 449-460.

Sigafoos, J., Didden, R., & O'Reilly, M. (2003). Effects of speech output on maintenance of requesting and frequency of vocalizations in three children with developmental disabilities. *Augmentative and Alternative Communication, 19*, 37-47.

Matson, J. L., & LoVullo, S. V. (2009). Encopresis, soiling and constipation in children and adults with developmental disability. *Research in Developmental Disabilities, 30,* 799-807.

Nevéus, T., von Gontard, A., Hoebeke, P., Hjälmås, K., Bauer, S., Bower, W., … Djurhuus, J. C. (2007). The standardization of terminology of lower urinary tract function in children and adolescents: Report from the standardization committee of the international children's continence society (ICCS). *Neurourology and Urodynamics, 26,* 90-102.

Van der Meulen, B. F., Ruiter, S. A. J., Lutje Spelberg, H. C. , & Smrkovsky, M. (2002). *Bayley Scales of Infant Development – Second Edition – Dutch Version* (BSID-II-NL). Lisse, the Netherlands: Swets & Zeitlinger.

Williams, C. A. (2010). The behavioral phenotype of the Angelman syndrome. *American Journal of Medical Genetics, 154C*, 432-437.

Chapter 6

Uroflowmetric assessment in participants with Angelman syndrome

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Abstract

Objective: To asses possible bladder dysfunctions and lower urinary tract symptoms (LUTS) in individuals with Angelman syndrome (AS), since in previous studies on toilet training and continence in AS remarkable voiding characteristics were found.

Method: Uroflowmetric analysis, a non-invasive technique to assess the voiding pattern, was conducted in six participants with AS.

Results: Pathological uroflow patterns were found in five participants; staccato flows in three participants, interrupted flows in one and both interrupted and staccato flows in another participant. Small quantities or urine were found in four participants, large amounts in one and one participant had normal voided volumes.

Conclusions: Results indicate that different conditions such as dysfunctional voiding are present in AS and future studies should further assess these in greater detail. Possible treatment of LUTS and incontinence includes adequate liquid intake, timed voidings, treatment of constipation and allowing enough time on toilet to stimulate relaxation.

1. Introduction

Angelman syndrome (AS) is a neurological disorder, caused by the absence or malfunctioning of chromosomes in the 15q11-13 region (Lalande & Calciano, 2007). Participants with AS have severe intellectual disability (ID), motor deficits, and speech is absent. Uncontrollable burst of laughter and hyperactive behavior are common (Williams, 2010).

Individuals with AS have severe deficits in adaptive behavior skills (e.g. communication, social skills, and continence) (Peters et al., 2004). Radstaake et al. (2013a) conducted a questionnaire study to assess frequency and characteristics of incontinence in AS. Results revealed that 54% of individuals (n = 71) between 5 and 55 years of age were incontinent for urine during the day, while 78% (n = 69) of the matched controls were incontinent. Results further pointed out that individuals with AS could stay dry for a significant longer duration than individuals with severe ID of other origin. Lower urinary tract symptoms (LUTS; e.g. straining, interrupted stream, hesitancy) were frequently mentioned by primary caregivers of AS.

The results of the questionnaire study corroborate clinical findings during a study on toilet training in AS (Radstaake, Didden, Moore, Anderson, & Curfs, 2013b). In this study, seven individuals with AS (aged 6-25 yr) were toilet trained, resulting in increases in correct in-toilet voids in all participants and low(er) frequencies of urinary accidents in five participants. Large amount of fluids (up to 2500 ml) did not always lead to higher voiding frequencies. Despite increased fluids, holding maneuvers were rarely seen in all participants. More noteworthy, urinary accidents often consisted of large quantities and seemed to be uninterruptable. In contrast, in-toilet urine flows were frequently interrupted and when small amounts of fluids were taken some participants showed signs of straining while voiding.

Above voiding characteristics (e.g. apparent absent holding maneuvers, voluminous and interrupted urine flows, and observed low voiding frequencies) may be indicative of a dysfunction of both the storage and emptying phase of the bladder. Abnormal voiding patterns (i.e. flows) can be categorized in normal (bell or tower shaped pattern) or pathological (plateau, staccato and interrupted pattern) urine flow (uroflow) patterns (see Austin et al. (2014) for examples) (Abrams et al., 2002; De Jong, Klijn, & Vijverberg, 2012; Nevéus et al., 2006). Several factors are associated with bladder dysfunction; level of ID, motor disabilities, swallowing difficulties, and urinary tract infections (UTI; Chen, Mao, Homayoon, & Steinhardt, 2004; Van Laecke, Raes, Vande Wall, & Hoebeke, 2009; Yang, Meng, & Chou, 2010). These variables increase the risk for bladder dysfunction. Abnormal voiding patterns are best explained as a result of physiological malfunctions in the urinary tract system (Feldman & Bauer, 2006).

Uroflowmetry gives an indication of possible disorders of the voiding phase only (not the storage phase). Different conditions can be associated with abnormal uroflow patterns. A plateau type of uroflow can be indicative of functional or structural bladder outlet obstruction. Both staccato and interrupted curves are typical of dysfunctional voiding. In this latter condition, the urethral sphincters and the pelvic floor muscles contract paradoxically during voiding – instead of relaxing. Finally, in an underactive bladder a complete emptying of the bladder is not possible, resulting in interrupted curves.

Uroflowmetry has been used to assess bladder dysfunction in children with ID (Yang et al., 2010) and in children with ID and motor disability (Van Laecke et al., 2001). In uroflowmetry, velocity, volume, and pattern of the uroflow are measured and deviations can be detected (Nevéus et al., 2006). Findings revealed that abnormal bladder emptying and a small bladder capacity more frequently occurred in children with severe ID compared to children

without ID or children with milder ID. In both studies, abnormal voiding patterns occurred in high frequencies (35.2% - 87.5%) in children with ID. In the study of Yang et al. (2010) interrupted flow was the most frequent occurring abnormal uroflow pattern. The study by Laecke et al. (2001) did not discriminate between different uroflow patterns.

The assessment of the above mentioned voiding characteristics in AS all rely on observations of parents and/or toilet trainers. To assess voiding patterns in individuals with AS reliably and objectively, we conducted uroflowmetry in six individuals. This is the first study to conduct this kind of assessment in a specific syndrome group in which severe ID is present. The aim of this study is to investigate if pathological uroflow patterns are present in six participants with AS. Such patterns could have implications for treatment and toilet training, e.g. optimal hydration and regular voiding routines, treatment for constipation, pelvic floor muscle awareness training, or medicinal treatment (Chase, Austin, Hoebeke, & McKenna, 2010).

2. Methods

2.1. Participants

Participants were six individuals with AS of whom two participated in our toilet training study (Radstaake et al., 2013b). Individuals with AS were asked to enroll in this study because they matched the inclusion criteria: (a) being twelve years or older, (b) voiding in the toilet on regular times, and (c) being able to void on different toilets. The other participants were recruited by asking members of the Prader Willi/Angelman Foundation in the Netherlands to participate. Six parents gave their consent, two of them were excluded as the participant was too young or lived too far away. Participants were two males and four females; their mean age was 29 years (see Table 1 for participant characteristics). All participants were diagnosed with AS by

chromosomal testing and had severe ID. Five could walk independently, one female used a stroller. Five participants were continent of urine during the day.

Table 1. Participant characteristics.

Participant	Age in years	Mobility	Continent	Living arrangements
1	13	Ambulant	Yes	Home
2	26	Ambulant	Yes	Institution
3	42	Ambulant	Yes	Institution
4	15	Ambulant	Yes	Home
5	36	Ambulant	No	Institution
6	43	Stroller – dependent	Yes	Institution

2.2. Setting

Data collection took place at the daycare centre and/or home of the participants. No changes were made to the bathrooms and toilets. An item (a chair, towel) was placed upon the regular toilet to indicate that the participant could not sit on that toilet seat, but had to sit on the toileting chair which was connected to the measuring equipment. To prevent disruption of daily routines, each participant's daily schedule was followed and the researcher was only present during toileting moments.

2.3. Procedure

The participants were taken to the bathroom at their regular toileting times, where uroflowmetric assessment was conducted. No extra fluids were given as not to influence the regular voiding patterns. All participants stayed on the toilet for 5-20 minutes or until voiding occurred. They remained seated for at least 15 seconds after the termination of the urine flow. In five out of six participants three voids were measured to make sure the assessment was reliable. In participant 4 only two voids were assessed, as both uroflow patterns were virtually identical and the mother of the child indicated that this was the way her child always voided. The

researcher observed if holding maneuvers and signs of straining were present before or during the toileting visit.

The uroflow data were analysed by a paediatrician (third author) according to the diagnostic criteria of the Standardization Committee of the International Children's Continence Society (Austin et al., 2014; Nevéus et al., 2006). Besides the pattern, the voided volume was measured. The voided volume was labeled as normal when its quantity was between 65 and 150% of the estimated bladder capacity (EBC). The EBC was set on 390 ml (Abrams et al., 2002). Quantities below 65% were labeled as small, quantities above 150% as large. Finally, the maximum flow rate was assessed and regarded as normal if the square of the maximum flow rate equaled or exceeded the voided volume (Austin et al., 2002).

3. Results

Results can be found in table 2. Pathological urometric findings were reported in participant 1, 2, 3, 5 and 6. Participant 1 showed both staccato and interrupted flow patterns, participant 2 showed interrupted flow patterns in all three voids. In participant 3, 5 and 6 both bell shaped and staccato shaped patterns were found. No pathological flow patterns were found in participant 4; both uroflows were bell shaped. Out of the 17 recorded voids, seven were normal uroflow patterns and ten were pathological patterns in which six were staccato and four were interrupted patterns.

Table 2. Outcomes of uroflowmetric assessment per participant.

Partici-pant	No. void	Normal			Pathological		Voided volume[1]	Maximum flow rate	Time to void
		Bell	Tower	Plateau	Staccato	Interrupted			
1	1					x	172; small	18.7	< 1 min
	2				x		350; normal	26.9	< 1 min
	3				x		131; small	17.1	3 min
2	1					x	173; small	24.7	5 min
	2					x	133; small	18.0	unknown
	3					x	197; small	13.4*	5 min
3	1	x					847; large	51.1	< 1 min
	2	x					362; normal	37.3	< 1 min
	3				x		638; large	47.2	< 1 min
4	1	x					420; normal	47.1	< 1 min
	2	x					449; normal	40.7	< 1 min
5	1	x					131; small	22.5	>10 min
	2				x		107; small	15.7	>10 min
	3				x		160; small	24.1	30 sec
6	1	x					77; small	13.5	>10 min
	2				x		125; small	12.5	6 min
	3	x					78; small	13.5	>10 min

Note. [1] small < 234 ml, normal 234-540 ml, large >541 ml; * relative small maximum flow rate.

Small voided volumes were found in participant 2, 5 and 6. Participant 1 had both small and normal voided volumes. In participant 3 both large and normal voided volumes were found. Only in participant 4 all voided volumes were of a normal quantity. Time between sitting on the toilet and voiding differed between and within participants. According to the maximum flow rate, only one flow rate is regarded as relatively low (Table 2).

Holding maneuvers were only seen in participant 3, before she voided the largest quantity of urine, she bended over while walking and refused to sit on the ground to play with her toys. No signs of straining were seen in all participants. A common feature was that participants often fidgeted when they were placed on the toilet, several were given a toy to play with and all except participant 1 were left alone in the toilet. Right before voiding, they stopped with whatever they were doing, sat still, looked very concentrated, and started voiding. Some participants (1, 2, 4 and 5) laughed or looked in the measuring cup directly after voiding.

4. Discussion

This is the first study to assess the uroflow patterns of participants with Angelman syndrome. Results indicate that pathological uroflow patterns were present in five out of six participants with AS. Also, some persons with AS had both normal, bell-shaped, as well as pathological uroflow patterns, which, too, is an indication that these abnormalities are most likely to be functional. In structural or neurogenic disorders, only pathological curves would be expected. Also, patients showed signs of hesitancy, i.e. difficulty in the initiation of micturition, which is in accordance with previous findings (Radstaake et al., 2013a). In four participants, relative small quantities of urine were found, a large amount was found in one participant, and also one participant had normal quantities of urine.

Different conditions could be responsible for these findings. Small bladder volumes could be due to overactive bladder (OAB) with typical signs of frequency i.e. repeatedly small voids and hesitancy (Austin et al., 2014). OAB is often associated with spontaneous detrusor contractions during the storage phase and is treated with anticholinergics. Indeed, van Laecke et al. (2009) reported positive results of anticholinergics in children with intellectual disability. Large bladder volumes could be the result of habitual voiding postponement and urine retention, which is treated by timed voidings. Staccato uroflow patterns are typical signs of dysfunctional voiding, caused by paradoxical pelvic floor and sphincter contractions during voiding. In typically developing children, uroflow and pelvic-floor-EMG biofeedback is highly effective and treatment of choice (Chase et al., 2010). Interrupted curves are indicative of underactive bladder, i.e. detrusor decompensation. Timed and relaxed voidings need to be instituted. In many cases, additional clean intermittent catherisation is needed to enable bladder emptying.

Behavior characteristics of the individuals with AS may also explain why their voiding patterns were pathological. First, in-toilet voiding in individuals with AS is often a taught skill; they void because they get a reward for it, but in the process of toilet training might not learn to fully empty their bladder or to accurately interpret and act upon the sensation of a full bladder. As a result, the partial emptying becomes a habit, instead of contracting their detrustor muscle and letting gravity empty their bladder, leading to pathological voiding patterns. Second, the interrupted and staccato flow patterns might stem from their behavioral phenotype (Williams, 2010); hyperactive and ataxic movements might disturb the control over the detrusor muscle resulting in discontinuing voids, although hyperactive movements were not observed while voiding. In addition, it took some participants more than 10 minutes to start voiding (i.e. hesitancy) and all participants fidgeted on the toilet and only started voiding when they sat still, indicating that relaxation is an important aspect in voiding. Some participants in the present study also reacted upon the initiation of voiding, they giggled or looked into the measuring cup. All the above mentioned behavioral characteristics might have influenced the voiding patterns of our participants.

When our results are compared to the result of the studies of van Laecke et al. (2001) and Yang et al. (2010), some similarities can be found. First, in the study of van Laecke et al. seven out of 11 children (aged 3.2-10.5) with severe ID showed abnormal voiding patterns, compared to five out of six individuals older than twelve in our study. Four children with an IQ between 36 and 45 participated in the study of Yang et al., and 56.2% of their uroflow patterns showed an abnormal voiding pattern, compared to 58.8% in our study. Second, according to the type of uroflow pattern; the van Laecke et al. study mentioned that an interrupted voiding pattern is the most common found dysfunctional voiding pattern and the Yang et al. study reports 60.7%

dysfunctional, staccato or interrupted voids, but does not further discriminate between the voiding patterns. In our study, staccato shaped patterns were found most frequently. Third, a relative large number of small voided volumes was found in all three studies; in all 11 children with severe ID in Yang et al., in 35 out of 38 children in the study of Laecke et al., and in our study in four out of six participants. Accurate comparisons between these studies is troubled by the low participant numbers and age differences as the aforementioned studies only studied children and in our study the mean age of participants was 29 years. It can be concluded that abnormal voiding patterns and small voided volumes are common in individuals with severe ID, including individuals with AS and more research needs to be done to assess voiding patterns at different ages.

A diagnosis of the specific type of disorder is needed to plan an effective treatment. The management of bladder dysfunction is important as it can lead to large quantities of residual urine, overflow incontinence, and urinary tract infections (Feldman & Bauer, 2006). Indeed, in our previous questionnaire study 18 out of 71 participants had suffered one or more UTI (2013a). Several treatment options are mentioned in the literature (see Chase et al. (2010) for a detailed review), of which the most relevant for individuals with AS will be outlined below. Constipation should be treated as it is a risk factor for urine incontinence (see Van Laecke et al., 2009) and high incidences of solid stools were mentioned in our previous study (Radstaake et al., 2013a). Care should also be taken to promote adequate fluid intake; both the Yang et al. (2010) and van Laecke et al. (2001) study mention insufficient hydration due to swallowing problems, environmental and poor self-care to be a very likely reason for bladder capacity problems. In addition, another study of van Laecke et al. (2009) showed that increased fluid intake led to urinary continence and normalized voided volumes in children with ID. Further behavioral

interventions consist of a regular voiding regimen at timed intervals, a well adjusted voiding position in order to promote the relaxation necessary for voiding. When these interventions are unsuccessful in ameliorating voiding dysfunctions and normalizing voided volumes, medications such as anticholinergics could be used.

Some important clinical and research implications can be drawn from this study. First, both staccato and interrupted voiding patterns are a risk for UTIs due to residual urine. As it was considered too invasive, no assessments were done to examine residual urine volume after each void. Based on the results of this study, this type of assessment is advised in future studies. Also, in future studies combined uroflowmetry and pelvic-floor-EMG would provide more information on the interaction of detrusor and sphincter during micturition. Second, out of the five participants with pathological voiding patterns, four were continent of urine during the day. This corroborates the findings of van Laecke et al. (2001), in which more abnormal voiding patterns were found in continent individuals, compared to those who were incontinent. Even if incontinence is not present, LUTS and abnormal emptying patterns are a risk factor for UTIs, and in consequence, for upper urinary tract problems. Based on this association, it is advised to plan specific interventions based on the underlying pathology. Van Laecke et al. (2001) proposed that children with ID are impaired in their reaction to stimuli, including reacting upon a full bladder. Increases in voided volumes will make it easier for them to interpret signals of the need to void, which aids to urinary continence. It could also be assessed how increased fluid intake influences voiding patterns and residual urine.

The results of this study have to be seen in light of the following limitations. A relative small number of participants was used and no matched control group was included, limiting the generalizability of our results. When compared to the existing studies on uroflowmetry no major

differences were found, whereas larger participant numbers of AS might indicate a more distinct voiding pattern. As mentioned before, uroflowmetric assessment can be seen as a basic first step and more invasive diagnostic measures (e.g., sonography, electromyography, intravesical urodynamics, video urodynamic study, cystoscopy, radiological investigations) could further define the underlying malfunctions causing the dysfunctional voiding patterns when indicated (see Chen, Shei-Di Yang, & Chang, 2010). But due to the invasiveness of these assessments and the explorative nature of this study, these assessments were not conducted in our participants. Also, in most patients they are not indicated.

This study aimed at assessing uroflow patterns in individuals with AS, as clinical observations in previous studies indicated bladder dysfunctions and large voided volumes of urine. The uroflowmetric measurement shows that interrupted and staccato patterns were found in individuals with AS, but that voided volumes were often small. During the toilet training study (Radstaake et al., 2013b), individuals were taught to void and were given large amounts of fluids; this could both have influenced the voided volumes. The amount of time that our participants could stay dry was not tested in this study, as this would influence their voiding patterns. Although abnormal voiding was found in this study and utilizing a bladder scan in a future study is advised, care should be taken when more invasive diagnostic measures are used. Therapy always depends on an exact diagnosis. In dysfunctional voiding, some interventions such as biofeedback and pelvic floor muscle training are not realistic for individuals with AS due to their severe ID. In OAB, anticholinergic medication is advisable. In severe underactive bladder, catherisation has to be considered. However, for all conditions, increasing fluid intake, timed, and relaxed voiding are relatively benign interventions and should always be tried first.

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6. Declaration of interest

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7. References

Abrams, P., Cardozo, L., Fall, M., Griffiths, D., Rosier, P., Ulmsten, U., … Wein, A. (2002). The standardization of terminology of lower urinary tract function: Report from the standardization sub-committee of the International Continence Society. *Neurology and Urodynamics, 21*, 167-178.

Austin, P. F., Bauer, S., Bower, W., Chase, J., Franco, I., Hoebeke, P., … Nevéus, T. (2014). The standardization of terminology of bladder function in children and adolescents: Update report from the standardization committee of the international children's continence society (ICCS). *The Journal of Urology, 191*, 1863-1865.

Chase, J., Austin, P., Hoebeke, P., & McKenna, P. (2010). The management of dysfunctional voiding in children: A report from the standardization committee of the International Children's Continence Society. *Journal of Urology, 183*, 1296-1302.

Chen, J. J., Mao, W., Homayoon, K., & Steinhardt, G. F. (2004). A multivariate analysis of dysfunctional elimination syndrome, and its relationships with gender, urinary tract infection and vesicoureteral reflux in children. *The Journal of Urology, 71*, 1907–

1910.

Chen, Y. S., Shei-Dei Yang, S., & Chang, S. (2010). Overactive bladder during childhood: When and how it should be treated. *Incontinence and Pelvic FloorDysfunctions, 4,* 13-17.

De Jong, T. P. V. M., Klijn, A. J., & Vijverberg, M. A. W. (2012). Lower urinary tract dysfunction in children. *European Urology Supplements, 11*, 10-15.

Feldman, A. S., & Bauer, S. B. (2006). Diagnosis and management of dysfunctional voiding. *Current Opinion in Pediatrics, 18*, 139-147.

Lalande, M., & Calciano, M. A. (2007). Molecular epigenetics of Angelman syndrome. *Cellular and Molecular Life Sciences, 64*, 947-960.

Nevéus, T., von Gontard, A., Hoebeke, P., Hjälmas, K., Bauer, S., Bower, W., … Djurhuus, J. C. (2006). The standardization of terminology of lower urinary tract function in children and adolescents: report from the Standardization Committee of the International Children's Continence Society (ICCS). *The Journal of Urology, 176*, 314-243.

Peters, S. U., Goddard-Finegold, J., Beaudet, A. L., Madduri, N., Turcich, M., & Bacino, C. A. (2004). Cognitive and adaptive behavior profiles of children with Angelman syndrome. *American Journal of Medical Genetics,128A*, 110-113.

Radstaake, M., Didden, R., Giesbers, S., Korzilius, H., von Gontard, A., Lang, R., … Curfs, L. M. G. (2013a) Incontinence in participants with Angelman syndrome and non-specific ID: A comparative study. *Research in Developmental Disabilities, 11,* 4184–4193.

Radstaake, M., Didden, R., Peters-Scheffer, N., Moore, D., Anderson, A., & Curfs, L. M. G. (2013b). Toilet training in participants with Angelman syndrome: A case series. *Developmental Neurorehabilitation, 17,* 243-250.

Van Laecke, E. V., Golinveaus, L., Goossens, L., Raes, A., Hoebeke, P., & Vande Walle, J.

(2001). Voiding disorders in severely mentally and motor disabled children. *The Journal of Urology, 1*, 2404–2406.

Van Laecke, E., Raes, A., Vande Walle, J., & Hoebeke, P. (2009). Adequate fluid intake, urinary incontinence, and physcial and/or intellectual disability. *The Journal of Urology, 182,* 2079-2084.

Williams, C. A. (201). The behavioral phenotype of the Angelman syndrome. *American Journal of Medical Genetics, 154C,* 432-437.

Yang, P., Meng, N., & Chou, E. C. (2010). Voiding dysfunctions in children with mental retardation. *Neurourology and Urodynamics, 29,* 1272-1275.

Chapter 7

Educational priorities for individuals with Angelman syndrome: A study of parents' perspectives

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Abstract

Education of individuals with intellectual disability should be based in part on parent priorities. To this end, the educational priorities of 77 parents of children with Angelman syndrome (AS) were assessed. Priorities were gathered from a questionnaire asking parents to rate their child's ability and the priority for training/treatment across a range of adaptive and maladaptive domains. A factor analysis examined if parents prioritized the training of skills in which their child showed a major, moderate or minor deficit. Results showed that parents valued training in developmental milestones (communication, locomotion, continence and eating) and recreational activities. Parents of children under the 18 years emphasized training in communication skills, while parents of adults with AS also valued daytime (physical) activities. Training for communication, recreational and ingestion skills was prioritized when children showed emerging skills; training for motor skills was prioritized when children were highly dependent; and training for self-care skills was prioritized when children were more independent in the self-care domain. Treatment for sleep and eating/overweight problems were prioritized in the behavioral problems domain. The outcomes of this study should be used to guide clinicians in the development and implementation of individual education plans (IEP) for individuals with AS, so that IEPs are aligned with parental preferences. Future research implications are discussed.

1. Introduction

Angelman syndrome (AS) is a neurodevelopmental disorder caused by the absence or malfunctioning of the maternal copy of the UBE3A gene (Lalande & Calciano, 2007). Epilepsy and sleep problems are common in the AS (Didden, Korzilius, Smits, & Curfs; Williams, 2010). The behavioral phenotype consists of a severe to profound intellectual disability (ID), severe speech and motor deficits, hyperactive behaviors, and an apparent happy demeanor (Pelc, Cheron, & Dan, 2008; Williams, 2010). Parents also report on frequent eating problems and non-compliance (Clarke & Marston, 2000; Summers, Allison, Lynch, & Sandler, 1995; Walz, Beebe, Byars, & Dykens, 2005).

Aspects of the behavioral phenotype can be found in the adaptive behavioral profile of AS, although studies are somewhat inconsistent. Gasca et al. (2010) found relatively high scores for "personal life skills", mediocre scores for "community life skills" and "motor skills" and low scores for "social and communication skills" for individuals with AS aged 1-17. Whereas Peters et al. (2004) studied individuals aged 5 months to 10 years and found that socialization skills were better developed than communication, daily living and motor skills; the latter being the least developed. After studying 28 individuals aged 16-40 years, Clayton-Smith (2001) found that with age, hyperactive movements decreased, the attention span increased, communication improved and that independence in self-help skills showed great variability. This variability in self-care or personal life skills was also found in Peters et al. and Gasca et al.; it was hypothesized that intervention/education might explain this variance (Gasca et al.). An increasing number of studies have shown that functional (i.e. adaptive) skills can be taught to individuals with AS and that behavioral problems can be diminished using behavioral interventions (Didden, Sikkema, Bosman, & Duker, 2001; Radstaake et al., 2013, Radstaake,

Didden, Moore, Anderson, & Curfs, 2014; Radstaake, Didden, Oliver, Allen, & Curfs, 2012; Summers & Szatsmari 2009).

Which (adaptive) skill is taught and how to do this in individuals with ID is typically organized in an Individual Education Plan (IEP; Gallagher & Desimone, 1995). Due, in part, to the potential value of parental participation in their child's IEP process (Siebes et al., 2006), research has focused on determining parent priorities in relation to what is taught to their child. For example, Pituch and colleagues used the *Treatment Priorities Survey* to identify educational priorities of parents of children with Prader-Willi syndrome (PWS; Pituch et al. 2010a), Cri-du-Chat syndrome (CdC; Pituch et al., 2010b) and Autism Spectrum Disorders (ASD; Pituch et al., 2011). Different priorities were found. Specifically, in parents of children with PWS, education/treatment for social skills at work, eating disturbances and overweight were prioritized. In CdC personal safety, toileting and the ability to describe feelings and events were considered important and in ASD parents indicated that making friends, personal safety and pedestrian safety skills should be prioritized. Overall, the parent reported priorities seemed to correspond to the unique characteristics of these three different syndromes (O'Brien, 2002).

Two studies have been conducted to assess parental perspectives on the educational priorities for children with AS. Calculator and Black (2010) studied the communication priorities in AS and reported that parents rated the ability to express wants and needs as most important. In general, parents valued the acquisition of skills concerning the initiation and maintenance of social interaction, and they also highlighted the teaching of functional skills. Besides the selection of skills, parents indicated that they wanted to be involved in the decisions being made about their child's educational program. In a study covering a wider range of skills, Leyser and Kirk (2011) reported that the major goals for parents were that their child (a) had social skills

and a social life with friends, (b) had happiness and enjoyment in life, (c) was as independent as possible, (d) was able to communicate, and (e) was safe and secure. Although the majority of parents indicated that the IEP process was helpful, 25% of parents (n = 17) expressed dissatisfaction, indicating that improvements can be made. Both studies were less than comprehensive in terms of the range of adaptive skill domains covered. The studies also did not examine priorities in relation to the child's current abilities, which could show if parents do indeed favor the training in adaptive skills domains that are relatively weak, for instance, motor skills (Peters et al., 2004; Gasca et al., 2010), or that parents favor training in domains in which children show mediocre or emerging skills.

The present study aimed to address these limitations and therefore extend the literature into parental priorities for the education of children with AS. To this end, we used an adapted version of the *Treatment Priorities Survey* (Pituch et al., 2010a) to assess the priorities of parent's in the care for their child with AS. The aims of this study are threefold: (a) to identify skills and behaviors that parents deemed to be important priorities for their child's education or treatment, (b) to analyze if parents adopted a deficit-based logic (i.e. favoring the teaching of skills in which the child shows major deficits) or an emerging-skills logic (i.e. favoring the teaching of skills in which the child shows emerging abilities) in their priorities, and (c) to assess if differences in parental priorities can be found between children and adults with AS. Information of this kind may be useful for developing IEPs reflecting the parent priorities. This in turn may guide the type of competencies that will be required of educators if they are to effectively address the priorities of parents of children with AS.

2. Methods

2.1. Participants

Respondents were members of the Angelman syndrome Parent Association in the Netherlands. The survey was sent to all 154 members of this association. After six weeks, the response rate was 44% (n = 65), and all non-respondents were sent a reminder by email. Four weeks later, 82 questionnaires (response rate 53%) had been returned. Five of these submissions were excluded from analyses because in three submissions the child's diagnosis of AS had not confirmed by genetic testing, in one questionnaire all answers concerning the skills/behaviors were left blank and in the fifth questionnaire parents declared to have two children with AS and it was unclear for whom (son, daughter, or both) they had completed the questionnaire. A total of 77 completed questionnaires were therefore used for the present study.

2.2. Questionnaire

The *Treatment Priorities Survey* (Pituch et al., 2010a) was adapted to fit the behavioral profile of individuals with AS (e.g., in the communication skills domain "speech" was replaced by "speech or communication through another communication mode (e.g., gestures, speech generating device, picture exchange system)"). The job skill domain was removed entirely as the severe ID associated with AS restricts the amount of job skills to be expected of individuals with AS. Activities that could possibly be placed under "job skills" in AS such as helping with household activities and handicraft were already present in other domains. The questionnaire was translated into Dutch and consisted of four parts.

In Part A, parents were asked about the demographic and diagnostic characteristics of their child (gender, age, living and daycare arrangements, severity of ID, confirmation of AS and

subtype). Part B asked about the parents' characteristics (e.g., gender, age, level of education and knowledge of their child's disability and content of IEP). Part C consisted of nine subsections corresponding to the following nine adaptive behavior domains derived from the International Classification of Functioning, Disability and Health Checklist (World Health Organization, 2003): (a) self-care skills, (b) domestic living skills, (c) community living skills, (d) recreational skills, (e) motor skills, (f) social skills, (g) communication skills, (h) academic skills, and (i) behavioral problems. For each domain, three to eight specific skills/behaviors were listed (e.g., expressing wants and needs, naming objects, and answering questions for the communication skills domain). For each listed skill/behavior, parents were asked to indicate their child's ability on a 5-point scale (ranging from 0, totally independent, to 4, totally dependent). For behavioral problems, parents were asked to rate the severity of each behavior on a 5-point scale (0 = not a problem; 4 = major problem). Parents were also asked rate the extent to which each skill/behavior was an educational/treatment priority on a 5-point scale (0 = no at all a priority to 4 = very high priority) and to indicate if any education/ treatment for that skill/behavior was currently part of the IEP. Part D was an open-ended section in which parents could add comments on the education of their child, the IEP, the questionnaire, or on other relevant topics.

2.3. Data analysis

2.3.1. Within group analysis

Data were analyzed with IBM SPSS V19. Descriptive analyses were used to display parent and child characteristics. Mean skill/behavior ability and priority ratings were calculated. The 10 skills and 5 behavioral problems with the highest priority ratings were identified. For each high priority rating it was calculated how many children received training or treatment for

that skill/behavior as part of their IEP. To clarify if age affected parent priorities, priorities for children (aged < 18) and adults (aged ≥ 18) were given separately. For the behavioral problems independent sample *t*-test were done to assess if children with severe behavioral problems more often received treatment for that behavior compared to children with less severe or no behavioral problems.

Factor analysis on all nine behavioral domains was conducted to facilitate interpretation. No factor analysis was done for the entire dataset, as the domains were considered to be too different (e.g., communication versus motor skills) and the relatively small sample size was unlikely to produce stable results. The ratings on the ability scale and the priority scale were analyzed in separate factor analyses. Prior to conducting the factor analyses, the dataset was checked for missing data. Items on current ability or priority regarding a skill/behavior that were left blank or rated as "not applicable" for more than 50% were individually analyzed and were excluded from factor analysis, if not considered relevant to the domain for clinical or theoretical reasons. When a certain skill was indicated as "not applicable", some parents did and others did not rate the priority of training this skill and mention if it was present in the IEP. As parents responded differently to "not applicable" skills and therefore might have interpreted this question differently, the scores on its priority rating and question on its presence in the IEP were treated as "not applicable".

For the factor analysis, principal axis factoring with oblique rotation (delta = 0) was used as the factors were expected to correlate and this type of rotation is appropriate when underlying variables are considered to be the motivation for responses to a number of items. Only factors with eigenvalues higher than 1 were retained in the analyses and items were considered to be

representative for a factor when the factor loading exceeded .40. Factor scores were computed by calculating the means on the items.

To assess if parents prioritized education/training or treatment for skills/behaviors that scored low, moderate, or high on the ability scale, the relations between ability and priority ratings were assessed. Cases with a missing ability and/or priority rating were excluded. When this led to the exclusion of more than 50% of the cases, analysis on which prioritization logic parents used for that given skill was terminated. A two-step approach was conducted. First, scatter plots were observed and when linear associations were expected, correlations between ability and priority ratings were analyzed using Pearson correlations. When significant correlations were found, non-linear regression analysis was done to assess the additional variance explained by the quadratic term. Second, in line with previous studies on educational priorities (see Pituch et al., 2010a, 2010b, 2011), when correlations were not found and scatter plots indicated non-linear associations, non-linear regression analysis was done to test for quadratic associations. When quadratic associations were found, this indicated that parents prioritized emerging skills; parents gave higher priorities to education/training when their child showed a moderate ability for that skill, relative to a higher or lower ability. Each ability/priority relation was analyzed separately per factor. To test for the family-wise-error rate, an alpha of 0.01 was used for the Pearson correlations. Due to the additional degree of freedom, an alpha of 0.05 was used for the quadratic regression analysis.

3. Results

3.1. Respondent characteristics

Respondent characteristics can be found in Table 1. The mean age of the respondents (n = 75) was 52.0 years (SD = 11.0 years, range 27-84 years), the age of two parents was unknown. One respondent was the child's sister, she was 52 years old and indicated that she was involved in her brother's IEP process. As siblings of children with an ID often take over the parenting role once their parents age, this respondent was not excluded from analysis. As the gender of the parent was only relevant to describe the respondents and was not used in any other analysis in this study, the parent with unknown relation to the child remained included in the dataset. The mean age of the parents of the children (aged < 18 years) was 42.3 years (SD = 5.9 years, range 27-55 years); mean age of the parents of the adults (aged ≥ 18) was 58.50 years old (SD = 8.5 years, range 37-84).

Table 1. Respondent characteristics.

		All ages *n* (%) *N* = 77	< 18 years *n* (%) *n* = 30	≥ 18 years *n* (%) *n* = 47
Relation to the child	Mother	61 (80)	28 (93)	33 (72)
	Father	14 (18)	2 (7)	12 (26)
	Sister	1 (1)		1 (2)
	Unknown	1		
Education	University	33 (43)	14 (47)	19 (41)
	High school or post-secondary	38 (50)	13 (43)	25 (54)
	Lower than high school	5 (7)	3 (10)	2 (4)
	Unknown	1		1
Knowledge of disability	(Very) extensive	59 (77)	32 (73)	37 (80)
	Average	16 (21)	7 (23)	9 (20)
	Below average	1 (1)	1 (3)	
	Unknown	1		1
Knowledge of IEP[1]	(Very) extensive	50 (56)	18 (60)	32 (70)
	Average	25 (33)	11 (37)	14 (30)
	Below average	1 (1)	1 (3)	
	Unknown	1		1

[1]IEP = Individual Education Plan.

Table 2. Child and IEP characteristics.

		All ages *n* (%) (*N* = 77)	< 18 years *n* (%) (*n* = 30)	≥ 18 years *n* (%) (*n* = 47)
Gender	Male	39 (51)	18 (60)	21 (47)
	Female	36 (49)	12 (40)	24 (53)
Age	<5	3 (4)	3 (10)	
	5-7	3 (4)	3 (10)	
	8-10	9 (12)	9 (30)	
	11-13	9 (12)	9 (30)	
	14-17	6 (8)	6 (20)	
	18-25	19 (25)		19 (40)
	26-47	28 (36)		28 (60)
Living arrangement	Institution	41 (58)	5 (17)	35 (74)
	Home	36 (34)	25 (83)	11 (26)
Main education/treatment setting	Daycare facility	39 (51)	5 (17)	34 (72)
	School/specialized daycare centre	27 (35)	23 (77)	4 (9)
	Residential setting	16 (21)	3 (10)	13 (28)
	Home	8 (10)	4 (13)	4 (9)
	Otherwise	3 (4)	2 (7)	1 (2)
Subtype	Deletion	60 (83)	24 (83)	36 (84)
	Uniparental disomy	5 (7)	1 (3)	4 (9)
	Mutation	5 (7)	4 (14)	1 (2)
	Imprinting error	1 (1)	-	1 (2)
	unknown	6	1	5
Level of intellectual disability	Profound	40 (55)	11 (41)	29 (63)
	Severe	33 (45)	16 (59)	17 (37)
	Unknown	4	3	1
Additional impairments and diagnoses	Epilepsy	62 (85)	23 (82)	39 (93)
	Motor deficits	56 (77)	22 (79)	34 (81)
	Tremors	27 (37)	9 (32)	18 (43)
	Scoliosis	19 (26)	8 (29)	11 (76)
	Vision impairments	11 (15)	5 (18)	6 (14)
	Attention deficit hyperactivity disorder	3 (4)	-	3 (7)
	Autism	2 (3)	1 (4)	1 (2)
Communication mode	Simple gestures and vocalizations	70 (91)	27 (90)	43 (96)
	Some words	7 (9)	4 (6)	3 (7)
	(Simplified) sign language	7 (9)	4 (6)	3 (7)
	Exchanging pictures	5 (6)	2 (6)	3 (7)
	Speech generating device	2 (3)	-	2 (4)
IEP[1] goals	Teaching skills	66 (92)	27 (96)	39 (87)
	Treating challenging behaviors	35 (49)	8 (29)	27 (61)
	Maintaining acquired skills	5 (7)	1 (4)	4 (9)
	Having a good quality of life	2 (3)	1 (4)	1 (2)
	Motor skills	2 (3)	1 (4)	1 (2)
	Communication skills	1 (1)		1 (2)

Note. When numbers do not add up to the total group count, this is due to missing values; when numbers add up higher than the total group count, parents could give several answers to that item; [1]IEP = Individual Education Plan.

3.2. Child characteristics

Child characteristics can be found in Table 2. The children had a mean age of 21 years and 4 months (*SD* = 11;4, range 2-47). The mean age of the children (aged < 18 years) was 10.0 years (*SD* = 4.0, range 2-16), mean age of the adults was 28.6 years (*SD* = 8.1 years, range 18-47). From the parents whose child lived at home, 16 (42%) had some professional home care support, of which ten were parents of children under 18.

3.3. Presence and content of IEP

Seventy-three parents indicated that their child had an IEP; three parents (4%) indicated that their child did not have an IEP. In all three, the IEP was currently being developed. Respondents of children who did not have an (actual) IEP were nonetheless asked to fill in the remainder of the questionnaire and to indicate in Part B if their child currently received education/ treatment for that skill/behavior, while not currently part of their IEP. IEP goals can be found in Table 2. Compared to the children, more adults had goals concerning "treatment of behavioral problems". It is important to note that while many of the "children" with AS were in fact adult offspring of the respondents, most nonetheless had an IEP to guide the education/treatment/habilitation process.

3.4. High priority skills and behavioral problems

In Table 3, the 10 skills with the highest priority ratings are listed. They represent skills from the communication, recreational, self-care, motor and academic skills domain. Percentages of children receiving education/training for these priority skills ranged from 41.7% (naming persons) to 78.3% (expressing wants and needs). For children under 18, parents mainly

highlighted skills from the communication domain (6 skills), the remaining skills were from the self-care, ingestion, motor and academic domains. Training in these skills was often given, ranging from 92.2 (expressing wants and needs) to 38.5% (describing feeling and events). In adults, most prioritized skills came from the communication and recreational domains (both 3 skills), skills from the motor domain (2 skills) and ingestion and self-care domains (both 1 skill) were highlighted as well. Percentages of individuals receiving training for these skills were slightly smaller, ranging from 68.3 (expressing wants and needs) to 37.5% (naming objects).

Table 4 shows the five behavioral problems that received the highest priority for treatment. Similar percentages of receiving treatment were found (30.0 to 34.9%). Higher priorities were given (46.9 to 61.1%), when parents assigned their children's behavioral problems as "2: reasonable problem" or more severe. Independent samples *t*-test revealed that for sleep problems ($t(49.6) = 3.46$, $p < .01$), eating problems ($t(51) = 2.89$, $p < .01$) and aggression ($t(58) = 3.35$, $p < .01$) a significant higher proportion of the children received training when their severity was rated "2" or higher. For overweight ($t(54) = 1.58$, $p = .12$) and non-compliance ($t(56) = 1.88$, $p = .07$), these numbers did not reach significance. Differences in priority behaviors for treatment between both age groups emerged, although they were small. Overweight, non-compliance, eating and sleep problems were found in both groups, for children under 18 "resistance to change" and for adults "aggression" complemented the top 5.

3.5. Factor analysis

Since less than 50% of the respondents responded to the following items, these were removed from analysis: outdoor chores – priority, sport – ability, sport – priority, wheelchair use – ability and – priority. Many items in the communication skills domain were removed on both

Table 3. Ten highest priority skills and percentage of children receiving training for that skill.

	All ages (N = 77)			< 18 years (n = 30)			≥ 18 years (n = 47)		
Rank	Skill	Mean (SD) [1]	IEP (%)[2]	Skill	Mean (SD)	IEP (%)	Skill	Mean (SD)	IEP (%)
1	Expressing wants and needs	3.01 (1.19)	78.3	Expressing wants and needs	3.16 (1.11)	92.9	Expressing wants and needs	2.90 (1.26)	68.3
2	Following simple directions	2.79 (1.32)	65.5	Following simple directions	2.76 (1.48)	70.8	Following simple directions	2.81 (1.96)	61.3
3	Naming objects	2.56 (1.50)	56.9	Naming objects	2.70 (1.46)	81.8	Outdoor activities	2.52 (1.30)	67.5
4	Walking	2.38 (1.61)	60.9	Starting a conversation	2.59 (1.54)	46.7	Naming objects	2.45 (1.55)	37.9
5	Continence	2.36 (1.31)	52.1	Naming persons	2.55 (1.50)	66.7	Swimming	2.37 (1.11)	58.5
6	Outdoor activities	2.35 (1.28)	69.7	Eating	2.48 (1.15)	82.8	Continence	2.33 (1.26)	48.8
7	Listening to teacher	2.34 (1.12)	61.7	Walking	2.48 (1.64)	65.5	Walking	2.30 (1.60)	57.5
8	Eating	2.32 (1.19)	64.0	Listening to teacher	2.46 (1.10)	65.4	Eating	2.21 (1.21)	52.2
9	Swimming	2.28 (1.26)	58.0	Continence	2.39 (1.40)	57.1	Toy play	2.15 (1.04)	65.0
10	Naming persons	2.27 (1.47)	47.1	Describing feelings and events	2.33 (1.59)	38.5	Cycling	2.14 (1.35)	62.1

[1]A skill with a mean priority above 2.0 indicates that treatment for that particular skill is of above average importance for parents; [2] percentage of participants receiving education/treatment in that skill or behavior as part of their Individual Education Plan (IEP).

Table 4. Descriptives of five most challenging behaviors and percentages of children with Angelman syndrome receiving treatment for that behavior.

group	Challenging behavior	Mean severity (SD)[1]	% Treatment	% Treatment (n)[2]
AS all ages (N = 77)	Sleep problems	1.87 (1.59)	30.0	46.9 (32)
	Overweight	1.54 (1.42)	30.0	55.0 (20)
	Eating problems	1.51 (1.51)	34.9	61.1 (18)
	Non-compliance	1.45 (1.24)	30.6	56.5 (23)
	Aggression	1.39 (1.55)	30.2	61.1 (18)
AS aged < 18 (n = 30)	Overweight	1.76 (1.36)	44.0	70.0 (10)
	Resistance to change	1.67 (1.31)	20.8	38.5 (15)
	Sleep problems	1.58 (1.59)	27.3	46.2 (13)
	Non-compliance	1.52 (1.01)	44.0	63.6 (12)
	Eating problems	1.46 (1.53)	34.8	66.7 (7)
AS aged ≥ 18 (n = 47)	Sleep problems	2.02 (1.60)	31.6	47.4 (21)
	Eating problems	1.53 (1.52)	35.0	58.3 (13)
	Aggression	1.45 (1.60)	30.8	60.0 (10)
	Non-compliance	1.41 (1.38)	21.6	50.0 (12)
	Overweight	1.39 (1.46)	20.0	40.0 (10)

[1]A skill with a mean priority above 2.0 indicates that treatment for that particular skill is of above average importance for parents; [2] Percentage of treatment calculated over the number of parents who indicated that the severity of the behavioral problem of their child was "2; a reasonable problem" or more severe.

ability and priority: asks for information when needed, can describe feelings/events, initiates conversations, and answers questions. Low numbers of reported items were also found in the academic skills domain: cutting - ability, pasting - ability, puzzling – ability, understanding the clock – ability, and all items on priority were excluded. All other items were included in the factor analysis.

Table 5 shows the results of the factor analysis and the corresponding factor loadings. The Kaiser-Meyer-Olkin Measure of Sampling Adequacy was above .50 for all factors, indicating that the data were adequate for factor analysis (George & Mallory, 1995). Except for personal safety, crawling, and naming persons, factor loadings were larger than .40.

Of the 14 domain-based ability and corresponding priority ratings, 11 domains were represented by a single factor. In the remaining three domains two factors were found. For the self-care skills, one factor concerned self-care and the other ingestion (r = .27). Responses to the recreational skills were also explained by two correlated factors (r = .39), one factor was related to indoor, the other to outdoor activities. The two factors for social skills (r = .35) were more difficult to interpret; one appeared to be more related to individuals, whereas the other factor was more related to groups of people.

For the behavioral problem domain, five factors were found to underlie the responses to the severity levels. These five factors were difficult to interpret and several items loaded on more than one factor. No factor analysis for the priority ratings could be done because the responses to these items were too different. Therefore, it was decided to conduct separate analyses for all items of the behavioral problem domain.

Table 5. Factor loadings for the ability and priority items in Angelman syndrome.

Domain	Item	Factor 1	Factor 2
Self-care skills abilities	Washing oneself	.88	
	Caring for body	.82	
	Toileting	.82	
	Dressing oneself	.79	
	Eating	.68	
	Drinking	.64	
Self-care skills priorities	Washing oneself	.94	.05
	Caring for body	.94	.09
	Dressing oneself	.94	-.17
	Toileting	.56	.06
	Drinking	-.04	.98
	Eating	.06	.81
Domestic living skills abilities	Household chores	.80	
	Shopping	.80	
	Outside chores	.88	
	Shopping	.81	
	Household chores	.75	
Community living skills abilities	Use public transportation	1	
	Use community businesses	.88	
	Pedestrian safety	.58	
	Personal safety	.39	
Community living skills priorities	Use public transportation	.80	
	Pedestrian safety	.79	
	Use community businesses	.75	
	Personal safety	.52	
Recreational skills abilities	Playing with friends	.85	-.10
	Toyplay	.84	.08
	Watching television	.65	.06
	Swimming	-.10	.87
	Outdoor activities	.27	.61
Recreational skills priorities	Outdoor activities	.88	
	Swimming	.80	
	Watching television	.51	
	Playing with friends	.50	
	Toyplay	.47	
Motor skills abilities	Walking the stairs	.82	
	Walking	.81	
	Lifting and carrying objects	.77	
	Fine motor skills	.72	
	cycling	.70	
	Sitting upright	.46	
	Crawling	.26	
Motor skills priorities	Lifting and carrying objects	.87	
	Fine motor skills	.80	
	Sitting upright	.72	
	Walking	.70	
	Walking the stairs	.69	
	Crawling	.60	
	Cycling	.57	
Social skills abilities	Seeks out interaction with others	.90	-.09
	Shows affection to caregivers	.86	-.08
	Accepts interaction	.67	.23
	Interacts appropriately with unfamiliar people	-.13	.87

	Makes friends	.07	.50
	Interacts appropriately with familiar people	.44	.45
Social skills priorities	Accepts interaction	.94	
	Interacts appropriately with familiar people	.89	
	Seeks out interaction with others	.87	
	Interacts appropriately with unfamiliar people	.84	
	Shows affection to caregivers	.83	
	Makes friends	.68	
Communication skills abilities	Following directions	.75	
	Manding	.68	
	Naming objects	.60	
	Naming persons	.39	
Communication skills priorities	Manding	.90	
	Naming objects	.88	
	Naming persons	.76	
	Following directions	.71	
Academic skills abilities	Coloring	.84	
	Playing music instruments	.65	
	Puzzling	.54	
	Listening	.45	

3.6. Prioritization logic

We assessed the logic that parents used in their prioritization: a deficit-based logic or a prioritization of emerging skills. First, it was analyzed for which domains significant linear correlations were found between the ability and priority ratings. A negative association was found between ability and priority ratings of self-care skills (r = -.39, p < .01, n = 65); the more dependent the child was, the lower the priority ranking for education/training. Positive associations were found for the prioritization of training for social skills concerning individuals (r = .39, p < .01, n = 60) and for motor skills (r = .46, p < .01, n = 42); the more dependent the child, the higher the priority rating. The linear regression models explained 15%, 15% and 21% of the variation in the priority ratings for training for that particular domain, respectively. No quadratic association was present as the additional variance explained by this term was 5% at maximum and the smallest p-value was .06. Associations could not be assessed for the academic

skills domain, as in more than 50% of the cases the ability and/or priority rating were missing or rated “not applicable”.

Second, for the remaining domains, we assessed whether quadratic terms explained the associations between the ability and priority ratings. This was the case for ingestion (feeding) skills ($p < .05$, $n = 64$), indoor ($p < .01$, $n = 43$) and outdoor recreational skills ($p < .05$, $n = 61$), and communication skills ($p < .05$, $n = 42$). The quadratic terms respectively explained 8%, 16%, 9%, and 10% of the variance in priority ratings, respectively. When children showed emerging skills, higher priority ratings were given compared to when children required a lot or no assistance to carry out the skills.

No linear or quadratic associations were found for community living skills ($r = -.26$, $p = .09$, $n = 44$; $p = .58$, $n = 43$, $R^2 < .01$) and social skills concerning groups ($r = .19$, $p = .18$, $n = 51$; $p < .30$, $n = 50$, $R^2 = .02$). For the domestic living skills, no analysis could be done as more than 90% of the respondents indicated that their child was totally dependent.

All behavioral problems were analyzed separately, as no factors could be determined. For each behavioral problem, a significant ($p < .01$) positive linear relation was found between the ability and priority rating. The more severe the behavioral problem, the higher the treatment priority. Correlations ranged between .28 (aggression) and .97 (passiveness and elopement), with 10 out of 14 correlations above .80.

4. Discussion

Parents of children with AS prioritized training in skills from the communication, recreational, self-care (i.e. continence, eating), motor and academic (i.e. listening to the teacher) domains. With regard to behavioral problems, treatment for sleep problems, overweight and

eating problems, non-compliance and aggression were given the highest priority. The prioritized training skills mainly represent developmental milestones (i.e. toileting, eating, communicating, walking) and later in life daytime activities (i.e. swimming and outdoor activities) and the majority of children were reportedly receiving education/training on these skills. These priorities regarding adaptive skill training seem to reflect the behavioral phenotype of AS (Williams, 2010) and similar priorities were found in the study by Leyser and Kirk (2011). The top priority rating for 'expressing wants and needs' is in accordance with the findings of Calculator and Black (2010). Out of all three studies concerning parent priorities it can be concluded that training in basic adaptive skills (e.g. communicating, walking) and enjoyable daytime activities are highly important for parents of children with AS, with an emphasis on communication skills throughout the lifespan.

The reported behavioral problems are in line with previous research by Clarke and Marston (2000) and Summers et al. (1995), although aggression was not found to be a major problem in the study by Clarke and Marston, and treatment for hyperactive behaviors was not given a high priority in our study. An explanation for both differences may be that previous studies explored the *presence* of behavioral problems while we assessed *priorities* for treatment. Although hyperactive behavior may be a more prominent problem in AS, parents most likely see aggression as a bigger problem which requires treatment. Sleep problems and associated treatment opportunities have often been documented in the AS population (Allen, Kuhn, DeHaai, & Wallace, 2013, Braam, Didden, Smits, & Curfs, 2008; Clarke & Marston, 2000; Didden et al., 2004; Summers et al., 1995; Walz et al., 2005), but eating problems are less well studied. Berry et al. (2005) found that individuals with AS more often than individuals with similar ID showed food fads (an interest in one specific food item), were selective eaters, ate non-food objects,

gorged foods, and had an increased appetite, findings overlapping with those of Clarke and Marston. Williams et al. (2006) also reported on "abnormal food related behaviors" and "obesity (in the older child)" and indicated that these were present in 20-80% of individuals with AS. In all probability, these documented eating problems relate to the high priorities parents gave to 'overweight' and 'eating skills' in our study. Further, parents gave high priorities to motor exercises in adulthood (e.g., swimming, cycling, walking), presumably to prevent or reduce overweight. This may be even more important when children age, as adults with AS were described as being "reluctant to exercise", resulting in weight gains (Clayton-Smith, 2001). More research should be done to examine the nature and extend of eating problems and overweight in AS in order to develop and assess treatment options as well as possibilities for prevention of such problems.

It appeared that the parents of children with AS used a deficit-based logic with respect to the prioritization of skills from the motor domain and the social skills domain concerning individuals. That is, high priorities for training were given when children had limited ability (i.e. major deficits). An explanation may be found in the severe motor deficits in AS, and parents may look upon locomotion as an important starting point in development, therefore prioritizing training in this skill domain. Also, motor deficits are apparent in all individuals with AS. Motor functioning is the least developed adaptive behavioral skill in children (Peters et al., 2004) and parents may believe that training is essential and perhaps the starting point in the development of motor skills. Early intervention in motor development was also advised by Beckung, Steffenburg, and Kyllerman (2004) to prevent long-term problems. For the social domain, an explanation might be that skills this domain represents attachment issues and these might be important for parents as they symbolize the relationship with their child. For self-care skills, higher priorities

were given when children were relatively independent. Parents may take over these actions when their child is totally dependent as they believe their child is unable to acquire them at the moment.

For ingestion, indoor and outdoor recreational and communication skills, however, parents prioritize skills when their child was showing some emerging ability. This logic appears consistent with Vygotsky's (1978) notion of the zone of proximal development. When the child initiates an action, this might be a good time to implement training to further develop the skill as there is likely to be motivation on the part of the child (Bondy & Frost, 2001; Iovannone, Dunlap, Huber, & Kincaid, 2003). Regarding communication skills, many children with AS show non-verbal communicative behaviors (Didden et al., 2009). Parents may be highly susceptible to these as they are aware of their child's speech deficit and may want to stimulate communication as soon as their child shows signs of readiness. When behavioral problems emerge, communication training can also be implemented to replace challenging behaviors with socially accepted communicative behaviors (Radstaake et al. 2012, 2013).

In comparing the results of this study with those studying the educational priorities of children with PWS, CdC, and ASD similarities and differences can be found (Pituch et al., 2010a, 2010b, 2011). Overall, parents of children with AS gave less priority scores above 3.0, suggesting that parents highly value the acquisition of a few particular skills or that parents have lower expectations of their children. A review on long-term educational plan goals for individuals with profound and multiple disabilities (van der Putten, Vlaskamp, & Poppes, 2009) showed that these individuals (N = 145) had an average of two long term goals, of which 14% were reached after one year. This indicates that several long term goals might not be feasible for individuals with severe ID and parents may adapt to this in their prioritization of skills. Second, parents of children with severe ID might have lower expectations and might be satisfied with

every developmental gain that their child makes. Indeed, several parents mentioned that the main goal for their child was to be happy and to have meaningful daytime activities. These types of comments from parents would seem similar to those reported by Leyser and Kirk (2011). Differences also emerge in the domains parents value for training.

In general, parents of children with PWS or ASD seem more orientated on social inclusion and value domains such as job skills, academic skills, recreational skills and community living skills. Parents of children with CdC or AS also highlight some of these skills, but appear to focus more on communication and self care skills. An explanation for this might be the differences in level of ID, which is more severe in CdC and AS. As can be seen, the behavioral phenotype also appears to influence the parental priorities in AS, PWS, CdC, and ASD (O'Brien, 2002). For instance 'communication skills'; in PWS all priority scores were linearly related or independent to their ability scores, but in ASD (communication and academic), CdC (communication and domestic living), and AS (communication, recreational and ingestion) skills were in a quadratic way related to their ability score, i.e. parents valued training in these skills when their child showed emerging abilities for that skill. Communication skills are most impaired in AS, CdC and ASD as compared to PWS, which may account for this difference. Overall, it is clear that parents of children with these four syndromes value goals aimed at adaptive behaviors and that level of ID and behavioral phenotypes are likely to play part in deciding which adaptive behavior(s) to address.

Outcomes of the present study have to be seen in light of the following shortcomings. First, the non-respondents were not analyzed and generalization of the conclusions is limited. Participants were all members of the Angelman syndrome Parent Association in the Netherlands; which presumably gives them easier access to information regarding training and treatment. Also,

parents were relatively highly educated which may have influenced our results. Indeed, parental level of education and social economic status have shown to influence the decisions parents make regarding their child's education (Mutua & Dimitrov, 2001; Szumski & Karwowski, 2012). Second, on many skills the majority of parents indicated that their child was totally dependent and training had no priority, indicating that we have been unable to make an adaptation of the questionnaire that fully fitted the AS behavioral profile. This may influence the validity of our results. For future research it is advised to group the skills into smaller responses as this might result in parents being able to prioritize more specific training targets. The low priority ratings cannot be attributed to poor internal validity, as most of the domains were explained by one factor and for the majority of the items high factor loadings were found. In following studies concerning parental preferences, the educational priorities of individuals with non-specific ID should be assessed, to allow for discriminations between ID and syndrome specific educational priorities when comparing the results of those of syndrome-groups.

We advise that caretakers and teachers of individuals with AS are informed about the behavioral characteristics of AS and the treatment preferences of parents, so that they can adjust IEPs accordingly. Training should focus on developmental milestones and on determining meaningful and enjoyable daytime activities, for instance activities with water and plastics, as this has shown to be a preference for individuals with AS (Clayton-Smith, 1993; Didden, Korzilius, Sturmey, Lancioni, & Curfs, 2008; Williams et al. 2010) and physical activities to prevent obesity. In addition, treatment for behavioral problems should be given, since they have shown to be successful for sleep problems (Braam et al., 2008), challenging behavior and communication (e.g., Radstaake et al., 2012, 2013) and incontinence (Didden et al., 2001; Radstaake et al., 2014). Teachers should be educated on these behavioral treatments, including

principles of prompting, shaping and reinforcing, since research has indicated that they can successfully administer behavioral treatments to enhance adaptive skills in individuals with ID (see e.g., Lalli, Browder, Mace, & Brown, 1993; Lydon, Healy, O'Reilly, & Lang, 2012; Ringdahl & Sellers, 2000) and AS (Radstaake et al., 2013). In administering these behavioral treatments, some behavioral characteristics of AS (e.g., short attention span, non-compliance) may interfere with accurate implementation of behavioral treatments (Summers et al., 1995). Interventions such as supervisory or video feedback, self-monitoring and instruction have shown to increase correct trainer behavior, which in turn had a positive effect on the child's progress (van Vonderen, Duker, & Didden., 2010; van Vonderen, Duker, Didden, Lang, & Lancioni, 2011).

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6. References

Allen, K. D., Kuhn, B. R., DeHaai, K. A., & Wallace, D. P. (2013). Evaluation of a behavioral treatment package to reduce sleep problems in children with Angelman Syndrome. *Research in Developmental Disabilities, 34*, 676-686.

Beckung, E., Steffenburg, S., & Kyllerman, M. (2004). Motor impairments, neurological signs, and developmental level in individuals with Angelman syndrome. *Developmental Medicine & Child Neurology, 46*, 239-243.

Berry, R. J., Leitner, R. P., Clarke, A. R., & Einfeld, S. L. (2005). Behavioral aspects of Angelman syndrome: A case control study. *American Journal of Medical Genetics Part*

A, 132A, 8-12.

Bondy, A., & Frost, L. (2001). The Picture Exchange Communication System. *Behavior Modification, 25,* 725-744.

Braam, W., Didden, R., Smits, M.G., & Curfs, L.M.G. (2008). Melatonin for chronic insomnia in Angelman syndrome: a randomized placebo-controlled trial. *Journal of Child Neurology, 23*, 649-654.

Calculator, S. N., & Black, T. (2010). Parent's priorities for AAC and related instruction for their children with Angelman syndrome. *Augmentative and Alternative Communication, 26*, 30-40.

Clarke, D., & Marston, G. (2000). Problem behaviors associated with 15q- Angelman syndrome. *American Journal on Mental Retardation, 105*, 25–31.

Clayton-Smith, J. (1993). Clinical research on Angelman syndrome in the United Kingdom: Observations on 82 affected individuals. *American Journal of Medical Genetics, 46*, 12-15.

Clayton-Smith, J. (2001). Angelman syndrome: Evolution of phenotype in adolescents and adults. *Developmental Medicine & Child Neurology, 43,* 476-480.

Gallagher, J., & Desimone, L. (1995). Lessons learned from implementation of the IEP: Applications to the IFSP. *Topics in Early Childhood Special Education, 15,* 353-378.

Didden, R., Korzilius, H., Smits, M. G., & Curfs, L. M. G. (2004). Sleep problems in individuals with Angelman syndrome. *American Journal on Mental Retardation, 109,* 275-284.

Didden, R., Korzilius, H., Sturmey, P., Lancioni, G., & Curfs, L. M. G. (2008). Preference for water-related items in Angelman syndrome, Down syndrome and non-specific intellectual disability. *Journal of Intellectual and Developmental Disability, 33*,

59-64.

Didden, R., Sigafoos, J., Korzilius, H., Baas, A., Lancioni, G. E., O'Reilly, M. F., … Curfs, L. M. G. (2009). Form and function of communicative behaviors in individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disability, 22,* 526-537.

Didden, R., Sikkema, P. E., Bosman, I. T. M., & Duker, P. C. (2001). Use of a modified Azrin-Foxx toilet training procedure with individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 14*, 64-70.

Gasca, C. B., Obiols, J. E., Bonillo, A., Artigas, J., Lorente, I., Gabau, E., … Turk, J. (2010). Adaptive behavior in Angelman syndrome: Its profile and relationship to age. *Journal of Intellectual Disability Research, 54*, 1024-1029.

George, D., & Mallory, P. (1995). *SPSS/PC+ step by step: A simple guide and reference*. Belmont, CA: Wadsworth.

Iovannone, R., Dunlap, G., Huber, H., & Kincaid, D. (2003). Effective educational practices for students with Autism Spectrum Disorders. *Focus on Autism and Other Developmental Disabilities, 18,* 150-165.

Lalande, M., & Calciano, M.A. (2007). Molecular epigenetics of Angelman syndrome. *Cellular and Molecular Life Sciences, 65*, 947-960.

Lalli, J. S., Browder, D. M., Mace, F. C., & Brown, D. K. (1993). Teacher use of descriptive analysis data to implement interventions to decrease student's problem behaviors. *Journal of Applied Behavior Analysis, 26*, 227-238.

Leyser, Y., & Kirk, R. (2011). Parents' perspectives on inclusion and schooling of students with Angelman syndrome: Suggestions for educators. *International Journal of Special Education, 26,* 1-14.

Lydon, S., Healy, O., O'Reilly, M. F., & Lang, R. (2012). Variations in functional analysis methodology: A systematic review. *Journal of Physical and Developmental Disability, 24,* 301-326.

Mutua, K., & Dimitrov, D. M. (2001). Prediction of school enrolment of children with intellectual disabilities in Kenya: The role of parents' expectations, beliefs, and educations. *International Journal of Disability, Development and Education, 48,* 179-191.

O'Brien, G. (Ed.). (2002). *Behavioral Phenotypes in Clinical Practice*. London: Mac Keith Press.

Pelc, K., Cheron, G., & Dan, B. (2008). Behavior and neuropsychiatric manifestations in Angelman syndrome. *Neuropsychiatric Disease and Treatment, 4*, 577-584.

Peters, S. U., Goddard-Finegold, J., Beaudet, A. L., Madduri, N., Turcich, M., & Bacino, C. A. (2004). Cognitive and adaptive behavior profiles of children with Angelman syndrome. *American Journal of Medical Genetics Part A, 128A*, 110-113.

Pituch, K. A., Green, V. A., Didden, R., Lang, R., O'Reilly, M., Lancioni, G., ... Sigafoos, J. (2010a). Rehabilitation priorities for individuals with Prader Willi syndrome. *Disability and Rehabilitation, 32*, 2009-2018.

Pituch, K. A., Green, V. A., Didden, R., Whittle, L., O'Reilly, M., Lancioni, G., … Sigafoos, J. (2010b). Educational priorities for children with Cri-du-Chat syndrome. *Journal of Developmental and Physical Disabilities, 22*, 65-81.

Pituch, K. A., Green, V. A., Didden, R., Lang, R., L., O'Reilly, M., Lancioni, G., ... Sigafoos, J. (2011). Parent reported treatment priorities for children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 5***,** 135-143.

Radstaake, M., Didden, R., Lang, R., O'Reilly, M., Sigafoos, J., Lancioni, G. E., … Curfs, L. M.

G.. (2013). Functional analysis and functional communication training in the classroom for three children with Angelman syndrome. *Journal of Developmental and Physical Disabilities, 25*, 49-53.

Radstaake, M., Didden, R., Peters-Scheffer, N., Moore, D., Anderson, A., & Curfs, L. M. G. (2014). Toilet training in participants with Angelman syndrome: A case series. *Developmental Neurorehabilitation, 17,* 243-250.

Radstaake, M., Didden, R., Oliver, C., Allen, D., & Curfs, L.M.G. (2012). Functional analysis and functional communication training in individuals with Angelman syndrome. *Developmental Neurorehabilitation, 15,* 91-104.

Ringdahl, J. E., & Sellers, J. A. (2000). The effects of different adults as teachers during functional analysis. *Journal of Applied Behavior Analysis, 33*, 247-250.

Siebes, R. C., Wijnroks, L., Ketelaar, M., van Schie, P. E. M., Gorter, J. W., & Vermeer, A. (2006). Parent participation in paediatric rehabilitation treatment centers in the Netherlands: A parent's viewpoint. *Child: Care, Health and Development, 33,* 196-205.

Szumski, G., & Karwowski, M. (2012). School achievement of children with intellectual disability: The role of socioeconomic status, placement, and parents' engagement. *Research in Developmental Disabilities, 33*, 1615-1625.

Summers, J. A., & Szatsmari, P. (2009). Using discrete trial instruction to teach children with Angelman syndrome. *Focus on Autism and Other Developmental Disabilities, 24*, 216-226.

Van der Putten, A., Vlaskamp, C., & Poppes, P. (2009). The content of support of persons with profound intellectual and multiple disabilities: An analysis of the number and content of

goals in the educational programmes. *Journal of Applied Research in Intellectual Disabilities, 22*, 391-394.

Van Vonderen, A., Duker, P., & Didden, R. (2010). Instruction and video feedback to improve staff's trainer behavior and response prompting during one-to-one training with young children with severe intellectual disability. *Research in Developmental Disabilities, 31*, 1481-1490.

Van Vonderen, A., Duker, P., Didden, R., Lang, R., & Lancioni, G. (2011). Self-management and supervisory feedback improves trainer implementation of communication rehabilitation. *Developmental rehabilitation, 14*, 29-35.

Vygotsky, L. S. (1978). *Mind and society: The development of higher psychological processes.* Cambrigde: Harvard University.

Walz, N. C., Beebe, D., Byars, K., & Dykens, E. (2005). Sleep in individuals with Angelman Syndrome: Parent perceptions of patterns and problems. *American Journal on Mental Retardation, 110*, 243-252.

Williams, C. A. (2010). The behavioral phenotype of Angelman syndrome. *American Journal of Medical Genetics, 154C,* 432-437.

Williams, C. A., Driscoll, D. J., & Dagli, A. I. (2010). Clinical and genetic aspects of Angelman syndrome. *Genetics in Medicine, 12*, 385-395.

Williams, C. A., Angelman, H., Clayton-Smith, J., Driscoll, D. J., Hendrickson, J. E., Knoll, … Zori, R. T. (1995). Angelman syndrome: Consensus for diagnostic criteria. *American Journal of Medical Genetics, 56*, 237-238.

World Health Organization. (2003). *ICF Checklist, Version 2.1a. Clinical Form for International Classification of Functioning, Disability and Health*. Geneva: Author.

Chapter 8

General discussion

In this thesis, we focused on the analysis and treatment of challenging behavior in individuals with AS. We assessed the behavioral function of challenging behavior in seven children with AS. Results indicated that receiving tangibles maintained the challenging behavior of four children, receiving attention maintained the challenging behavior of two children and three children showed challenging behavior to escape from a demand. In two children, two behavioral functions were found. Functional communication training (FCT) was successfully implemented in both natural and clinical settings by teachers and researchers and had a small positive effect (decrease) on the frequency of challenging behavior in one child, a medium effect in two children and a large effect in five children. Next to communication skills, urinary continence was trained using principles based on learning theory. Individualized toilet training protocols using the response restriction method were administered in seven individuals with AS. Training led to an increase in in-toilet voids in all individuals and to a decrease in urinary accidents in six individuals. In three individuals positive results regarding in-toilet voids and urinary accidents were maintained over a period of 3 to 18 months. Compared to individuals with a non-specific intellectual disability, more daytime urinary continence was found in AS. More daytime continence was found in individuals with AS with a higher age and higher level of adaptive behavioral functioning. Nocturnal incontinence was the most common form of incontinence in AS. Dysfunctional voiding patterns (i.e. interrupted and staccato urine flow

patterns) were found in six out of seven individuals with AS during uroflowmetry. Results of our studies on incontinence indicated that lower urinary tract symptoms were often present in individuals with AS. Parents of children with AS prioritized training in communication, recreational, self-care and motor skills, and highlighted the treatment of eating and sleeping problems, child's overweight, non-compliance and aggression. In their prioritization, parents primarily focused on skills in which their child showed emerging abilities or severe deficits rather than on skills in which their child showed minor deficits.

Results of studies indicate that challenging behavior can serve multiple social functions in AS and that children can be taught functional communication skills as a result of which challenging behaviors decrease. This result suggests that challenging behaviors generally serve a social communicative function in AS. Further, urinary incontinence is not part of the behavioral phenotype of AS. Next to this, continence may be fostered in individuals with AS using individualized toilet training protocols. Lower urinary tract symptoms and dysfunctional voiding patterns frequently occur in AS, indicating that bladder dysfunctions might be present in AS. The preferences of parents according to the training of skills and treatment of challenging behaviors in the care for their child with AS appear to reflect the behavioral phenotype of AS.

In the following parts, the results of our studies concerning assessment and treatment of challenging behavior and incontinence are discussed. This is followed by a discussion of the parental perspectives concerning the child for their child with AS. This chapter ends with the limitations and future directions of the studies and a discussion of the clinical implications.

8.1. Role of communication in reducing challenging behavior

In two studies, we conducted functional behavioral analysis (FBA) on challenging behaviors displayed by 7 children with AS. In four children, the challenging behavior functioned to obtain a tangible, in three children to escape from a task and in another two children to receive attention. In two children, two behavioral functions were found. In three out of four children in which FBA was conducted in the classroom, initial FBA gave inconclusive results and adaptations had to be made (i.e. peers were asked to play elsewhere). Contrary to what we expected based on previous studies (Strachan, Shaw, Burrow, Horsler, Allen, & Oliver, 2009; Tunnicliffe & Oliver, 2011), attention was not the primary behavioral function in all children. In a study on social approach behaviors in AS (Heald, Allen, Villa, & Oliver, 2013), the frequency of these behaviors were found to differ within children, which also argues against the "eagerness for attention assumption" in AS. In the two children in which attention was found to maintain their challenging behavior, the high- and low-attention conditions were conducted in a contrived setting with unfamiliar adults. In the children in which the high- and low-attention conditions were held in the classroom with peers (i.e. less contrived setting), attention was *not* the behavioral function. Due to the distractibility of children with AS (Summers, Allison, Lynch, & Sandler, 1995; Mount, Oliver, Berg, & Horsler, 2011; Williams, 2010), it is possible that the reinforcer magnitude of adult attention was influenced by the presence of peers. Adult attention might be more reinforcing and attractive when peers are not around; when peers are around the children with AS might look at and be distracted by them and might therefore be less focused on receiving attention from adults.

Besides the presence of peers, other contextual FBA variables (e.g. type of setting, familiarity of adult) might also have affected outcomes regarding the behavioral function.

Several studies have assessed the functions of challenging behavior in both classroom and contrived settings in children with autism (see Lang, Sigafoos, Lancioni, Didden, & Rispoli, 2010). Results of these studies indicated that challenging behaviors can have different functions in different settings (i.e. playground vs. classroom, therapy room vs. classroom) and that familiarity of the person conducting the sessions can influence both the rate as well as the function of the challenging behavior (Ringdahl & Sellers, 2000). These findings suggest that the variables controlling the challenging behavior may vary across settings and that FBA results cannot be generalized from one setting to another. Our results suggest that multiple functions can maintain the challenging behavior in AS. Classrooms without peers can serve as a setting for conducting FBAs by teachers, thereby enhancing the ecological validity (i.e., the correspondence between the behavioral function found in FBA and in the natural context) of the FBA results as compared to FBA in contrived settings (see Lang et al., 2010)

Prior to the occurrence of challenging behavior, behaviors such as making eye contact, physical contact and reaching for tangibles were seen in participants with AS. We conceptualized these behaviors as precursors to challenging behaviors. Precursors are behaviors occurring prior to the challenging behavior and are elicited and followed by the same environmental variables (i.e. antecedents and reinforcers) as the challenging behavior, making precursors and challenging behaviors functionally equivalent (Carr & Durand, 1985; Petty, Allen & Oliver, 2009). We used burst analyses to explore which behaviors were precursors. In burst analysis, all target behaviors (e.g. challenging or communicative behaviors) are pooled together (the "burst") and periods between target behaviors are divided into percentiles (Oliver, Hall, & Murphy, 2005). The probability of a certain behavior (e.g. precursor) can thereby be assessed prior to, during and after the occurrence of the target behavior. The designated precursors showed a peak in

probability before the onset of the challenging behavior and a decline afterwards, except in 'looking at tangible'. We used precursors as the starting point for prompting in functional communication training (FCT). During FCT, the children were successfully taught to replace their challenging behavior by exchanging a referent picture or object, or by pressing the button of the Big Mack ®. The potential of using precursors as onsets of training and the positive effect of the training on challenging behavior was also found in studies concerning individuals with ID but without AS (Borrero & Borrero, 2008; Langdon, Carr, & Owen-deSchryver, 2008). In the children in our study, challenging behaviors decreased following the teaching of a communicative (replacement) behavior, as both were found to be functionally equivalent: the tendencies in probabilities of the antecedents (i.e. the absence of tangibles or attention or presence of a demand) were similar before and after both challenging and communicative behavior as shown by burst analyses.

The behaviors designated as precursors resemble the non-verbal behaviors outlined by Didden et al. (2009). In their study, parents reported that for instance touching and making eye contact were used by their child with AS to focus attention on themselves and pointing and reaching were employed to request for an item. Based on our findings, these non-verbal behaviors should not merely be seen as "attention seeking behaviors" corresponding to the social disposition of children with AS, but they should also be seen as onsets for communication training to increase communication skills and / or to treat challenging behavior. The precursors should be seen as emerging communication skills (Keenan, 2002). Starting training upon their emergence would take into account the preference of parents to initiate communication training when their child shows emerging communicative abilities (see §8.3).

8.2. Effective continence training

In the questionnaire study we found that incontinence is not part of the behavioral phenotype of AS. More urinary daytime incontinence was found in a control group that was matched on age and level of ID; no significant differences between groups emerged on the other types of incontinence. Noctural enuresis (NE) was the most common form of incontinence in AS; 89% of individuals was incontinent at night. In our sample of 71 individuals with AS, 46% was continent for urine during the day. We found that the likelihood of being continent for urine and feces during the day in AS increases with age and level of adaptive functioning as measured by the Vineland Screener (Scholte & van Berckelaer-Onnes, 2008). These findings seem consistent with those of previous studies (Buntinx et al., 1995; Didden, Korzilius, Smits, & Curfs, 2004; Laan, den Boer, Hennekam, Renier, & Brouwer, 1996), including the high frequencies of NE and elevated number of continent individuals in adults with AS as compared to children with AS. We hypothesized that the decrease in hyperactivity and increase in attention span in adulthood makes individuals with AS more prone to learning new skills (including voiding skills and continence), thereby explaining the higher frequencies of continence in adulthood, as compared to children (Clayton-Smith, 2001; Laan et al., 1996). The marjority of individuals with AS (45 out of 71) shows in-toilet voids.

We successfully trained seven individuals with AS (aged 6-25 years) in their natural environment using an individualized response restriction toilet training protocol. Results revealed that in all individuals a marked increase in in-toilet voids occurred following training, while in two individuals urinary accidents still occurred during the generalization phase. In three individuals, positive results regarding in-toilet voids and accidents were maintained over a longer period of time (3-18 months). The other children relapsed to some extent, which could partially

be attributed to environmental factors (e.g. change of day-care group, stressful family events such as divorce). Another reason for the relapses could be that training principles were not consequently carried out by caretakers once the formal training was terminated. Parents and caretakers are highly significant in maintaining training results in the period following the generalization phase, as accidents often still occur in individuals with ID (Averink, Melein, & Duker, 2005). In the study by Didden, Sikkema, Bosman, and Duker (2001) on toilet training in AS, two post-training phases were implemented in which interventions were slowly faded out by caretakers. In these periods, the caretakers administered consequences for urinary accidents and reinforcers for in-toilet voids until urinary accidents were absent for a month. Increases in correct toileting in all participants were maintained over a period up to 2.5 years. In our study, we did not implement a post-training phase, which could explain the differences in follow-up results between our and Didden et al.'s study.

When baseline frequencies of urinary accidents of individuals with AS in our study are compared to those of individuals with severe ID (see e.g., Averink, Melein, & Duker, 2005; Duker, Averink, & Melein, 2001), frequencies of accidents in individuals AS are relatively low. These findings corroborate those of the questionnaire study: voiding frequencies were lower and time-between-voids was longer in individuals with AS, as compared to individuals with non-specific ID. During toilet training, individuals sometimes did not void during training hours nor did they display holding maneuvers, despite drinking up to 2.5 liters of water. Taken together: individuals with AS were found to void less frequently and retained their urine for longer periods of time than individuals with severe ID of other origin.

In both the questionnaire and toilet training study lower urinary tract symptoms (LUTS) were observed. Participants with AS showed signs of hesitancy (i.e. difficulty to initiate voiding,

while there is a “need to go”), straining (i.e. having to make extensive efforts to apply abdominal pressure to start voiding), and interrupted stream. Other frequently mentioned LUTS by parents of children with AS were: (a) takes too little time to void and (b) urgency (i.e. a compelling need to void). Both LUTS were not seen during our toilet training study. Observed LUTS frequencies were lower in the matched control group. These results suggest that it takes much effort to initiate and maintain a steady urine flow in individuals with AS.

To further assess their urine flow, uroflowmetry was conducted in six individuals with AS. Results revealed that in five individuals small voided volumes and pathological uroflows (i.e. staccato and interrupted urine flows) were found. These findings are in line with studies concerning uroflowmetry in individuals with severe ID (van Laecke et al., 2001; Yang, Meng, & Chou, 2010), the only difference being that in AS relatively more staccato uroflows were found opposed to more interrupted uroflows as in the study by van Laecke et al. (2001). Staccato and interrupted uroflow patterns are caused by paradoxical pelvic floor and sphincter (i.e. muscle controlling the outlet of urine) contractions during voiding and by an underactive detrusor (i.e. bladder muscle that contracts during voiding), respectively (Chase, Austin, Hoebeke, & McKenna, 2010). The pathological uroflows are most likely functional in nature, as pathological and normal uroflow patterns were found in the individuals in our study. The presence of both normal and pathological uroflow patterns in individuals signifies that the behavior of individuals with AS affects the urine flow, as when structural or neurogenic disorders were in effect, all uroflow patterns in individuals would be pathological. In summary, all three studies on incontinence in AS indicate that urinary continence can be achieved by individuals with AS. Second, lower urinary tract dysfunctions and dysfunctional voiding patterns frequently occur in AS.

8.3. Parental preferences

Results of our study on parental preferences in individuals with AS suggest that parents highly value the acquisition of skills representing developmental milestones (i.e. walking, eating, communicating, and toileting) and when their children reach an adult age parents want caretakers to focus on providing/teaching meaningful daytime activities for their (adult) children. These results are in line with those of previous research on parental preferences in AS (see Calculator & Black, 2010; Leyser & Kirk, 2011). For most adaptive skill domains (i.e. communication, recreational and ingestion skills), parents want caretakers to teach their child skills when s/he already showed emerging abilities in that domain. In these domains, parents appear to adopt Vygotski's (1987) notion on proximal development. Emerging abilities might be an indication of heightened motivation to learn a new skill, which is beneficial for the learning process of these skills (Bondy & Frost, 2001; Iovannone, Dunlap, Huber, & Kincaid, 2003). This might especially be the case when newly acquired skills lead to some type of positive reinforcement such as social interaction, recreational activities and food. For example, Didden, Korzilius, Kamphuis, Sturmey, Lancioni, and Curfs (2006) found that interacting with staff, receiving praise, swimming, and outdoor trips were on average highly preferred by children with AS, as indicated by their parents. In other skills (i.e. motor and social skills) parents highly valued training when their child showed severe deficits in that domain. The social skills domain appears to represent skills related to attachment issues (i.e. items on affection/interaction), which are important to parents as they symbolize the relationship they have with their child. Interaction is also the starting point of communication, further explaining why parents deem it important that these skills are taught when their child shows deficits in this domain. Gross motor skills are

delayed in AS and motor skills are the least developed adaptive behavior skill in children under the age of six (Peters et al., 2004; Williams, Driscoll, & Dagli, 2010), which suggests that training is needed to foster motor development in AS. Early intervention in AS regarding motor development was also advised by Beckung, Steffenburg, and Kyllermann (2004) to prevent long-term motor problems. This may explain why parents prioritize training in motor skills when their child shows severe deficits.

With regard to challenging behaviors, parents prioritize treatment of sleep problems and eating problems, being overweight, aggressive behavior and non-compliance. Their priorities regarding sleeping and eating problems, aggressive behavior and non-compliance are in accordance with the high prevalence of such behaviors in AS (see Clarke & Marston, 2000; Summers et al., 1995). Sleep problems, eating problems and aggressive behaviors are more common in AS than in individuals with non-specific ID (see Arron, Oliver, Moss, Berg, & Burbidge, 2011; Berry, Leitner, Clarke, & Einfield, 2005; Didden et al., 2004; Pelc, Cheron, & Dan, 2008), which may explain the heightened priorities for treatment of these behaviors given by parents in our study. In older children with AS, obesity occurs in 20-80% (William, Driscoll, & Dagli, 2010) and reluctance to exercise in adulthood has been previously reported (Clayton-Smith, 2001), which could account for the high priority parents gave to the treatment of being overweight. Surprisingly, parents in our study did not prioritize hyperactive behaviors for treatment. Hyperactive behaviors are common in AS (Clarke & Marston, 2000; Summers et al., 1995) and are more frequent in AS compared to individuals with non-specific ID (Berry et al., 2005). Parents are aware of these behaviors, but they do not prioritize them for treatment. Except for hyperactive behaviors, the priorities for training and treatment in AS as prioritized by parents

seem to reflect the frequently reported behavioral problems in AS that is the behavioral phenotype of AS (Pelc et al., 2008; Williams, 2010; Williams et al., 2010).

When compared to individuals with other genetic syndromes (Cri-du-Chat, Autism spectrum disorder and Prader-Willi syndrome), parents of children with AS not only appear to prioritize a smaller number of skills, but they also assign lower priorities to the teaching of adaptive skills (Pituch et al., 2010a; 2010b; 2011). Several reasons can account for these findings. Due to the severe intellectual disability (ID), attention deficits and non-compliant behaviors (Berry et al., 2005; Summers et al., 1995), parents may have lower expectations of their child and want to focus on a small number of adaptive skills as they believe it is unachievable for their child to attain more goals. Focusing on the training of several adaptive skills might not be feasible for individuals with severe ID (see Van der Putten, Vlaskamp, & Poppes, 2009) and parents might adapt to this in their prioritization of skills. Second, many parents of children with AS experience relatively high amounts of stress and loss of control (Griffith et al., 2011; Van den Borne et al., 1999; Wullfaert, Scholte, & van Berckelaer-Onnes, 2010). Having high hopes and prioritizing multiple skills for training may result in disappointment and (further) feelings of loss of control, presumably leading to more stress in parents. Parents may thus focus on a small number of goals based on what their child can do, instead of what s/he cannot do (see e.g., King et al., 2006). Parents in our study mainly prioritized the teaching of emerging skills instead of prioritizing the teaching of skills in which their child show a severe deficit, which resembles a focus on what their child can do. Additionally, when compared to studies on the above three syndromes the level of ID in AS was most severe and the emphasis on emerging abilities was most pronounced in AS (Pituch et al., 2010; 2010a; 2011). This might indicate that parents of

children with severe ID more likely prioritize the training of emerging skills than parents of children with a milder level of ID.

The number and type of adaptive skills that parents prioritize and the logic that parents adopt in their prioritization (i.e. focus on emerging skills) appear to be both associated with the behavioral phenotype and severity of the ID in AS. Despite their severe to profound ID, individuals with AS can be taught adaptive behaviors (see Didden et al., 2001; Summers, 2012; Summers & Szatsmari, 2009).

8.4. Limitations and future perspectives

Several limitations should be mentioned. In the communication and toilet training studies we adapted the training protocols according to individual and environmental characteristics. Combined with the low participant numbers in our training studies, this limits generalization of the training results to the AS population or to individuals with comparable levels of ID. Further, we did not compare research settings or interventions within individuals. For instance, we did not conduct FBA conditions in contrived and natural environments in individuals with AS, restricting the comparison of the functions found in both environments. Nor did we apply both "positive practice" and "remains seated on toilet until voiding occurred" after a urinary accident during toilet training in the same individual, which makes it impossible to indicate which intervention (intervention package described by Didden et al. [2001] versus that described in the present thesis) is most successful in decreasing urinary accidents in AS. More research is necessary to evaluate which intervention or training setting is most successful, although this will highly depend on individual characteristics as well.

Children in our study were taught to request for a break or for food, but they have not been taught *when* they can do this. Heald, Allen, Villa and Oliver (2013) have shown that individuals with AS can discriminate between when social approach behaviors will and when such behaviors will not be reinforced. The researchers used different color jackets to indicate the availability and non-availability of attention and the children learned to respond correspondingly. Children with AS should thus be taught when to request for attention, tangibles or a break and when these objectives are not available.

Our studies on incontinence primarily focused on urinary incontinence, but results of our questionnaire study also indicated high rates of fecal and nighttime incontinence. As for nighttime urinary incontinence, there might be an association with sleep problems which are common in AS (see Didden, Korzilius, Smits, Curfs, & Dykens, 2004). Braam, Didden, Smits, and Curfs (2008) prescribed melatonin to eight individuals with AS, which led to an increased quality and quantity of sleep. Several studies have shown that melatonin supplementation influences nighttime voiding in that it decreased nighttime voiding in elderly people (Drake, Mills, & Noble, 2004; Sugaya, Nishijima, Miyazato, Kadekawa, & Ogawa, 2007), and increased bladder capacity and decreased the urine quantitity in rats (Matsuta et al., 2010). It has not yet been studied if melatonin supplementation has an effect on the frequency and quantity of nighttime voids in AS.

Although parental priorities in AS appear to reflect both the behavioral phenotype of AS and the severe ID, it is not yet clear if the priorities of parents differ from those of parents of children with comparable ID. To investigate which priorities specifically relate to AS, the same study should be conducted in parents of children with ID with mixed etiologies. This kind of

information would help clinicians to further adjust the IEPs according to the preferences of parents with AS.

8.5. Clinical implications

Our studies indicate that individuals with AS are capable of learning adaptive skills. We primarily focused on challenging behavior, communicative behavior and continence. These topics appeared to be in line with the training and treatment preferences as designated by parents of children with AS. In the care for children with ID, such as AS, collaboration between parents and caretakers concerning goals and how to address them is essential (Matson, Mahan, & LoVullo, 2009; Siebes et al., 2006). Clinicians should therefore take these preference into account and should adhere to the below recommendations when designing individual education plans (IEP) for individuals with AS.

With regard to communication skills, training should start as soon as children show emerging skills such as pointing and reaching (see Didden et al., 2006 for more examples), as decreased communicative abilities places them at risk for developing challenging behaviors (McClintock, Hall, & Oliver, 2003). Williams, Peters and Calculator (2009) advised to target communication skills in the classroom when opportunities emerge as the motivation to acquire a certain objective will be high at that moment (i.e. attention, escape, food, or a toy); for instance, when they walk towards the refrigerator to get a drink the child could be taught to sign “drink” or to exchange a picture of object which refers to a drink. Some children will need individual training to acquire these communication skills, but motivation for the required objective is highly important, due to the distractibility in AS. In our studies, FBA was successful in assessing the behavioral function, which thereby indicated which objective was highly reinforcing to the child.

With regard to FBA, it is advised to keep the number of sessions as small as possible. The children in our study were easily distracted (Berry et al., 2005; Pelc et al., 2008), limiting the duration and number of sessions that could be conducted. To shorten the time needed for FBA, it is advised to design individually adjusted FBA conditions (Hagopian, Rooker, deLeon, & Jessel, 2013) as opposed to conducting standard experimental FBA based on Iwata, Dorsey, Slifer, Bauman and Richman's (1994) procedure. Individually adjusted FBA conditions have been successful in assessing the behavioral function in children with ID when no function was found during standard FBA procedure (Hagopian et al., 2012). The individualized FBA conditions should be based on observations in the natural environment and interviews with parents and / or caretakers (Schlichenmeyer, Roscoe, Rooker, Wheeler, & Dube, 2013).

We advise to perform the FBA sessions in the natural environment with familiar teachers. Lang et al. (2009) advised to conduct FBA in the same setting in which treatment is implemented in order to prevent discrepancies in behavioral functions between settings. As children benefit most from FCT when taught skills are generalized to their natural environment, it seems logical to conduct FBA in their natural environment. However, distractions from peers should be minimized, as FBAs in classrooms with peers gave inconclusive results in three out of four children and adjustments had to be made, thereby prolonging FBA duration. In order to increase the effectiveness and the efficiency of FBA in children with AS, individual preferences should be taken into account when designing FBA conditions. The conditions should be held in the context in which the challenging behavior normally occurs, while keeping distractions from peers to a minimum. Our studies indicated that the challenging behavior in AS has a communicative function and can be decreased by teaching the child a more socially accepted means of communication. Challenging behavior should not only be seen as "being part of AS",

but it should be carefully assessed in order to find its behavioral function and treat it accordingly using procedures such as FCT.

Several recommendations can be made to increase urinary continence and decrease LUTS and dysfunctional voiding (i.e. pathological uroflows) in individuals with AS. Treatment is important as LUTS and dysfunctional voiding can lead to urinary tract infections (see Chase et al., 2010; Foxman, 2002) and incontinence may have adverse effects (e.g. pain, discomfort and dependency on caregivers; Cicero & Pfadt, 2002; Kroeger & Sorenson-Burnworth, 2009). The recommendations are based on the components of urotherapy, which refers to the nonsurgical and non-pharmacological intervention for lower urinary tract malfunction (Chase et al., 2010; Néveus et al., 2006). Urotherapy is effective in treating urinary incontinence, reducing urinary tract infections and it reduces constipation (see Chase et al., 2010; Mulders, Cobussen-Boekhorst, de Gier, Feitz, & Kortmann, 2011). The elements of urotherapy that apply to AS will be outlined below.

First, fluid intake should be optimized. In our uroflowmetry study, voided volumes were small, which could be due to insufficient liquid intake. Previous research has shown that increased liquid intake can foster urinary continence and lead to normal voided volumes in ID (van Laecke, Raes, vandeWalle, & Hoebeke, 2009). Optimal liquid intake is also important in the prevention and treatment of constipation (Anti et al., 2011), which seems required as the majority of individuals in the questionnaire study were reported to have a solid stool. Solid stools are a risk factor for urinary incontinence and when treated, can decrease urinary incontinence (Chase et al., 2010; Kroeger & Sorenson-Burnworth, 2009; Loening-Baucke, 1997). In AS, swallowing problems are reported in 20-80% of individuals with AS (Williams, Driscoll, & Dagli, 2010), which can lead to insufficient hydration (van Laecke et al., 2001) especially since

abilities to communicate thirst are reduced. Van Laecke et al. (2001) attributed insufficient liquid intake in individuals with severe cognitive and motor disabilities to their environment. Caretakers of individuals with AS should be susceptible to insufficient liquid intake, especially in the presence of swallowing problems, small voided volumes and solid stools.

Second, caretakers should implement a regular toileting regimen. Results of our studies imply that individuals with AS retain their urine for prolonged intervals, have low voiding frequencies and rarely display holding maneuvers, suggesting that they might not sense a need to void. Some individuals with AS did show self-initiated voiding but care should be taken that they void on a regular basis. As communication deficits might limit their ability to communicate a need to void, learning how to communicate a need to void should be taught during toilet training. Timed voiding can also prevent dysfunctional voiding patterns (Chase et al., 2010).

Third, relaxation is needed to arrange an optimal voiding position (Chase et al., 2010). During uroflowmetry it took several participants more than 5 minutes to start voiding and according to their parents and caretakers this was a normal interval, indicating that individuals with AS may need sufficient time to initiate voiding. The behavioral phenotype of AS includes ataxic, tremulous movements and frequent hand flapping (Williams, 2010), which presumably counteracts the muscle contractions and relaxations necessary for voiding (see Chase et al., 2010). This could account for the pathological uroflow patterns and the high frequencies of interrupted stream, hesitancy, straining and taking too little time to void. When voiding is terminated prematurely, residual urine could lead to urinary tract infections (Chase et al., 2006; Hansson, Hjalmas &, Jodal et al. 1990), which is a risk factor for urinary incontinence (Brown, Grady, Ouslander, Herzog, Varner, & Edward, 1999). By consequence, individuals with AS should be given enough time to start voiding and to fully empty their bladder.

Next to these urotherapeutic components, reinforcement and fading techniques are useful in designing toilet training protocols for individuals with ID, such as individuals with AS (von Gontard, 2013). Individuals in our study were prompted to void and were immediately reinforced to constitute an association between in-toilet voiding and a reward. Fading principles were applied when reducing time on toilet, reducing the magnitude of reinforcement, increasing the reinforcement interval and decreasing liquid intake. Criteria for fading, scheduled consequences for urinary accidents, and training setting depended on individual characteristics and training success. Together with the compelling genotype and behavioral phenotype of AS, individual characteristics necessitate clinicians to be flexible in the application of toilet training protocols (see Klassen et al., 2006; von Gontard, 2013). In order to reliably assess frequency and volume of both in-toilet voids and urinary accidents during the day, participants with AS should be assessed throughout the day, using uroflowmetry and a "bladder diary", in which all voids are documented (see Néveus et al., 2006).

8.6. References

Anti, J., Pignataro, G., Armuzzi, A. Valenti, A., Iascone, E., Marmo, R., … Gasbarrini, G. (1998). Water supplementation enhances the effect of high-fiber diet on stool frequency and laxative consumption in adult patients with functional constipation. *Hepatogastroenterology, 45,* 727-732.

Arron, K., Oliver, C., Moss, J., Berg, K., & Burbidge, C. (2011). The prevalence and phenomenology of self-injurious and aggressive behaviour in genetic syndromes. *Journal of Intellectual Disability Research, 55*, 109-120.

Averink, M., Melein, L., & Duker, P. C. (2005). Establishing diurnal bladder control with the response restriction method: Extended study on its effectiveness. *Research in Developmental Disabilities, 26*, 143-151.

Beetz, R. (2003). Mild hydration: a risk factor for urinary tract infection? *European Journal of Clinical Nutrition, 57*, S52-S58.

Beckung, E., Steffenburg, S., & Kyllerman, M. (2004). Motor impairments, neurological signs, and developmental level in individuals with Angelman syndrome. *Developmental Medicine & Child Neurology, 46*, 239-243.

Berry, R. J., Leitner, R. P., Clarke, A. R., & Einfeld, S. L. (2005). Behavioral aspects of Angelman syndrome: A case control study. *American Journal of Medical Genetics Part A, 132A,* 8-12.

Bondy, A., & Frost, L. (2001). The Picture Exchange Communication System. *Behavior Modification, 25,* 725-744.

Borrero, C. S. W., & Borrero, J. C. (2008). Descriptive and experimental analyses of potential precursors to problem behavior. *Journal of Applied Behavior Analysis, 41,* 83-96.

Braam, W., Didden, R., Smits, M. G., & Curfs, L. M. G. (2008). Melatonine for chronic insomnia in Angelman syndrome: A randomized placebo-controlled trial. *Journal of Child Neurology, 23*, 649-654.

Brown, J., Grady, D., Ouslander, J. G., Herzog, A. R., Varner, R. E., Edward, R., & Posner, S. F. (1999). Prevalence of urinary incontinence and associated risk factors in postmenopausal women. *Obstetrics & Gynecology, 94*, 66-70.

Buntinx, I. M., Hennekam, R. C. M., Brouwer, O. F., Stroink, H., Beuten, J., Mangelschots, K., & Fryns, J. P. (1995). Clinical profile of Angelman syndrome at different ages. *American*

Journal of Medical Genetics, 56, 176-183.

Calculator, S. N., & Black, T. (2010). Parent's priorities for AAC and related instruction for their children with Angelman syndrome. *Augmentative and Alternative Communication, 26,* 30-40.

Carr, E. G., & Durand, M. V. (1985). Reducing behavior problems through functional communication training. *Journal of Applied Behavior Analysis, 18*, 111-126.

Chase, J., Austin, P., Hoebeke, P., & McKenna, P. (2010). The management of dysfunctional voiding in children: A report from the standardization committee of the International Children's Continence Society. *Journal of Urology, 183*, 1296-1302.

Cicero, F. R., & Pfadt, A. (2002). Investigation of a reinforcement-based toilet training procedure for children with autism. *Research in Developmental Disabilities, 23*, 319-331.

Clarke, D., & Marston, G. (2000). Problem behaviors associated with 15q- Angelman syndrome. *American Journal on Mental Retardation, 105*, 25–31.

Clayton-Smith, J. (2001). Angelman syndrome: Evolution of phenotype in adolescents and adults. *Developmental Medicine & Child Neurology, 43,* 476-480.

Didden, R., Korzilius, H., Kamphuis, A., Sturmey, P., Lancioni, G., & Curfs, L. M. G. (2006). Preferences in individuals with Angelmans syndrome assessed by a modified Choice Assessement Scale. *Journal of Intellectual Disability Research, 50*, 54-60.

Didden, R., Korzilius, H., Smits, M. G., & Curfs, L. M. G. (2004). Sleep problems in individuals with Angelman syndrome. *American Journal on Mental Retardation, 109*, 275-284.

Didden, R., Sigafoos, J., Korzilius, H., Baas, A., Lancioni, G. E., O'Reilly, M. F., & Curfs, L. M. G. (2009). Form and function of communicative behaviors in individuals with Angelman

syndrome. *Journal of Applied Research in Intellectual Disability, 22,* 526-537.

Didden, R., Sikkema, P. E., Bosman, I. T. M., & Duker, P. C. (2001). Use of a modified Azrin-Foxx toilet training procedure with individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 14*, 64-70.

Drake, M.J., Mills., I. W., & Noble, J. G. (2004). Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement. *The Journal of Urology, 171*, 1199-1202.

Duker, P. C., Averink, M., & Melein, L. (2001). Response restriction as a method to establish diurnal bladder control. *American Journal on Mental Retardation, 3*, 209-215.

Dykens, E. M. (1995). Measuring behavioral phenotypes: Provocations from the "new genetics". *American Journal on Mental Retardation, 99,* 522-532.

Foxman, B. (2002). Epidemiology of urinary tract infections: incident, morbidity, and economic costs. *The American Journal of Medicine, 113*, 5-13.

Griffith, G. M., Hastings, R. P., Oliver, C. Howlin, P., Moss., J. Petty, J., & Tunnicliffe, P. (2011). Psychological well-being in parents of children with Angelman, Cornelia de Lange and Cri du Chat syndromes. *Journal of Intellectual Disability Research, 55*, 397-410.

Hagopian, L. P., Rooker, W. G., Jessel, J., & DeLeon, I. G. (2013). Initial functional analysis outcomes and modification in pursuit of differentiation: A summary of 176 inpatient cases. *Journal of Applied Behavior Analysis, 46*, 88-100.

Hansson, S., Hjalmas, K., Jodal, U., & Sixt, R. (1990). Lower urinary tract infection in girls with untreated asymptomatic or covert bacteriuria. *The Journal of Urology, 143*, 333-335.

Heald, M., Allen, D., Villa, D., & Oliver, C. (2013). Discrimination training reduces high rate social approach behaviors in Angelman syndrome: Proof of principle. *Research in*

Developmental Disabilities, 34, 1797-1803.

Iovannone, R., Dunlap, G., Huber, H., & Kincaid, D. (2003). Effective educational practices for students with Autism Spectrum Disorders. *Focus on Autism and Other Developmental Disabilities, 18,* 150-165.

Iwata, B. A., Dorsey, M. F., Slifer, K. J., Bauman, K. E., & Richman, G. S. (1994). Towards a functional analysis of self-injury. *Journal of Applied Behavior Analysis, 27*, 197-209.

Keenan, T. (2002). *An introduction to child development*. Londen: Sage.

King, G. A., Zwaigenbaum, L., King, S., Baxter, D., Rosenbaum, P., & Bates, A. (2006). A qualitative investigation of changes in the belief systems of families of children with autism or Down syndrome. *Child: Care, Health and Development, 32*, 353-369.

Klassen, T. P., Kiddoo, D., Lang, M. I., Friesen, C., Russell, K., Spooner, C., & Vandemeer, B. M. (2006). *The effectiveness of different methods of toilet training for bowel and bladder control.* (Evidence Report/Technology Assessment No. 147). Rockville MD: Agency for Healthcare Research and Quality.

Kroeger, K. A., & Sorensen-Burnworth, R. (2009). Toilet training individuals with autism and other developmental disabilities. *Research in Autism Spectrum Disorders, 3,* 607-618.

Laan, L., den Boer, A. Th., Hennekam, R., Renier, W. O., & Brouwer, O. F. (1996). Angelman syndrome in adulthood. *American Journal of Medical Genetics*, *66,* 356-360.

Lang, R., O'Reilly, M., Lancioni, G., Rispoli, M., Machalicek, W., Chan, J. M., … Franco, J. (2009). Discrepancy in functional analysis results across two settings: Implications for intervention design. *Journal of Applied Behavior Analysis, 42*, 393-397.

Lang, R., Sigafoos, J., Lancioni, G., Didden, R., & Rispoli, M. (2010). Influence of assessment setting on the results of functional analysis of problem behavior. *Journal of Applied*

Behavior Analysis, 43, 565-567.

Langdon, N. A., Carr, E. G., & Owen-deSchryver, J. S. (2008). Functional analysis of precursors for serious problem behavior and related intervention. *Behavior Modification, 32*, 804-827.

Leyser, Y., & Kirk, R. (2011). Parents' perspectives on inclusion and schooling of students with Angelman syndrome: Suggestions for educators. *International Journal of Special Education, 26,* 1-14.

Loening-Baucke, V. (1997). Urinary incontinence and urinary tract infection and their resolution with treatment of chronic constipation of childhood. *Pediatrics, 100*, 228-232.

Matson, J. L., Mahan, S., & LoVullo, S. V. (2009). Parent training: A review of methods for children with developmental disabilities. *Research in Developmental Disabilities, 30*, 961-968.

Matsuta, Y., Yusup, A., Tanase, K., Ishida, H., Akino, H., & Yokoyama, O. (2010). Melatonine increases bladder capacity via GABAergic system and decrease urine volume in rats. *The Journal of Urology, 184*, 386-391.

McClintock, K., Hall, S., & Oliver, C. (2003). Risk markers associated with challenging behaviors in people with intellectual disabilities: a meta-analytic study. *Journal of Intellectual Disability Research, 47*, 405-416.

Mount, R., Oliver, C., Berg, K., & Horsler, K.(2011). Effects of adult familiarity on social behaviours in Angelman syndrome. *Journal of Intellectual Disability Research, 55*, 339-350.

Mulders, M. M., Cobussen-Boekhorst, H., de Gier, R. P. E., Feitz, W. F. J., & Kortmann, B. B. M. (2011). Urotherapy in children: Quantitative measurements of daytime urinary

incontinence before and after treatment: According to the new definitions of the Internationals Children's Continence Society. *Journal of Pediatric Urology, 7*, 213-218.

Nevéus, T., von Gontard, A., Hoebeke, P., Hjälmas, K., Bauer, S., Bower, W., … Djurhuus, J. C. (2006). The standardization of terminology of lower urinary tract function in children and adolescents: Report from the Standardization Committee of the International Children's Continence Society (ICCS). *The Journal of Urology, 176*, 314-243.

Oliver, C., Hall., S., & Murphy, G. (2005). The early development of self injurious behavior: Evaluating the role of social reinforcement. *Journal of Intellectual Disability Research, 49,* 591-599.

Pelc, K., Cheron, G., & Dan, B. (2008). Behavior and neuropsychiatric manifestations in Angelman syndrome. *Neuropyschiatric Disease and Treatment, 4*, 577-584.

Peters, S. U., Goddard-Finegold, J., Beaudet, A. L., Madduri, N., Turcich, M., & Bacino, C. A. (2004). Cognitive and adaptive behavior profiles of children with Angelman syndrome. *American Journal of Medical Genetics, 128A*, 110-113.

Petty, J., Allen, D., & Oliver, C. (2009). Relationship among challenging, repetitive, and communicative behaviors in children with severe intellectual disabilities. *American Journal on Intellectual and Developmental Disabilities, 114*, 356-368.

Pituch, K. A., Green, V. A., Didden, R., Lang, R., O'Reilly, M., Lancioni, G., et al. (2010a). Rehabilitation priorities for individuals with Prader-Willi syndrome. *Disability and Rehabilitation, 32*, 2009-2018.

Pituch, K. A., Green, V. A., Didden, R., Whittle, L., O'Reilly, M., Lancioni, G., & Sigafoos, J. (2010b). Educational priorities for children with Cri-du-Chat syndrome. *Journal of Developmental and Physical Disabilities, 22*, 65-81.

Pituch, K. A., Green, V. A., Didden, R., Lang, R., L., O'Reilly, M., Lancioni, G. & Sigafoos, J. (2011). Parent reported treatment priorities for children with autism spectrum disorders. *Research in Autism Spectrum Disorders, 5***,** 135-43.

Ringdahl, J. E., & Sellers, J. A. (2000). The effects of different adults as therapists during functional analysis. *Journal of Applied Behavior Analysis, 33*, 247-250.

Schlichenmeyer, K. J., Roscoe, E. M., Rooker, G. W., Wheeler, E. E., & Dube, W. V. (2013). Idiosyncratic variables that affect functional analysis outcomes: A review (2001-2010). *Journal of Applied Behavior Analysis, 46*, 339-348.

Scholte, E.M., & van Berckelaer-Onnes, I. A. (2008). *Vineland-Screener 0-6 jaar*. Leiden: PITS.

Siebes, R. C., Wijnroks, L., Ketelaar, M., van Schie, P. E. M., Gorter, J. W., & Vermeer, A. (2006). Parent participation in paediatric rehabilitation treatment centers in the Netherlands: A parent's viewpoint. *Child: Care, Health and Development, 33,* 196-205.

Strachan, R., Shaw, R., Burrow, C., Horsler, K., Allen, D., & Oliver, C. (2009). Experimental functional analysis of aggression in children with Angelman Syndrome. *Research in Developmental Disabilities, 30,* 1095-1106.

Summers, J. (2012). Neurodevelopmental outcomes in children with Angelman syndrome after 1 year of behavioural intervention. *Developmental Neurorehabilitation, 15*, 239-252.

Summers, J., Allison, J., Lynch, P., & Sandler, L. (1995). Behavior problems in Angelman syndrome. *Journal of Intellectual Disability Research, 3,* 97-106.

Summers, J. A., & Szatsmari, P. (2009). Using discrete trial instruction to teach children with Angelman syndrome. *Focus on Autism and Other Developmental Disabilities, 24*, 216-226.

Sugaya, K., Nisijma, S., Miyazato, M., Kadekawa, K., & Ogowa, Y. (2007). Effects of melatonin and rilmazafone on nocturia in the elderly. *The Journal of International Medical Research, 35*, 685-691.

Tunnicliffe, P., & Oliver, C. (2011). Phenotype-environment interactions in genetic syndromes Associated with severe or profound intellectual disability. *Research in Developmental Disabilities, 32*, 404-418.

Van den Borne, H. W., van Hooren, R. H., van Gestel, M., Rienmeijer, P., Fryns, J. P., & Curfs, L. M. G. (1999). Psychosocial problems, coping strategies, and the need for information of parents of children with Prader-Willi syndrome and Angelman syndrome. *Patient Education and Counseling, 38*, 205-216.

Van der Putten, A., Vlaskamp, C., & Poppes, P. (2009). The content of support of persons with profound intellectual and multiple disabilities: An analysis of the number and content of goals in the educational programmes. *Journal of Applied Research in Intellectual Disabilities, 22*, 391-394.

Van Laecke, E. V., Golinveaus, L., Goossens, L., Raes, A., Hoebeke, P., & Vande Walle, J. (2001). Voiding disorders in severely mentally and motor disabled children. *The Journal of Urology, 166*, 2404-2406.

Van Laecke, E. V., Raes, A., vande Walle, J., & Hoebeke, P. (2009). Adequate fluid intake, urinary incontinence and physical and/or intellectual disability. *Journal of Urology, 182*, 2079-2084.

Von Gontard, A. (2013). Urinary incontinence in children with special needs. *Nature Reviews Urology, 10*, 667-674.

Von Gontard, A., & Neveus, T. (2006). *Management of disorders of bladder and bowel control in childhood.* London: MacKeith Press.

Vygotsky, L. S. (1978). *Mind and society: The development of higher psychological processes.* Cambridge: Harvard University.

Williams, C. A. (2010). The behavioral phenotype of Angelman syndrome. *American Journal of Medical Genetics, 154C*, 432-437.

Williams, C. A., Driscoll, D. J., & Dagli, A. I. (2010). Clinical and genetic aspects of Angelman syndrome. *Genetics in Medicine, 12*, 385-395.

Williams, C. A., Peters, S. U., & Calculator, S. N. (2009). *Facts about Angelman syndrome, 7th Edition*. Retrieved from: http://www.angelman.org/_angelman/assets/File/facts%20about%20as%202009%203-19-10.pdf.

Wullfaert, J., Scholte, E. M., & Van Berckelaer-Onnes, I. A. (2010). Maternal parenting stress in families with a child with Angelman syndrome or Prader-Willi syndrome. *Journal of Intellectual and Developmental Disability, 35*, 165-174.

Yang, P., Meng, N., & Chou, E. C. (2010). Voiding dysfunctions in children with mental retardation. *Neurology and Urodynamics, 29,* 1272-1275.

Summary

1. Behavioral treatment of challenging behavior

In order to assess the function of challenging behavior in children with Angelman syndrome (AS), functional behavioral analysis (FBA) was performed in seven children. During these analyses analogues were used, in which situations out of everyday life were replicated while systematically manipulating antecedents and consequences of challenging behavior. In this way, it was assessed if the children displayed challenging behavior to acquire attention or tangibles or to escape from demands. In four children FBA was administered by their teachers and took place in their own classroom, in the other children a researcher worked with the children in a therapy room. Challenging behavior consisted of several topographies such as hair pulling, pinching, making disruptive vocalizations and back arching. Results revealed that behavior was primarily motivated by tangibles (food or toys) in four children, by escape in two children and two children showed challenging behavior to receive attention. All children showed challenging behaviors in several conditions, indicating that challenging behavior may serve multiple functions. In five children clear precursors (i.e. behaviors reliably preceding the challenging behavior) could be identified, in the other two these were less clear. Precursors included reaching for an object and making physical or eye contact with the trainer.

After determining the primary function of the challenging behavior, the child was taught to replace challenging behavior by a replacement behavior; a socially accepted mode of communication such as exchanging a picture or three dimensional object or by using a speech generating device or computer. This training is known as Functional Communication Training

(FCT). The children were prompted to display the replacement behavior when they showed a precursor, no consequences were scheduled for challenging behavior. This training led to a decline in challenging behavior with a small effect size in one child, a medium effect size in two children and a large effect size in five children. Analysis further showed that the tendencies of the probabilities of the maintaining variables (e.g. not receiving attention or demands for a task) were comparable before and after both challenging and replacement behavior, indicating that both were functionally equivalent. Both studies indicate that challenging behavior in Angelman syndrome can have a positive or negative social function and that new modes of communications can replace challenging behavior. In teaching these new forms of communication, precursors can be used as the onset of prompting and familiar teachers can successfully perform FBA and FCT in the classroom.

2. Incontinence and toilet training

We analyzed the prevalence of urinary and fecal incontinence in individuals with AS (n = 71) and non-specific intellectual disability (ID, n = 69). Individuals with AS showed less urinary incontinence during the day, compared to their matched controls. Differences were also found in the number of voids or defecations; individuals with AS appear to void and defecate less often during the day. This applies to both continent and incontinent individuals. In accordance, individuals with AS who voided on the toilet postponed voiding for a significant longer duration of time than individuals with non-specific ID who voided on the toilet. Overall, nearly half of the individuals with AS (46%) were continent for urine during the day and the majority (63%) showed in-toilet voids. Nocturnal incontinence was the most common form of incontinence in AS (89%). Remarkable findings were also found according to voiding characteristics; many

individuals with AS showed lower urinary tract symptoms (LUTS), including straining, interrupted stream, taking too little time to void, hesitancy and urgency. Combined with the low voiding frequencies and long intervals between voiding, these could indicate bladder dysfunctions. Based on the results of this study, neither form of incontinence is part of the behavioral phenotype of AS.

In our toilet training study, we trained seven individuals (aged 6-25 years) with Angelman syndrome to acquire daytime urinary continence. We adjusted the Response Resictrion training protocol to the behavioral phenotype of AS and to the individual characteristics of each participant. Each training took place in the participant's own environment and consisted of several of the following elements; diaper removal, increased liquid intake, not leaving the toilet until voiding occurred, response restriction, toy play while seated on toilet seat, most-to-least prompting to void, reinforcements for correct voids and positive practice after an urinary accident. When training progressed, liquid intake and time-on-toilet was decreased and the reinforcement interval was prolonged until the child went to toilet with intervals of one-and-a-half to two hours. After three or four weeks of training, the number of correct voids increased and number of accidents decreased in five participants. In one participant the number of accidents remained low (zero during baseline, one during generalization) and in one participant no difference occurred in number of accidents. Follow up (after 3 to 18 months) revealed that in three participant positive results regarding in-toilet voids and accidents were maintained, the other participants relapsed and caretakers attributed this mainly to changes in the participant's environment. Remarkable voiding characteristics during toilet training included the absence of holding maneuvers despite increases in liquid intake, low voiding frequencies during baseline,

voluminous and uninterruptable urinary accidents and signs of straining when little fluids were drunk.

Some of these voiding characteristics were also found during our uroflowmetry study. In this study we conducted uroflowmetry, a non-invase method to assess the voiding pattern and volume of a urinary void, in six individuals with AS. In five individuals, pathological voiding patterns were found. In four individuals a staccato voiding pattern (in which different peaks in speed occur during the void) and in two individuals an interrupted voiding pattern (in which different episodes of voiding occur) was found, one individual showed only normal voiding patterns. Different type of voiding patterns (staccato, interrupted, or normal) were also found within the participants, which indicates that the abnormal patterns are functional instead of the result of a structural or neurogenic disorder. Small voided volumes occurred in five participant, one participant had relative voluminous voids. Findings also revealed that in three individuals it took five or more minutes before voiding was initiated.

3. Parental preferences in the care for children with AS

To assess the priorities of parents in the care for their child with AS, the "Treatment PrioritiesSurvey" was used. In this survey, 77 parents of children with AS were asked to give ability and priority ratings to skills from adaptive and maladaptive behavior domains. Parents of children below the age of 18 mainly highlighted the training of skills from the communication, self-care, ingestion, motor and academic domains. For adults with AS, skills from the communication, recreational, motor and self-care domain were highlighted. In general, parents highlighted the acquisition of developmental milestones (e.g. walking, eating, toileting). In older individuals, the emphasis on teaching the child to communicate remained, but was

complemented by participating in meaningful daytime activities. Parents indicated that physical activities such as walking, cycling and swimming were highly important. Training for motor skills and social skills concerning individuals was prioritized when children showed a major deficit, training for communication, ingestion and recreation skills was prioritized when children showed emerging abilities and training for self-care skills was deemed most important when children showed relative independence in this domain. Treatment was prioritized for eating problems and overweight, as well as for sleep problems, incompliance, and aggression. The more severe the behavioral problem, the higher the priority for training.

4. Overall summary

Above mentioned studies describe how the capabilities of individuals with Angelman syndrome can be strengthened and expanded. They show that techniques derived from the Applied Behavior Analysis can effectively be applied in individuals with Angelman syndrome, in both clinical and natural settings. Individualization of training procedures is necessary due to their behavioral phenotype and individual characteristics. Our studies targeted adaptive skills such as communication and incontinence, skills which were also highlighted for training by parents.

Samenvatting

1. Gedragsmatige behandeling van probleemgedrag

Bij zeven kinderen met het Angelman syndroom (AS) is functionele gedragsanalyse (FA) uitgevoerd om de functie van hun probleemgedrag te onderzoeken. Bij deze analyses werden situaties uit het dagelijks leven nagebootst, waarbij de antecedenten en de consequenties van het probleemgedrag systematisch werden gemanipuleerd. Op deze manier kon worden onderzocht of de kinderen het probleemgedrag lieten zien om aandacht of geliefde voorwerpen te krijgen of om aan een taak te ontsnappen. Bij vier kinderen werden de analyses uitgevoerd in hun eigen klaslokaal en zij werkten samen met hun eigen leerkrachten. De andere kinderen werkten met een onderzoeker in een prikkelarme therapieruimte. Het probleemgedrag had meerdere verschijningsvormen zoals haren trekken, knijpen, ongewenste geluiden maken en de rug overstrekken. Uit de analyses bleek dat het probleemgedrag bij vier kinderen vooral gericht was op het verkrijgen van speelgoed of eten, twee kinderen lieten het gedrag zien om te ontsnappen aan een taak en bij twee kinderen was het probleemgedrag er met name op gericht om aandacht te krijgen. Alle kinderen lieten probleemgedrag zien in meerdere condities, wat aangeeft dat het gedrag verschillende functies kon hebben. Bij vijf kinderen waren er duidelijke voorlopers (d.i. gedragingen die vaak voorafgaan aan het probleemgedrag) te onderscheiden, bij de andere twee kinderen waren deze voorlopers minder duidelijk te herkennen. Voorbeelden van voorlopers waren reiken naar een gewenst voorwerp en fysiek en oogcontact maken met de onderzoeker of begeleider.

Toen de primaire functie van het probleemgedrag bekend was, werd het kind geleerd om dit gedrag te vervangen door een meer sociaal geaccepteerde vorm van communicatie, bijvoorbeeld het uitwisselen van een klein voorwerp of foto of door gebruik te maken van een spraakcomputer. Deze training wordt Functionele Communicatie Training (FCT) genoemd. In deze training werden de kinderen gestimuleerd om het vervangende gedrag uit te voeren zodra zij een voorloper lieten zien, er werd door de trainers niet gereageerd op het probleemgedrag zelf. De training zorgde voor een afname van probleemgedrag bij alle kinderen: bij één kind was er een kleine effectgrootte, bij twee een middelmatige effectgrootte en bij vijf kinderen was er sprake van een grote effectgrootte.

De analyses lieten ook zien dat de tendensen in de kans op aanwezigheid van de instandhoudende variabelen (bv. geen aandacht krijgen, een taak moeten maken) voorafgaand en volgend op zowel het probleemgedrag als het vervangende gedrag vergelijkbaar waren, wat aangeeft dat beide gedragingen dezelfde functie hadden. Beide studies geven aan dat probleemgedrag bij mensen met AS zowel een positieve als een negatieve sociale functie kan hebben en dat nieuwe manieren van communiceren aangeleerd kunnen worden, waardoor het probleemgedrag afneemt. Zodra het kind een voorloper laat zien, kan de trainer hierop insteken door het kind te begeleiden bij het gebruiken van de nieuwe communicatievorm. Daarnaast kunnen voor het kind bekende begeleiders worden ingezet als uitvoerders van zowel FA als FCT in het klaslokaal.

2. Incontinentie en zindelijkheidstraining

We hebben het vóórkomen van incontinentie voor urine en ontlasting onderzocht bij mensen met AS (n = 71) en mensen met een verstandelijke beperking (VB) door een andere

oorzaak (*n* = 69). Vergeleken met de controlegroep, waren er minder mensen met AS incontinent voor urine gedurende de dag. Ook de mictie- en ontlastingfrequenties lagen lager in de AS groep, dit gold zowel voor zindelijke als onzindelijke mensen. Hierop aansluitend, gekeken naar de mensen die op het toilet plasten, bleven mensen met AS gemiddeld significant langer droog dan mensen met een VB. Bijna de helft van alle mensen met AS uit ons onderzoek (46%) was zindelijk voor urine overdag en de meerderheid plaste op het toilet (63%). De meest voorkomende vorm van incontinentie bij AS was incontinentie voor urine 's nachts. Gebaseerd op de resultaten van deze studie is incontinentie geen onderdeel van het gedragsfenotype van AS. Er werden ook een aantal opvallendheden gevonden in de karakteristieken van het plassen: meerdere mensen met AS lieten één of meerdere "lower urinary tract symptoms" zien waaronder; persen, onderbroken straal, te weinig tijd nemen om te plassen, veel tijd nodig hebben om te beginnen met plassen en het onmiddellijk moeten plassen bij aandrang. Tezamen met de lage mictie- en ontlastingfrequenties en de lange intervallen tussen micties, kunnen deze LUTS duiden op blaasdysfuncties.

We hebben een zindelijkheidstraining uitgevoerd bij zeven individuen (6-25 jaar) met AS, welke gericht was op zindelijkheid voor urine overdag. De training was gebaseerd op de response restrictie training en werd aangepast aan het gedragsfenotype en de individuele kenmerken van de trainee. Elke training vond plaats in de natuurlijke omgeving van de trainee een bestond uit één of meerdere van de volgende elementen: verwijdering van de luier, verhoogde vochtinname, niet verlaten van de badkamer totdat er geplast was, response restrictie, zittend op het toilet met speelgoed spelen, afnemende hulp bij het gaan plassen, beloningen voor plassen op het toilet en positieve oefening na een ongelukje. Op geleide van de voortgang van de training werd de vochtinname weer gereduceerd naar normale hoeveelheden, werd de tijd dat de

trainee op de badkamer moest blijven verkort en werd het beloningsinterval tussen twee toiletbezoeken verruimd totdat de trainee om de anderhalf tot twee uur naar het toilet ging. Na drie tot vier weken training waren de micties op het toilet toegenomen bij alle trainees en bij vijf trainees waren de ongelukjes afgenomen. Bij één trainee bleef het aantal ongelukjes laag (nul tijdens de basislijn, één tijdens de generalisatiefase) en bij een andere trainee bleef het aantal ongelukjes gelijk. Tijdens de nameting (3 tot 18 maanden na de training) bleek dat bij drie trainees de resultaten waren behouden, de andere trainees hadden een terugval gehad. Volgens de verzorgers van deze trainees kon de terugval onder andere worden verklaard door veranderingen in de omgeving van de trainee. Er werden verschillende opvallende mictiekarakteristieken geobserveerd gedurende de zindelijkheidstraining; sommige trainees plasten niet tot nauwelijks gedurende de basislijn, ondanks de verhoogde vochtinname werd niet gezien dat de trainees hun urine ophielden, ongelukjes waren vaak groot en niet te onderbreken en bij sommige trainees werd gezien dat ze erg moesten persen om te plassen als ze weinig hadden gedronken.

Een aantal van deze karakteristieken werden ook gevonden tijdens ons uroflometrie studie. Tijdens deze studie werd bij zes participanten met AS uroflowmetrie toegepast, een niet-invasieve techniek die het patroon, de hoeveelheid en de snelheid van een mictie meet en bepaald. Bij vijf participanten werden pathologische mictiepatronen gevonden. Bij vier participanten werd een staccato patroon gevonden, hierbij werden er verschillende pieken gezien in de snelheid van het plassen; bij twee participanten werd een onderbroken patroon gevonden, hierbij werd de urinestroom enkele malen onderbroken. Er werden verschillende type mictiepatronen (staccato, onderbroken, normaal) gevonden binnen de participanten, wat aangeeft dat de pathologische mictiepatronen functioneel van aard zijn en dat er waarschijnlijk geen neurogene of structurele oorzaak onder ligt. Bij vijf participanten werden kleine hoeveelheden urine gevonden, één

participant had een relatief volumineuze mictie. Uit observaties bleek verder dat het bij drie participanten vijf of meer minuten duurde voordat ze gingen plassen.

3. De voorkeuren van ouders in de zorg voor hun kind met AS

Om te onderzoeken welke prioriteiten ouders van kinderen met AS hebben in de zorg voor hun kind is de "Treatment Priorities Survey" afgenomen bij 77 ouders van een kind met AS. Zij werden gevraagd om aan te geven hoeveel hulp hun kind nodig had bij een bepaalde zelfredzaamheidvaardigheid en hoe belangrijk zij het vonden dat hun kind training kreeg om die vaardigheid zelfstandig(er) uit te kunnen voeren. Ook werd hen gevraagd naar de ernst van probleemgedragingen en naar welke prioriteit zij gaven aan een passende behandeling. Ouders van kinderen onder de 18 gaven de hoogste prioriteit aan training voor communicatieve, zelfzorg, voedsel- en vochtinname, motorische en schoolse vaardigheden. Voor volwassenen met AS werd het belangrijk gevonden dat zij training kregen op het gebied van communicatie, vrijetijdsbesteding, motoriek en zelfzorg. Over het algemeen werd er prioriteit gegeven aan het trainen van ontwikkelingsmijlpalen (bijv. eten, lopen, zindelijkheid). Bij oudere individuen met AS bleef de nadruk liggen op het trainen van communicatieve vaardigheden, maar werd ook het belang van trainen van zinvolle dagelijkse bezigheden benadrukt. Ouders gaven aan dat motorische activiteiten zoals wandelen, fietsen en zwemmen erg belangrijk waren. De prioriteit voor trainingen op het gebied van motorische vaardigheden en sociale vaardigheden gericht op individuen was het grootst als de kinderen veel hulp nodig hadden bij deze vaardigheden. Trainingen voor communicatieve, voedsel- en vochtinname en recreatieve vaardigheden kregen een hoge prioriteit wanneer de kinderen zich hierin begonnen te ontwikkelen. Ouders vonden de training in zelfzorg vaardigheden belangrijker wanneer hun kind hier al relatief zelfstandig in

was. Het behandelen van eetproblemen en overgewicht, slaapproblemen, ongehoorzaamheid en agressie kreeg een hoge prioriteit van ouders. Hoe ernstiger het probleemgedrag, hoe hoger de prioriteit voor de behandeling.

4. Tot slot

Bovengenoemde studies beschrijven hoe de mogelijkheden van individuen met AS kunnen worden versterkt en uitgebreid. Ze laten zien dat technieken uit de Toegepaste Gedragsanalyse effectief kunnen worden toegepast bij individuen met AS, in zowel klinische als natuurlijke omgevingen. Het is noodzakelijk om behandelprotocollen aan te passen op zowel het gedragsfenotype van AS als de individuele karakteristieken van de trainee. In onze studies hebben we ons vooral gericht op adaptieve vaardigheden als communicatie en zindelijkheid, omdat dit door ouders als belangrijk werd aangemerkt.

Dankwoord

Mijn dank begint bij Prof. dr. Robert Didden. Robert, dankzij jou kon een langgekoesterde wens in vervulling gaan: studeren in Engeland. Ik mocht naar de University of Birmingham om mijn masterscriptie te schrijven. Daar ben ik geweldig begeleid, zowel in het werk als daarbuiten door Dr. Debbie Allen en Prof. dr. Christopher Oliver. Nog steeds denk ik met zeer veel plezier terug aan die drie maanden in Birmingham. Eenmaal terug in Nederland gingen zaken in vogelvlucht. De Angelman Foundation was enthousiast en wilde een promotieonderzoek subsidiëren. Van de ene op de andere dag was ik geen student meer maar docent en promovenda aan de Radboud Universiteit te Nijmegen. Om het verhaal compleet te maken, je hebt me ook geholpen aan een baan als orthopedagoog bij Daelzicht, waar ik nu nog steeds werkzaam ben. Robert, je hebt een primaire rol gespeeld in mijn eerste jaren als orthopedagoog, je hebt me aan al mijn banen geholpen, me nog enthousiaster gemaakt voor dit vak, hebt me begeleid in mijn werk en in mijn schrijfwerk. Ik wil je danken voor je inzet, tijd en geduld met mij, tot in je weekenden aan toe. Zonder jou had ik hier niet gestaan.

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Maartje ten Hooven - Radstaake

Curriculum Vitae

Maartje ten Hooven – Radstaake werd geboren op 20 juli 1985 te Winterswijk. Na het VWO studeerde ze HBO-Verpleegkunde aan de Saxion Hogeschool in Enschede. Tijdens haar stages bij het Mappa Mondo huis te Wezep, een kinderhospice van het Rode Kruis, raakte ze verder geïnteresseerd kinderen met een ontwikkelingsachterstand. In 2006 begon ze aan de studie Pedagogische Wetenschappen en Onderwijskunde te Nijmegen. Gedurende deze studie werkte ze op diverse woon- en logeervoorzieningen van 's Heerenloo en de Driestroom en bij de buitenschoolse opvang van KION. Daarnaast bleef ze als vrijwilliger betrokken bij Mappa Mondo. Tijdens haar Masterjaar heeft ze drie maanden in Engeland gewoond en daar haar scriptieonderzoek uitgevoerd. Bij het Centre of Neurodevelopmental Disabilities aan de University of Birmingham heeft ze meegewerkt aan een onderzoek naar probleemgedrag bij kinderen met het Angelman syndroom. Dit onderzoek vond plaats onder leiding van Prof. dr. Chris Oliver en Dr. Debbie Allen.

Eenmaal terug in Nederland werd haar de mogelijkheid geboden dit onderzoek voort te zetten met een subsidie van de Angelman Foundation, wat heeft geresulteerd in dit proefschrift. Naast het onderzoek kon ze als docent aan de slag gaan bij de Radboud Universiteit te Nijmegen. Binnen het onderwijs geeft ze met name de klinisch gerichte vakken in zowel de Bachelor als de Masterfase van Pedagogische Wetenschappen. Na haar afstuderen ging ze ook aan de slag als orthopedagoog bij Daelzicht. Ze werkt hier met kinderen met een verstandelijke beperking en gedragsproblemen.

List of publications

Giesbers, S., Didden, R., Radstaake, M., Korzilius, H., von Gontard, A., Lang, R., … Curfs, L. M. G. (2012). Incontinence in individuals with Rett syndrome: A comparative study. *Journal of Developmental and Physical Disabilities, 24,* 287-300.

Radstaake, M., & Didden, R. (2012). Children with autism can be taught a complicated requesting task. *Evidence-Based Communication and Intervention, 6*, 126-128.

Radstaake, M., Didden, R., Bolio, M., Lang, R., Lancioni, G., & Curfs, L. M. G. (2011). Functional assessment en behavioral treatment of skin picking in a teenage girl with Prader Willi syndrome. *Clinical Case Studies, 10*, 67-78.

Radstaake, M., Didden, R., Giesbers, S., Korzilius, H. Peters-Scheffer, N, Lang, R., … Curfs, L. M. G. (2013). Incontinence in individuals with Angelman syndrome: A comparative study. *Research in Developmental Disabilities, 34,* 4184-4193.

Radstaake, M., Didden, R., Lang, R., O'Reilly, M., Sigafoos, J., Lancioni, G. E., Appels, N. & Curfs, L. M. G. (2013). Functional analysis and functional communication training in the classroom for three children with Angelman syndrome. *Journal of Developmental and Physical Disabilities, 25,* 49-63.

Radstaake, M., Didden, R., Oliver, C., Allen, D., & Curfs, L.M.G. (2012). Functional analysis and functional communication training in individuals with Angelman syndrome. *Developmental Neurorehabilitation, 15,* 91-104.

Radstaake, M., Didden, R., Peters-Scheffer, N., Moore, D., Anderson, A., & Curfs, L. M. G. (2014). Toilet training in participants with Angelman syndrome: A case

series. *Developmental Neurorehabilitation, 17,* 243-250.

Radstaake, M., Didden, R., Peters-Scheffer, N., Sigafoos, J., Korzilius, H., & Curfs, L. M. G. (2014). Educational priorities for individuals with Angelman syndrome: A study of Parents' perspectives. *Journal of Developmental and Physical Disabilities, 26*, 299-316.

Radstaake, M., Didden, R., von Gontard, A., & Curfs, L. M. G. (2014). Uroflowmetric assessment in participants with Angelman syndrome. *Developmental Neurorehabilitation.* Advance online publication. doi:10.3109/17518423.2013.874377.