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Behavioural flexibility in individuals with Angelman syndrome, Down syndrome, non-specific intellectual disability and Autism spectrum disorder

R. Didden,[1] J. Sigafoos,[2] V. A. Green,[2] H. Korzilius,[1] C. Mouws,[1] G. E. Lancioni,[3] M. F. O'Reilly[4] & L. M. G. Curfs[5]

1 *Radboud University Nijmegen, Nijmegen, the Netherlands*
2 *Victoria University of Wellington, Wellington, New Zealand*
3 *University of Bari, Bari, Italy*
4 *University of Texas at Austin, Austin, TX, USA*
5 *University of Maastricht, Maastricht, the Netherlands*

Abstract

Background Little is known about behavioural flexibility in children and adults with Angelman syndrome and whether people with this syndrome have more or less problems in being behaviourally flexible as compared with other people.
Method Behavioural flexibility scores were assessed in 129 individuals with Angelman syndrome using 11 items from the Behavioural Flexibility Rating Scale-Revised (Green *et al.* 2007). Level of behavioural flexibility scores in individuals with Angelman syndrome ($N = 129$) was compared with that of people with non-specific intellectual disability (ID) ($N = 90$), Down syndrome ($N = 398$) and Autism spectrum disorder ($N = 235$).
Results Comparative analyses show that individuals with Angelman syndrome were more flexible than those with non-specific ID ($P < 0.001$) and those with Autism spectrum disorder ($P < 0.01$). There were no differences in behavioural flexibility scores between individuals with Angelman syndrome and those with Down syndrome ($P = 0.94$).
Conclusion It is concluded that individuals with Angelman syndrome are comparatively flexible in their behaviour.

Keywords Angelman syndrome, Autism spectrum disorder, Behavioural flexibility, Behavioural phenotype, Down syndrome

Correspondence: Robert Didden, Radboud University Nijmegen, PO Box 9104, 6500 HE, Nijmegen, the Netherlands (e-mail: R.Didden@pwo.ru.nl).

Angelman syndrome (AS) is a genetic neurodevelopmental disorder with a prevalence of about 1 out of 12 000 (Clayton-Smith & Laan 2003; Williams 2005). Although 80% of the cases in which AS is suspected can be confirmed by laboratory testing, the cause of AS remains complicated. There are four known causes that all relate to the dysfunction of deletion of genes on chromosome 15. A deletion of the chromosome 15q11–q13 occurs most frequently (i.e. 75%). The remaining three causes include uniparental disomy (2–3%), methylamine imprinting mutation (2–3%) and UBE3A mutations (2–3%). In 15–20% of cases AS is suspected, but laboratory testing cannot confirm the expectation

(Williams 2005). AS is associated with developmental delay, lack of speech, hyperactivity and attention problems, movement of balance disorder, restlessness and epilepsy. Other characteristic features include excessive laughter, sleep disturbance, preference for water and an apparently happy demeanor (see e.g. Clayton-Smith & Laan 2003; Didden *et al.* 2004, 2008; Berry *et al.* 2005; Williams 2005; Horsler & Oliver 2006).

Currently, there appears to be little evidence-based information concerning the likely education and rehabilitation needs of individuals with AS. There is also relatively little literature related to provision of effective training programmes. For example, while there are some anecdotal reports from parents that children with AS may have problems in dealing with unexpected situations, there are currently no data confirming the nature, extent or circumstances of this potential problem. Several researchers have noted significant problems with behavioural flexibility and an increased risk for autism in individuals with AS (see Steffenburg *et al.* 1996; Cohen *et al.* 2005). It would seem critically important to ascertain whether individuals with AS exhibit problems in relation to unexpected changes in the environment, such as when objects are misplaced and cannot be located by the individual, or when a sudden and unexpected change in routine occurs. If individuals with AS do in fact have problems adjusting their behaviour to adapt to or cope with such changes in the environment, then it would suggest a need to develop effective procedures to address this behavioural concern. At present, however, it is unknown whether AS is associated with problems in behavioural flexibility.

Few instruments are available for assessing behaviour flexibility in individuals with severe intellectual disabilities (ID) and/or autism. Recently, Green *et al.* (2006, 2007) developed the Behaviour Flexibility Rating Scale (BFRS) and the Behaviour Flexibility Rating Scale – Revised (BFRS-R). The BFRS(R) is a tool with which behavioural flexibility may be measured in individuals with developmental disabilities. This instrument was developed in order to identify specific situations related to a resistance to change and to rate the extent to which individuals show problems with environmental changes. In their large sample ($n = 762$), they found that people with autism had substantially more problems with behavioural flexibility than individuals with Down syndrome confirming that problems with behavioural flexibility are indeed strongly associated with autism.

It remains to be assessed whether individuals with AS have an increased risk of problems with behavioural flexibility as compared with other individuals with severe ID. The aim of the present study, therefore, was to assess level of behavioural flexibility scores among a large group of people with AS ($n = 129$) and compare flexibility scores with that of individuals from three comparative groups: (1) non-specific ID ($n = 90$); (2) Down syndrome ($n = 398$); and (3) Autism spectrum disorder ($n = 235$). Eleven items match between the BFRS-R and the BFRS and these items were used to explore differences in behavioural flexibility scores between individuals with AS and individuals from the other diagnostic groups.

Method

Participants

Participants with AS were recruited through the Dutch Parent Organization of parents with children with AS. They were sent the Dutch version of the BFRS-R (Green *et al.* 2007); see Instrument) with an accompanying letter stating the general aim of the study and explaining how to complete the questionnaire. If an individual with AS lived in a residential facility, parents were asked to complete the BFRS-R together with a staff member who had worked with the individual for at least 6 months. Out of 154 questionnaires, 129 were returned (response rate 84%). Individuals had a mean age of 17.40 years (range: 2–52 years, SD = 10.67) and 48% were male. Most (i.e. 94%) lived at home with their parent(s) and 6% lived in a residential facility.

A comparison group consisting of individuals with non-specific (severe) ID was sought within several day care centers located in the eastern part of the Netherlands. The staff members and parents of 90 individuals with non-specific ID were asked to complete the BFRS-R and return it. Participants had a mean age in years of 13.87 (range: 2–52 years, SD = 11.39) and 60% were male. They were living at home (i.e. 86%) or in a residential facility (i.e. 14%). They functioned in the profound to moderate range of ID (most functioned in the severe range of

ID; level of functioning was based on outcomes of rating scales such as the *Sociale Redzaamheidsschaal-Z* (Kraijer & Kema 2004), a rating scale for measuring adaptive behaviours in people with ID and widely used in the Netherlands). They did not have a genetic disorder or the cause of the disability was unknown.

BFRS data collected in individuals with autism and those with Down syndrome as part of a study conducted by Green *et al.* (2006) were used in the present study. These data were collected through an internet survey via the Autism Society of America and related organizations and Autism Link, as well as the National Down Syndrome Society of America and related organizations. The survey yielded three groups of individuals with a confirmed primary diagnosis: (1) Down syndrome ($n = 398$); (2) Autism spectrum disorder ($n = 235$); and (3) Asperger syndrome ($n = 93$). Only data from the Down syndrome and Autism group were used in the present analyses. In the Down and Autism group, 60% and 87% of the individuals were male respectively.

Instrument

Data on individuals with AS and non-specific ID were collected using the BFRS-R (Green *et al.* 2007) which was translated into Dutch. It consists of 16 items addressing situations related to problems with behavioural flexibility. For each item, the caregiver had to indicate to what extent a situation causes a problem for the participant. The severity of each potentially problematic situation was rated on a four-point Likert scale ranging from 0 (i.e. not at all a problem) to 3 (i.e. the situation causes severe problems). (An operational definition is provided for each of the four points on the scale.) Results from preliminary studies indicate that the BFRS-R has good psychometric properties. We examined its properties in 76 direct care staff members and 56 parents who completed the BFRS-R for 70 children with developmental disabilities. Factor analysis revealed three factors (i.e. Flexibility towards objects, Flexibility towards the environment, and Flexibility towards persons) and results of several analyses indicated an excellent internal consistency and good intra-rater and inter-rater reliability of the total scale and its items. These data suggest that the BFRS-R may provide a useful and reliable rating of behavioural flexibility in individuals with developmental disabilities (see Peters-Scheffer *et al.* 2008). Data on individuals with Down syndrome and Autism spectrum disorder were collected using the BFRS (Green *et al.* 2006; Pituch *et al.* 2007) which consists of 15 items. Eleven items of the BFRS were retained in the revised version, the BFRS-R.

In order to be able to compare behavioural flexibility of AS and non-specific developmental disability with that of individuals with autism spectrum disorder and Down syndrome, we used the 11 items of the BFRS that were retained in the revised version of the BFRS-R. Cronbach's alpha for the 11 items was 0.87.

Statistical analyses

Mean total scores and mean scores of each of the 11 items were computed using SPSS (version 15). Relationships between Age, Gender and Living setting (where applicable) and mean total scores were explored for each diagnostic group using *t*-tests, and One-way ANOVA's. Then, One-way ANOVA's (followed by *post-hoc* comparisons to test differences between pairs of groups) were performed to test for differences in total mean scores and mean items scores between the four diagnostic groups.

There was a statistically significant difference between the four diagnostic groups in percentages of males and females, $\chi^2(3) = 79.14$, $P < 0.001$. While in the AS and Down syndrome groups the percentage of males and females were comparable, in the Autism and the non-specific ID group the number of males was higher than the number of females (see also Table 1). There also appeared an unequal distribution in age groups across the four diagnostic groups, $\chi^2(12) = 144.21$, $P < 0.001$. As a consequence, the Generalized Linear Model (GLM) was used to test the effects of the covariates Age and Gender in addition to the effects of Diagnostic group on level of behavioural flexibility scores.

Results

Within-group analyses

For each diagnostic group, we explored whether level of behavioural flexibility scores was related to

Table 1 Mean total scores, standard deviations, and number of individuals for diagnostic groups and gender, age, and setting

Variable	Angelman Mean (SD; *n*)	Autism Mean (SD; *n*)	Non-specific ID Mean (SD; *n*)	Down Mean (SD; *n*)
Gender				
Male	0.73 (0.62; 62)	1.16 (0.54; 188)*	1.00 (0.66; 54)	0.70 (0.48; 196)#
Female	0.65 (0.45; 67)	1.15 (0.67; 29)	0.98 (0.65; 36)	0.72 (0.45; 173)
Age				
0–5	0.41 (0.38; 12)	1.09 (0.56; 59)	0.98 (0.58; 32)	0.58 (0.39; 139)
6–11	0.77 (0.48; 31)	1.16 (0.59; 106)	1.01 (0.67; 18)	0.77 (0.46; 151)
12–18	0.70 (0.52; 38)	1.18 (0.54; 53)	0.62 (0.59; 9)	0.87 (0.45; 73)
19–25	0.67 (0.60; 23)	1.06 (0.62; 11)	1.24 (0.81; 19)	0.87 (0.54; 23)
25+	0.72 (0.64; 25)	1.10 (0.55; 6)	0.93 (0.70; 12)	0.74 (0.61; 11)
Living setting				
Home	0.73 (0.55; 121)	–	0.98 (0.62; 68)	–
Facility	0.73 (0.63; 8)	–	1.00 (0.77; 22)	–
Mean Total	0.69 (0.54; 129)	1.14 (0.57; 235)	1.00 (0.68; 90)	0.72 (0.46; 398)

ID, intellectual disability; –, no data available.
* 18 missing values, # 29 missing values.

Gender, Age, and Living environment (for AS and non-specific ID only). First, results of *t*-tests showed no significant differences for mean total score between males and females for AS, $t(110.93) = 0.84$, $P = 0.41$, Autism, $t(215) = 0.04$, $P = 0.97$, non-specific ID, $t(88) = 0.68$, $P = 0.90$, and Down syndrome, $t(367) = 0.45$, $P = 0.65$. It is concluded that Gender was not related to the level of behavioural flexibility scores in each diagnostic group.

Further, One-way ANOVA's showed no significant differences between age groups in AS, $F_{4,124} = 1.03$, $P = 0.40$, Autism, $F_{4,230} = 0.30$, $P = 0.83$, and non-specific ID, $F_{4,85} = 1.38$, $P = 0.21$. However, there was a difference in level of behavioural flexibility scores between age groups for Down syndrome, $F_{4,392} = 6.53$, $P < 0.001$. Games-Howell *post-hoc* tests for unequal variances were conducted and results showed that the age group 0–5 years had a statistically significantly lower mean flexibility score (i.e. were more flexible) than the age groups 6–11 years, 12–18 years, and 19–25 years respectively. There were no differences in flexibility scores between other age groups.

Finally, there were no differences in behavioural flexibility scores between those who lived at home and those who lived in a residential facility in AS, $t(127) = 0.01$, $P = 1.00$, and in non-specific ID, $t(88) = 0.10$, $P = 0.92$.

Between-group analyses

Results of One-way ANOVA for Diagnosis showed significant differences in mean total score between diagnostic groups, $F_{3,848} = 37.89$, $P < 0.001$. Results of Games-Howell *post-hoc* tests for unequal variances showed that the mean total score for AS was lower than the mean total score of Autism and non-specific ID ($P < 0.05$) (see Table 2 for means and SD's). In addition, total mean score in non-specific ID was significantly higher than the mean in Down syndrome and the mean flexibility score in Autism was significantly higher than in Down syndrome ($P < 0.05$). There were, however, no significant differences in total mean score between AS and Down syndrome ($P = 0.94$), and between Autism and non-specific ID ($P = 0.27$). Results of One-way ANOVA followed by Games-Howell *post-hoc* tests for Diagnosis and the separate flexibility items generally indicate that scores for AS were lower than for the other diagnostic groups (only for item 7 'Unexpected interaction' and item 8 'Separation from group' individuals with Down syndrome were more flexible; see Table 2 for more details). Results of our study show that individuals with AS and Down syndrome were most behaviourally flexible and those with Autism were least behaviourally flexible.

A GLM with Diagnosis, Gender, and Age as independent variables and mean total score as

Table 2 Mean item scores, standard deviations and results of multivariate analyses

Item	Diagnostic Group	Mean	SD	$F_{3,848}$	*Post-hoc#* (Games-Howell)
1. Object misplaced	AS	0.43	0.74	20.75***	AS < ID, AU, DS
	ID	0.99	1.06		AU > DS
	AU	1.06	1.38		ID > DS
	DS	0.66	0.76		
2. Planned event canceled	AS	0.83	1.00	26.64***	AS < AU
	ID	1.10	0.77		AU > DS
	AU	1.38	1.01		ID > DS
	DS	0.74	0.77		
3 Object replaced/ removed	AS	0.37	0.65	11.18***	AS < AU, ID
	ID	0.77	0.93		AU > DS
	AU	0.70	0.81		ID > DS
	DS	0.44	0.66		
4. Unavailable object	AS	1.14	0.97	15.50***	AS < ID
	ID	1.63	1.15		AU > DS
	AU	1.32	0.93		ID > DS
	DS	1.00	0.77		
5. Material has broken	AS	0.64	0.86	57.24***	AS < ID, AU, DS
	ID	1.03	0.94		AU > ID, DS
	AU	1.77	0.95		
	DS	1.05	0.79		
6. Change in routine	AS	0.71	0.87	18.84***	AS < AU
	ID	0.96	1.01		AU > DS
	AU	1.21	0.96		
	DS	0.70	0.78		
7. Unexpected interaction	AS	0.71	0.86	13.36***	AS > DS
	ID	0.89	0.98		AU > DS
	AU	0.82	0.87		ID > DS
	DS	0.47	0.66		
8. Separation from group	AS	0.88	0.95	11.12***	AS > DS
	ID	0.92	0.94		AU > DS
	AU	1.03	0.99		ID > DS
	DS	0.63	0.72		
9. Material brakes, activity stops early	AS	0.74	0.85	12.89***	AS < ID, AU
	ID	1.09	1.04		AU > DS
	AU	1.08	0.87		ID > DS
	DS	0.72	0.69		
10. Other person shows annoying behaviours	AS	0.82	0.90	19.50***	AS < AU, DS
	ID	1.07	0.88		AU > ID, DS
	AU	1.51	0.97		
	DS	1.07	0.85		
11. Material in incorrect place	AS	0.33	0.75	7.29***	AS < AU
	ID	0.51	0.80		AU > DS
	AU	0.69	0.84		
	DS	0.46	0.72		
Total mean score	AS	0.69	0.54	37.89***	AS < AU, ID
	ID	1.00	0.68		AU > DS
	AU	1.14	0.57		ID > DS
	DS	0.72	0.46		

AS, Angelman syndrome; ID, intellectual disability; AU, Autism spectrum disorder; DS, Down syndrome.
Only significant differences between groups are depicted (*P*'s < 0.05). *** *P* < 0.001.

dependent variable was performed for the total sample. There appeared a main effect of Diagnosis, $F_{3,764} = 9.82$, $P < 0.001$, and two interaction effects, namely Diagnosis*Age, $F_{12,764} = 2.09$, $P < 0.05$ and Diagnosis*Gender*Age, $F_{12,764} = 2.30$, $P < 0.01$. The interaction effect Diagnosis*Gender, $F_{3,764} = 1.82$, $P = 0.14$, and Gender*Age, $F_{4,764} = 0.52$, $P = 0.72$, were not statistically significant, nor was there a main effect of Gender, $F_{1,764} = 2.11$, $P = 0.15$, and Age, $F_{4,764} = 1.61$, $P = 0.17$. Results of these analyses suggest that the significant differences in total mean flexibility scores between diagnostic groups (see results of *post-hoc* tests) are to some degree influenced by age group and gender.

Discussion

This study is the first to empirically investigate behavioural flexibility in individuals with AS. It may be concluded that AS is not associated with an increased risk of problems with behavioural flexibility as suggested by anecdotal reports from parents and other caregivers and case studies (see Steffenburg *et al.* 1996; Cohen *et al.* 2005). When compared with a control group consisting of individuals with non-specific ID, individuals with AS are significantly more flexible in behaviour. Also, gender, place of residence and age are not related to behavioural flexibility scores in people with AS. In sum, problems with behavioural flexibility do not seem to belong to the behavioural phenotype of AS. This does not mean, however, that some individuals with AS do not have significant problems in this area. Several treatment options (e.g. relaxation training, antecedent control) are available for addressing problems with being behaviourally inflexible although empirical data on their effectiveness are lacking. For individuals with AS, behavioural approaches aimed at, for example, improving their self-control probably are not feasible. Future studies should investigate effectiveness of approaches that successfully address resistance to change and unexpected situations in individuals with developmental disabilities, including those people with AS that have problems in this area (Green *et al.* 2007).

Some methodological shortcomings of the present study should be mentioned. The first shortcoming concerns the lack of data on the predictive validity of the BFRS-R. It still remains to be assessed whether the BFRS-R is a valid instrument that measures problems with behavioural flexibility in daily situations. Future studies should be conducted addressing the predictive validity of the BFRS-R. The second shortcoming concerns the comparability of the various diagnostic groups. We were unable to match groups on some demographic characteristics of participants (e.g. level of ID, autism in people with non-specific ID) because precise data were not available. It may be possible that differences in level of behavioural flexibility between diagnostic groups may be (partly) influenced by differences in demographic characteristics. However, some variables that were not used as a matching variable (e.g. Gender, Age) were statistically tested for their effects. Results of these analyses showed a main effect for Diagnosis only on the level of behavioural flexibility. There were also two significant interaction effects, but as both contain the variable Diagnosis we may conclude that this variable affects behavioural flexibility scores more than Gender and Age do. Other variables, such as for example, level of intellectual and adaptive functioning and genetic subtype of AS (e.g. deletion, disomy), that were not included in the present analyses may be related to behavioural flexibility scores. Future studies on behavioural flexibility and/or AS should be conducted addressing these issues.

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