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Brief report: A longitudinal study of excessive smiling and laughing in children with Angelman syndrome

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Abstract

Elevated laughing and smiling is a key characteristic of the Angelman syndrome behavioral phenotype, with cross-sectional studies reporting changes with environment and age. This study compares levels of laughing and smiling in 12 participants across three experimental conditions (full social interaction (with eye contact), social interaction with no eye contact, proximity only) at two data points. No differences were noted in frequency of laughing and smiling over time in any condition. However, with age as a covariate, the frequency of laughing and smiling decreased over time in the full social interaction (with eye contact) condition only. As this is the first longitudinal study to explore these behaviors in Angelman syndrome, the results suggest a gene-environment-time interaction within the behavioral phenotype.

Keywords

Angelman syndrome; behavioral phenotype; intellectual disability, aging, behavior

Angelman syndrome (AS) affects approximately 1 in 10,000-12,000 live births and is associated with a loss of gene activity from the 15q11-13 region on the maternal chromosome (Petersen, Brondum-Nielsen, Hansen & Wulff, 1995; Steffenburg, Gillberg, Steffenberg & Kyllerman, 1996). The syndrome is associated with varying degrees of intellectual disability (typically severe to profound) with expressive speech more affected than receptive speech. Seizures are present in more than 80% of cases. The physical phenotype includes ataxic gait, hand-flapping, hypopigmentation and a number of craniofacial features. The behavioral phenotype is characterised by heightened levels of laughing and smiling, particularly in the presence of adult attention (Horsler & Oliver, 2006; Oliver, Demetriades & Hall, 2002; Oliver et al., 2007), increased sociability (Mount, Oliver, Berg & Horsler, 2007) and a short attention span (Walz & Benson, 2002).

Change in behavioral phenotypes with age has only been investigated in a small number of syndromes. The most researched example is cognitive decline in individuals with Down syndrome (e.g. Adams et al., 2008). Within Angelman syndrome, early parental or case reports (Clayton-Smith, 2001; Laan, den Boer, Hennekam, Renier & Brouwer, 1996) generally describe the continued presence of “happy” or sociable behavior as children age, although one cross-sectional study identified changes in the intensity of the “happy disposition” as children progress into adulthood (Buntinx et al., 1995). However, these methods lack objective measurement of the behavior of interest.

A recent study (Adams, Horsler & Oliver, 2011) compared the frequency of laughing and smiling in 24 children with AS in experimental settings. Confirming prior experimental studies, laughing and smiling were highest in the full social interaction condition compared to a restricted social interaction and adult close proximity only condition. The cross-sectional comparison showed that the oldest age group showed significantly less smiling and laughing

than the youngest age group within the social interaction condition only. This interaction between age, environment and behavior requires further investigation using a longitudinal design to accurately map these changes.

This study uses data from three previous studies in order to investigate change with age in laughing and smiling in individuals with Angelman syndrome within a longitudinal design. Based on previous cross-sectional studies (removed for anonymity) that show declines with age (particularly during adolescence) in the full social interaction condition only, we predict that older children with Angelman syndrome will show more significant reductions in levels of laughing and smiling than younger children with Angelman syndrome in the full social interaction condition only.

METHOD

Participants

This study presents the data coded from videos of three previous studies, two of which are used for each participant's baseline data (time 1) (removed for anonymity) and one used as the follow-up data collection (removed for anonymity). Twelve of the twenty individuals who participated in the two baseline studies consented to take part at time 2. Of those who did not agree to take part, six (30%) families did not reply, one (5%) family had moved to another country and one (5%) child had been moved to full time residential care.

The twelve participants with data at time 1 and time 2 all had de novo maternal deletion of chromosome 15q 11-13 (deletion subclass unknown). Detailed in Table I, at time 1, the mean age of the participants was 6.6 years (sd=2.9, range 3-12.1) and the mean adaptive behavior composite score from the Vineland Adaptive Behavior Scales was 12.4 (sd=2.85, range 8-

17.8). At time 2, the mean age of the participants was 10.9 years (sd=3.1, range 6.6-15.8) and mean adaptive behavior composite score was 32.9 (sd=6.69, range 24-47). All of the children lived at home with their parents and attended local schools. The mean time between time 1 and time 2 data collection was 46.3 months (sd=11.1, range=31-64).

(Insert Table 1 about here)

Procedure

Prior to recruitment, the (removed for anonymity), School of Psychology Ethics Committee confirmed that the study met the British Psychological Society's criteria for Ethical Conduct of Human Research.

Each participant was exposed to the experimental conditions used by (removed for anonymity) where they were observed (and videotaped) in three conditions with a familiar adult. These are: proximity only (adult sits adjacent to participant, maintaining a neutral facial expression and does not look, talk to or touch participant), a restricted social interaction condition (adult sits adjacent to participant while talking as per a normal social interaction, but maintains a neutral facial expression and does not look at the participant) and a social interaction condition (adult sits adjacent to participant while talking, giving physical contact, smiling, laughing and maintaining eye contact as per normal social interaction). The method of (removed for anonymity) differed slightly, but only the data from the above conditions with the familiar adult were used for this study in order to maintain consistency. The observations were all conducted at the child's home in a quiet room with minimal distractions.

This data were then analysed and data from time 1 were compared to time 2 (that used the same procedure as <removed for anonymity> in order to explore change with age in laughing

and smiling. To ensure consistency, the same familiar adult (always the child's mother, foster mother or adopted mother) was used at both Time 1 and Time 2.

This study focussed on the percentage of time in each condition that the child was showing laughing or smiling. Inter-observer agreement was assessed for Time 2 data by having a second observer simultaneously but independently recode behavior for 20% of all data collected. The sample of 20% included sessions from all conditions and all participants. Kappa indices were calculated based on a 10-second interval-by-interval comparison of observer records. Kappa coefficients for each behavior range from .78 to .83. As all indices were greater than .6, inter-observer reliability can be considered good (Landis & Koch, 1977).

RESULTS

Figure 1 shows the mean percentage of time that participants showed laughing and smiling behaviors in each of the three conditions at Time 1 and Time 2.

(Insert Figure 1 about here)

Kolmogorov-Smirnov tests indicated that the data were normally distributed. In order to identify whether laughing and smiling behaviors within the three environmental conditions change over time with age, repeated measures ANOVAs were undertaken with the duration of laughing and smiling behaviors in the three conditions for both time 1 and time 2. The results show no significant difference between time 1 and time 2 data in all three conditions

(eye contact ($F(1,11)=1.96$, $p=.19$); restricted ($F(1,11)=.66$, $p=.43$) and proximity only ($F(1,11)=2.8$, $p=.12$)).

As it has been identified that laughing and smiling differs with age in children with Angelman syndrome (Adams et al, 2011), the above analyses were repeated with child age at time 2 entered as a covariate.

The analysis of co-variance revealed a significant interaction between the co-variate and environment, suggesting that the relationship between the dependent variable and the co-variate is not linear (i.e. is different in one of the conditions) and consequently compromising the underlying assumptions of the analysis. Therefore, three separate repeated measures analyses of co-variance were carried out, one for each of the environmental conditions; proximity only, restricted social interaction and social interaction.

The results of these three analyses of co-variances highlighted that when age is taken into account, there is a significant main effect of time in the social interaction condition ($F(1,10)=5.59$, $p=.04$) but not in the restricted social interaction ($F(1,10)=.53$, $p=.49$) or proximity only ($F(1,10)=.15$, $p=.71$). The data indicate that, when factoring age at t2 into the analysis, the duration of laughing and smiling behaviors significantly declined over time in the social interaction condition. This suggests that the frequency of laughing and smiling behaviors in relation to eye contact and social interaction decrease with age.

DISCUSSION

This is the first longitudinal study evaluating changes in laughing and smiling in children with Angelman syndrome in controlled experimental conditions. The results show that when age at the follow-up assessment is taken into account, laughing and smiling decreases over

time in the full social interaction condition only. This supports previous cross-sectional studies (Adams et al., 2011) and qualitative reports (Buntinx et al., 1995).

Whilst it cannot be ignored that the sample size for this study was relatively small, with only 12 participants participating at time 1 and time 2. However, given the prevalence of Angelman syndrome, sample sizes using direct observational methods are rarely above that reported in this study. Given that a significant effect is observable with a small n , it highlights the importance and usefulness of studies with small sample sizes within such rare disorders. The strength of using direct observational assessments coupled with high levels of inter-rater reliability minimise additional threats to validity.

Although the data cannot clearly state that cause for such changes, the literature does suggest several areas that would be important for further research. It is well-established that puberty impacts upon physical, emotional and social development (e.g. Pailkoff & Brooks-Gunn, 1991) but there has been little research in this area in individuals with intellectual disabilities and none with individuals with Angelman syndrome. Additional health conditions, in particular, epilepsy, can also impact upon sociability. Whilst it could be considered a limitation that the stage of puberty nor the extent to which an individual was experiencing seizures were measured in this study, neither of these factors would explain why the change with age is only noted in the full social interaction condition only and not in the restricted social interaction or proximity only condition. Clayton-Smith (2001) notes increased anxiety with age, although this noted to be related to changes to routines and not social anxiety, so may not fully explain the specific changes seen with age. To begin to further understand what impact puberty, physical and mental health conditions such as epilepsy may have on behavioural presentation in rare genetic syndromes, these factors should be carefully considered and assessed in future studies using either cross-sectional or longitudinal designs (Adams & Oliver, 2011). It would also be valuable to consider what, if any, other behaviours

the adolescents may be engaging in (e.g. repetitive or restricted behaviours, hand-flapping) instead of the laughing and smiling, socially based behaviours.

The results support the previous studies showing that the laughing and smiling behaviors, widely accepted as part of the behavioral phenotype of Angelman syndrome, show variability across environments (e.g. Horsler & Oliver, 2006a,b). This study also adds to the wider growing body of literature highlighting the changes seen in behavioral phenotypes over time (e.g. Adams et al., 2011; Oliver, Woodcock & Adams, 2010). This highlights the importance of considering gene by behavior by environment by time interactions in delineating the profile within a behavioral phenotype, and further studies focussing upon the different genetic subtypes of Angelman syndrome may further delineate this profile.

The recognition of an evolving and changing behavioural phenotype has important clinical implications and requires clinicians to consider multiple factors before implementing interventions and highlights the importance of regular reviews and evaluations of treatment efficacy. For example, although Oliver et al. (2007) suggest eye contact as a potential reinforce for children with Angelman syndrome, Adams et al. (2010) suggest that the decline in laughing and smiling in the *social interaction* condition with age may reflect a decreased potency in eye contact and social attention as a reinforcer as the children reach adolescence. Early intervention is therefore necessary in order to maximise the potential reinforcing properties of social interaction within this population.

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Table 1: Demographic information for participants

Participant	Gender	Time 1		Time 2		Years Time 1 - Time 2
		Age (years)	Adaptive behavior composite ³	Age (years)	Adaptive behavior composite ³	
1 ¹	F	5.3	12.30	8.8	35.00	3.5
2 ¹	F	4.6	17.80	8.3	47.00	3.7
3 ¹	F	9.5	16.00	13.3	32.00	3.7
4 ¹	M	12.1	10.30	15.8	25.00	3.7
5 ¹	M	6.5	10.30	10.3	28.00	3.7
6 ¹	F	3.0	10.50	6.8	29.00	3.7
7 ¹	M	3.3	12.00	7.3	41.00	4.0
8 ²	M	9.0	16.00	13.9	34.00	4.8
9 ²	M	4.5	12.00	9.5	33.00	4.9
10 ²	M	10.3	11.00	15.3	24.00	4.9
11 ²	F	4.9	8.00	10.0	38.00	5.0
12 ²	M	6.3	12.00	11.4	29.00	5.1

¹ Recruited from (removed for anonymity)

² Recruited from (removed for anonymity)

³From Vineland Adaptive Behavior Scales

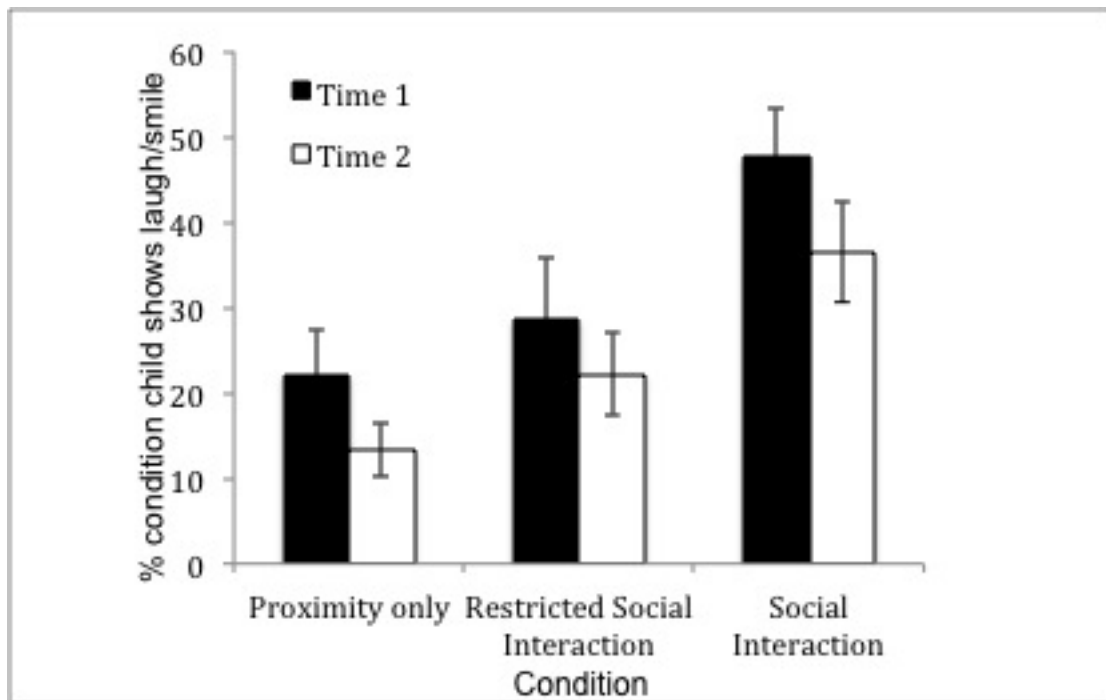


Figure 1. Mean percentage of time showing smiling and laughing behaviours (\pm standard error)