

Attenuated behaviour in Cornelia de Lange and fragile X syndromes

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Abstract

Background Catatonia-like presentations in people with autism have been increasingly recognised within research and diagnostic guidelines. The recently developed Attenuated Behaviour Questionnaire has identified that attenuated behaviour [autistic catatonia] is very prevalent in people with autism spectrum disorders (ASDs) and associated with repetitive behaviour. In the current study, we investigated attenuated behaviour within two genetic syndromes associated with ASD and examined ASD and repetitive behaviour as longitudinal predictors of attenuated behaviour.

Method The Attenuated Behaviour Questionnaire was completed by parents/carers of 33 individuals with Cornelia de Lange syndrome (CdLS) and 69 with fragile X syndrome (FXS). Information collected from the same informants 4 years previously was utilised to examine ASD and repetitive behaviour as predictors of later attenuated behaviour, controlling for age, gender and ability.

Results Catatonia-like attenuated behaviour was reported for individuals with CdLS (30.3%) and FXS (11.6%). Slowed movement was more prevalent in people with CdLS. No other phenotypic differences

were observed. Across the two groups, repetitive behaviour predicted the presence of attenuated behaviour 4 years later, after controlling for age, gender and ability.

Conclusions Attenuated behaviour can be identified in individuals with CdLS and FXS and may have an effect on both adaptive behaviour and quality of life. Repetitive behaviours predicted subsequent risk within both groups and should be assessed by services as part of a pro-active strategy of support.

Keywords attenuated behaviour, autism, catatonia, cornelia de lange syndrome, fragile X, movement disorder

Background

Although it is increasingly acknowledged that genetic aetiologies can be identified for at least 30–50% of individuals with intellectual disability (ID) (Arvio and Sillanpää 2003; Wellesley *et al.* 1991), potentially important information is lost by ignoring commonalities within and across specific genetic syndromes, particularly at the level of the behavioural phenotype associated with any given syndrome.

Research into syndrome-related phenotypes has revealed important information about common behaviours and health problems within different genetic syndromes, with implications for practice. For

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example, research has highlighted an increased risk for thyroid dysfunction in Down syndrome (Pueschel and Pezzullo 1985; Šare *et al.* 1978), gastrointestinal problems in Cornelia de Lange syndrome (CdLS; e.g. Bull *et al.* 1993; Cates *et al.* 1989), sleep problems in various genetic syndromes (e.g. De Leersnyder *et al.* 2001; Didden *et al.* 2004) and profiles of behaviour that challenges within particular genetic syndromes (e.g. Arron *et al.* 2011). Simultaneously, the identification of specific genetic syndromes underlying ID has become more effective with recent advances within clinical genetics (Allison *et al.* 2006), making such findings increasingly relevant as more and more people receive services with a diagnosed genetic syndrome.

Within a number of genetic syndromes, the nature of Autism Spectrum Disorder (ASD) has been studied extensively (Moss *et al.* 2009, 2013; Moss and Howlin 2009; Richards *et al.* 2015). Researchers have now begun to map the developmental trajectory of specific behavioural characteristics of ASD within genetic syndromes, reporting changes in repetitive behaviour and social behaviour over time (e.g. Adams *et al.* 2011; Cochran *et al.* 2015; Moss *et al.* 2015). Whilst the specific profile of ASD characteristics varies across genetic syndromes (e.g. Moss *et al.* 2009, 2013), there is increasing evidence that particular ASD characteristics may constitute cross-syndrome risk markers. Restricted and repetitive behaviours (RRB) are associated with increased risk of self-injurious behaviour across various syndromes as well as within idiopathic ASD and ID (Davies and Oliver 2016; Eden *et al.* 2014; Oliver *et al.* 2012; Richards *et al.* 2016), despite the differing profiles of SIB across these groups (Arron *et al.* 2011).

Whilst previous studies into behavioural phenotypes have provided important information about the behavioural features of ASD across different genetic syndromes, researchers have not yet attempted to define the syndrome specific profile of other characteristics that appear related to ASD. For example, there is increasing evidence for an overlap between presenting issues in ASD and neurological conditions. Research has identified an increased prevalence of Parkinsonian features in adults over 39 years of age with ASD (Starkstein *et al.* 2015), with common brain regions possibly affected in the two disorders (Hollander *et al.* 2009). In addition to repetitive behaviours (Hollander *et al.* 2009),

catatonic-like states have been reported in both disorders (Patterson 1986; Wing and Shah 2000), with the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association 2013) introducing an additional code to represent ASD with co-morbid catatonia. Whilst there are difficulties in diagnosing catatonia *per se* (Penland *et al.* 2006), it is clear that a significant number of individuals with ASD experience difficulties characterised by increased slowness, difficulties in initiating and completing movements, increased passivity and an increased reliance on prompting from others (Wing and Shah 2000).

In order to characterise these particular motor and behavioural manifestations in individuals with ASD, Breen and Hare (2017) developed the *Attenuated Behaviour Questionnaire* (ABQ), a third-party measure of catatonia-like features or 'attenuated behaviour' primarily derived from Wing and Shah's (2000) clinical studies. The authors reported that in a sample of young adults diagnosed with ASD, 48.3% were reported to meet a proposed clinical cut-off for autistic catatonia and that those who showed attenuated behaviour [autistic catatonia] also had significantly higher scores on a measure of RRB.

The current study expanded on Breen and Hare's (2017) initial work by examining the presence of attenuated behaviour [autistic catatonia] and disordered movement in two genetic syndromes in which ASD has been commonly reported and described, CdLS and Fragile X syndrome (FXS; e.g. Moss *et al.* 2009, 2013, under review; Richards *et al.* 2015). The study also built on the previous findings of a relationship between RRB and attenuated behaviour in ASD, examining this relationship across both syndrome groups and investigating the longitudinal predictive value of ASD characteristics in highlighting later risk for attenuated behaviour.

Aims and hypotheses

The primary aims of the current study were to (1) examine the prevalence and profile of attenuated behaviour [autistic catatonia] and disordered movement in CdLS and FXS, using the ABQ (Breen and Hare 2017), and (2) examine the putative relationship between attenuated behaviour and age, gender and ability level. In line with Breen and Hare's (2017) findings in ASD and previous research on

ASD characteristics as cross-syndrome risk markers, it was hypothesised that across the combined sample (CdLS and FXS) that RRB as measured by the Repetitive Behaviour Scale (RBS) at Time point 1 (T1) will be associated with the presence of attenuated behaviour as measured by the ABQ at Time point 2 (T2) and that the presence of probable ASD as indicated by Social Communication Questionnaire (SCQ) score at T1 will be associated with the presence of attenuated behaviour as measured by the ABQ at T2. Given the lack of extant research, no *a priori* hypotheses were proposed in relation to possible inter-syndromic differences in the presentation of attenuated behaviour in CdLS and FXS.

Methods

Participants

Parents or carers of children and adults with either CdLS or FXS were recruited via an existing research database of people diagnosed with specific genetic syndromes and their parents or carers (e.g. Moss *et al.* 2009, 2013, 2017). Only male participants with FXS were listed on the database, due to the absence of ID in at least half of female participants with FXS (Rousseau *et al.* 1994). Eligibility criteria for the study were (1) parent/carer of an individual with either CdLS or FXS, (2) provided T1 data on the *SCQ* and *Repetitive Behaviour Questionnaire* as part of a previous study (e.g. Moss *et al.* 2013, under

review), (3) child's genetic diagnosis confirmed by an appropriate healthcare professional (General practitioner, clinical geneticist or consultant paediatrician) and (4) residence in the UK or Republic of Ireland.

Recruitment

An initial letter was sent out to parents/carers regarding the T2 follow-up study. Follow-up calls to discuss the research were made up to 28 days after letters were sent. All data at T1 and T2 were collected via postal questionnaires. In total, 209 eligible participants were identified from the database, 140 (67.0%) of whom could be contacted, with 132 (94.3%) of these initially agreeing to take part. A total of 33 participants with CdLS and 69 participants with FXS were recruited, equating to a 77.3% completion rate. Demographic characteristics of the sample are presented in Table 1. In total, 19 respondents (18.6%) were parents/carers of children with CdLS or FXS aged under 16 years and 83 (81.4%) were parents/carers of adults with CdLS or FXS. The age range of individuals with CdLS was 8–53 years and the range was 8–51 years in the FXS group. Whilst there was no significant difference between the CdLS and FXS groups in terms of the average age ($t(100) = 1.54, P = .13$), there was a significant difference in the gender distribution across the two groups ($\chi^2 = 62.09, P < .001$). There was no significant difference between the two groups in the

Table 1 Demographics and characteristics of individuals recruited at T2

		Cornelia de Lange	Fragile X
	<i>n</i>	33	69
Gender	% male (<i>n</i>)	30.3 (10)	100 (69)
Age (years)	Mean (SD)	27.73 (11.20)	24.39 (9.78)
	Range	8–53	8–51
Wessex score ¹	Mean (SD) range	10.56 (2.75) 5–15	13.36 (1.74) 5–15
Possible ASD ²	% meeting cut-off (<i>n</i>)	75.0 (24)	86.6 (58)
Mean ABQ-CAB score (SD)		5.15 (5.89)	2.69 (4.43)
Mean ABQ-CF score (SD)		3.48 (3.49)	1.97 (3.41)
Mean ABQ-CS score (SD)		3.10 (3.49)	1.80 (3.25)

¹One CdLS participant has missing Wessex data.

²One CdLS participant and two FXS participants had missing data for ASD cut-off.

T2, Time point 2; ASD, autism spectrum disorder; ABQ, Attenuated Behaviour Questionnaire; CAB, Core Attenuated Behaviour; CF, Core Frequency; CS, Core Severity; CdLS, Cornelia de Lange syndrome; FXS, fragile X syndrome.

proportion of individuals meeting the ASD cut off ($\chi^2 = 2.04$, $P = .17$).

Ethical approval

Ethical approval was granted for this study by Coventry and Warwickshire Research Ethics Committee and by the University of Manchester.

Measures

Data collected at T1 were obtained from parents'/carers' responses on the following questionnaires as part of an ongoing programme of research using the same families and which has been previously reported in Moss *et al.* 2009 and Moss *et al.* 2013. The measures used include the following: *The RBS* (Moss and Oliver 2008) is a 19-item-questionnaire that measures the frequency and severity of RRB in adults and children with and without ID and comprises five subdomains of *stereotyped behaviour* (3 items), *compulsive behaviour* (8 items), *insistence on sameness* (2 items), *restricted preferences* (3 items) and *repetitive speech* (3 items). Items are scored on a 0 ('Never') to 4 ('More than once a day') scale of frequency, with higher scores indicating a greater frequency of RRB. The RBS has good internal consistency and reasonable concurrent validity with the Repetitive subscale of the Autism Screening Questionnaire (Berument *et al.* 1999; which was an earlier version of the SCQ) (Moss *et al.* 2009).

The Wessex Scale (Kushlick *et al.* 1973) is a 15-item-questionnaire that assesses several dimensions of ability in children and adults with IDs and comprises five subscales relating to *continence* (4 items), *self-help skills* (3 items), *mobility* (2 items), *speech* (1 item) and *literacy* (3 items) with two additional items to assess vision and hearing impairments. Items are scored on a scale from 1 to 3, with higher scores indicating a greater level of ability. The Wessex Scale has good inter-rater reliability when used with both children and adults (Palmer and Jenkins 1982). For purposes of comparison, a score of between 5 and 9 on the Wessex can be taken as indicating moderate to severe ID.

The SCQ (Rutter *et al.* 2003) is a 40-item informant-report screening questionnaire designed to identify individuals with ASD. It examines the severity of impairment across three domains of *communication* (13 items), *reciprocal social interaction*

(15 items) and *restricted, repetitive and stereotyped patterns* (8 items). Items are given a rating of 1 (Yes) or 0 (No), with 24 items being reverse scored. There are an additional six items that are only completed for individuals who can communicate verbally. Higher scores indicate a greater number of ASD features and a cut-off score of 15 on the 'lifetime' version is used to recommend screening for ASD (Berument *et al.* 1999). The SCQ showed concurrent validity with the Autism Diagnostic Interview (Le Couteur *et al.* 1989) when used in a sample of 200 participants with diagnoses including ASD, ID and various genetic syndromes (Berument *et al.* 1999). In the current study, participants were categorised into those with and without possible ASD based on the cut-off score of 15. Given the design of the longitudinal research programme, the actual date of completion of the SCQ varied depending on initial enrolment into the ongoing research programme.

Four years later, T2 data were collected from the same participants who were asked to complete *The ABQ* (Breen and Hare 2017), a 34-item, third-party report measure designed to measure the prevalence and frequency of the attenuated behaviours associated with 'autistic catatonia'. The 34 items of the ABQ assess motor symptoms (15 items), affective alterations (5 items) and behavioural alterations (14 items) in a similar way to the *Northoff Catatonia Scale* (Northoff *et al.* 1995) (for further information on items selection, please see Breen and Hare 2017). Each item includes operationalised behavioural descriptions (e.g. Item 2 'Difficulty initiating actions /"stuckness"/ akinesia' by 'Stopping mid-air half way through reaching for something & looking like they are trying to move but cannot or beginning to pick up a cup to drink but lifting it only half way and then putting it down again') to address concerns about inconsistent or vague definitions in other catatonia rating scales (Carroll *et al.* 2008). All ABQ items are rated on a five point (0–4) scale to capture information about the progressive nature of autistic catatonic symptoms (0 = No, never observed; 1 = No, not at the moment but it used to happen; 2 = Yes, but less than before; 3 = Yes, the same as before; 4 = Yes, more than before). The six most commonly reported items, all of which relate to motor movement dysfunction, are regarded as the 'core symptoms' of autistic catatonia and correspond to previous published diagnostic criteria (Hare and Malone 2004;

Wing and Shah 2000). Positive responses to these core items (i.e. being rated 2, 3 or 4) triggers supplementary questions relating to current *frequency* (i.e. the usual amount of time the symptom is present during waking hours) that ranged from all of the time to rarely. Current *severity* (i.e. the effect of the symptom on the individual's ability to perform tasks or activities) ranged from very to slightly severe.

Based on these items, a set of sub-scales can be computed for the ABQ, namely the *ABQ-CAB Core Attenuated Behaviour* (measure of the presence of each of the six core attenuated behaviours with individual item scores summed to yield a Core Attenuated Behaviour score with a range of 0–24), the *ABQ-CS Core Severity* (measure of the severity of the currently present core attenuated behaviours with individual severity scores summed to yield a Core Severity score with a range of 0–24) and the *ABQ-CF Core Frequency* (measure of the frequency of the currently present core attenuated behaviours with individual severity scores summed to yield a Core Frequency score with a range of Range 0–24).

As the focus of the current study was on the identification of attenuated behaviour in CdLS and FXS and identification of the relationship, if any, between this and other forms of motor dysfunction, only the six core items and the seven motor items were initially included, with attenuated behaviour being identified on the basis of the presence of a minimum of three of the six core items (Breen and Hare 2017). The ABQ has good sensitivity (0.65) and specificity (0.38) with regard to existing diagnoses of autistic catatonia and according to its developers '... appears to have potential as a valid and practical clinical measure with a degree of discriminant validity' (Breen 2014; Breen and Hare 2017). Moreover, as a measure of attenuated behaviour, it is not limited to use only in cases of autism, whether idiopathic or syndrome. As attenuated behaviour associated with autism appears to be onset from early adolescence onwards, the ABQ was originally developed using a sample of young adults aged 12–25 years, and at this stage of its development, there are no obvious reasons why it should be equally applicable to older (over 25 years old) populations. Parents/carers also completed a number of additional items at T2 relating to demographics and other relevant information including health problems and medications.

Procedure

At T2, participants were invited to complete an online survey including background questions and the ABQ. Postal questionnaires were sent when parents/carers were not able to complete the study online. Follow-up telephone calls were made 3 to 4 weeks after online/postal questionnaires were sent.

Data analysis

There were missing data for four participants in total and these participants were excluded from relevant analyses. When normality assumptions were not met for continuous variables, a non-parametric Mann–Whitney U Test was conducted to compare T1 scores of those with and without later attenuated behaviour at T2. In relation to dichotomous variables, where observed cell values were below five, a Fisher's Exact Test was used. For all other univariate analyses, Pearson's Chi-Squared and Independent Samples *T*-Tests were conducted to examine differences in T1 variables according to the presence of attenuated behaviour at T2. Based on the ratios in the current study (for those with or without attenuated behaviour), a total sample of 92 was required (with 15 participants in the smallest group) in order to detect a large effect (0.8) with 80% power and an alpha criterion of .05.

A logistic regression analysis was conducted, with T2 attenuated behaviour as the outcome variable. To control for confounding variables, age, gender and ability level were entered at Step 1, with the predictors of interest (syndrome group, ASD cut-off status and RBS score) entered at Step 2. A syndrome group × ASD cut-off interaction term was also added at Step 2, to examine any group differences in the relationship between meeting the ASD cut-off and having attenuated behaviour at T2. Based on the commonly accepted rule of 10 participants per predictor variable (e.g. Peduzzi *et al.* 1996), a sample size of 70 or more was required.

Results

Kolmogorov–Smirnov tests were conducted for each continuous variable. Neither age ($D(102) = .07$, $P = .20$) nor RBS total scores ($D(102) = .06$, $P = .20$) differed significantly from a normal distribution but ability level, as determined by Wessex self-help score,

did not meet the assumption of normality ($D(102) = .18, P < .001$).

Sample description

With regard to the number of individuals in each group scoring above the suggested cut-off point for 'autistic catatonia' on the ABQ-CAB sub-scale, 9/33 (27.3%) of the CdLS group and 6/69 (8.7%) of the FXS group scored over 8 on the ABQ-CAB (Breen and Hare 2017).

Examination of the prevalence and profile of attenuated behaviour and disordered movement in Cornelia de Lange syndrome and fragile X syndrome

Using the movement domain of the ABQ, the prevalence of various movement problems in the

CdLS and FXS groups (Table 2) was calculated, in line with the first aim of the study. There were no significant differences between the CdLS and FXS groups in terms of the reported prevalence of any movement problems ($P > .05$ for all comparisons).

The prevalence of attenuated behaviour symptoms, as assessed by the ABQ core domain, in both CdLS and FXS was delineated and compared (Table 3). There was a significant difference in slowness of movement ($\chi^2 = 7.32; P = .017$), which was significantly more prevalent in the CdLS group. Based on Breen and Hare's (2017) definition, ten (30.3%) individuals with CdLS and eight (11.6%) individuals with FXS met the cut-off on the ABQ for autistic catatonia. The difference in prevalence between groups was significant ($\chi^2 = 5.38$;

Table 2 Number of individuals with CdLS and FXS reported as showing specific movement problems at T2

		Cornelia de Lange	Fragile X
	<i>n</i>	33	69
Any movement problem	% (<i>n</i>)	84.4 (27)	79.1 (53)
Repetitive body movements (stereotypy)	% (<i>n</i>)	66.7 (22)	58.8 (40) [†]
Stiff posturing	% (<i>n</i>)	18.2 (6)	16.2 (11) [†]
Increased motor tics	% (<i>n</i>)	31.3 (10) [†]	44.1 (30) [†]
Waving or shaking extremities	% (<i>n</i>)	48.5 (16)	64.7 (44) [†]
Twisting/flicking of hands	% (<i>n</i>)	30.3 (10)	26.5 (18) [†]
Moving in jerky way	% (<i>n</i>)	21.2 (7)	32.4 (22) [†]
Unusual gait	% (<i>n</i>)	60.6 (20)	45.6(31) [†]

[†]One missing response for each of these items.

CdLS, Cornelia de Lange syndrome; FXS, fragile X syndrome; T2, Time point 2.

Table 3 Percentage of individuals with CdLS and FXS reported to show core symptoms of attenuated behaviour at T2

		CdLS	FXs
Total <i>n</i>		33	69
Freezing/very still like a statues	% (<i>n</i>)	15.2 (5)	5.8 (4)
Difficulty initiating actions/'stuckness'/akinesia	% (<i>n</i>)	24.2 (8)	14.5 (10)
Problems stopping actions once started	% (<i>n</i>)	39.4 (13)	21.7 (10)
Difficulty initiating movement	% (<i>n</i>)	15.2 (5)	4.3 (3)
Slowness in movement	% (<i>n</i>)	24.2 (8)*	5.8 (4)
Requires prompts to complete action	% (<i>n</i>)	42.4 (14)	34.8 (24)

* $P < .05$.

CdLS, Cornelia de Lange syndrome; FXS, fragile X syndrome; T2, Time point 2.

$P = .028$), reflecting a higher prevalence in the CdLS group.

Attenuated behaviour and age, gender and ability

The relationship between attenuated behaviour and age, gender and ability was investigated (Table 4), with no significant difference in age ($t(100) = 1.26$; $P = .21$) or ability level ($U = 561.00$; $P = .08$) at T1 for those with and without attenuated behaviour at T2 across the whole sample. In the CdLS group, there was a significant difference in gender for those with and without attenuated behaviour ($\chi^2 = 9.43$; $P = .004$), with a higher proportion of female participants showing attenuated behaviour.

Attenuated behaviour, autism spectrum disorder and restricted and repetitive behaviours

To test the hypotheses, a binary logistic regression was then conducted with presence/absence of attenuated behaviour at T2 as the dependent variable. Age, gender and ability score were entered at Step 1 with syndrome group, RBS score, ASD cut-off status and syndrome group*ASD cut-off status entered at Step 2. At Step 2, the overall model was significant ($\chi^2 (7) = 19.01$; $P = .008$) with a significant predictive effect for RBS score (OR = 1.07; 95% CI = 1.02–1.12; $P = .003$). Neither ASD cut-off status (OR = 1.20; 95% CI = .098–14.66; $P = .89$) nor syndrome group*ASD cut-off status (OR = .33; 95% CI = .01–12.05; $P = .54$) contributed significantly to the model. Syndrome group was no longer a significant predictor of T2 attenuated behaviour

after controlling for age, gender and ability level (OR = 1.16; 95% CI = .09–15.64; $P = .91$).

Discussion

The present study was designed with several specific aims and hypotheses, the first of which was to delineate the prevalence of attenuated behaviour in CdLS and FXS, with a second aim of investigating the predictive relationship between probable ASD and RRB, and subsequent attenuated behaviour. In line with the first aim of the study, varying prevalence rates were reported for the different signs of attenuated behaviour and disordered movement. Although the prevalence of attenuated behaviour appeared significantly higher in the CdLS group, this was not the case after controlling for confounding variables. The first hypothesis, that RRB at T1 scores would be associated with attenuated behaviour at T2, was supported by the current data even after controlling for age, gender and ability level. The second hypothesis, that the presence of probable ASD at T1 would be associated with attenuated behaviour at T2, was not supported over the corresponding null hypothesis.

Overall, the data from the current study indicated that compared with individuals with idiopathic ASD, of whom 48.3% displayed attenuated behaviour (Breen and Hare 2017), the prevalence of attenuated behaviour in individuals with CdLS and FXS was lower at 30.3% and 11.6%, respectively. Within the current sample, 75.0% and 86.6% of CdLS and FXS participants, respectively, met the screening cut-off for ASD. Therefore, the relative

Table 4 T1 characteristics according to presence of attenuated behaviour at T2

		Attenuated behaviour	
		Present	Absent
Total <i>n</i>		18	84
T1 Wessex ability level	Median (IQR)	6.5 (5–7)	7 (6–9)
T1 Age	Mean (SD)	23.83 (9.03)	20.48 (10.53)
Repetitive behaviour score	Mean (SD)	33.82* (16.48)	25.32 (14.03)

* $P < .05$.

T1, Time point 1; T2, Time point 2.

prevalence of attenuated behaviour was still lower than expected when compared with Breen and Hare's sample of 99 individuals with ASD, particularly for those with FXS. There was some evidence for a different profile of specific symptoms across the syndrome groups, in line with reports of differing profiles of ASD features in FXS and CdLS (e.g. Moss *et al.* 2009, 2013). Moreover, given the known features of the behavioural phenotypes of both FXS and CdLS, including hyper-arousal and hyper-activity (Arron *et al.* 2011), in the present study, the *least* commonly reported aspects of attenuated behaviour were periods of stiffness (FXS), slowness of movement (FXS) and difficulties initiating movement (FXS & CdLS). Also, whilst attenuated behaviour was seen only in a minority of participants, disordered movement was reported for 84.4% of CdLS and 79.1% of FXS individuals, respectively.

Strengths and limitations of the study

The current study was the first to explore the prevalence of attenuated behaviour in genetic syndromes associated with ASD and ID, as well as being the first to examine aspects of disordered movement in a large cohort of individuals with either CdLS or FXS. The results provided an important contribution to our understanding of the specific presentation of attenuated behaviour and related movement problems in CdLS and FXS. Although the recruitment strategy is likely to have maximised the potential number of participants completing T2 questionnaire data, the study was limited by the inability to control for T1 attenuated behaviour as a predictor of subsequent attenuated behaviour. The selection of other T1 measures was similarly limited by the reliance of historical data and the use of extant data for T1 may have introduced an element of multicollinearity into the logistic regression undertaken at T2. Future research should assess a wider range of predictor variables, as well as controlling for the presence of attenuated behaviour at T1. A further limitation is that the full psychometric properties of the ABQ, in particular inter-rater and test-retest reliability, have yet to be established. Similarly, this is the first study to use the ABQ with participants aged over 25 years, albeit that there do not appear any empirical grounds for limiting it to use

with people aged 12 to 25 years as per the original study by Breen and Hare (2017).

Clinical implications and directions for future research

The results of the current study suggest that episodes of catatonia-like attenuated behaviour are likely to be evident and potentially important for a minority of individuals with CdLS and FXS. Without additional support, episodes of attenuated behaviour and disordered movement have the potential to restrict people's independence and quality of life. Furthermore, these difficulties are likely to add to the level of care and assistance that individuals require from their family/carers on a day-to-day basis. Services must ensure that families receive appropriate support to enable them to provide the right level of care. However, whilst there are some descriptions of effective behavioural approaches (e.g. Hare and Malone 2004), there is currently a lack of evidence for safe and effective interventions for autistic catatonia *per se* (DeJong *et al.* 2014) and the development of practice-based evidence for supporting and intervention for attenuated behaviour is clearly a priority.

Within Community Learning Disability Teams, as well as statutory services more widely, reasonable adjustments should be made to facilitate physical access and engagement for individuals with CdLS and FXS experiencing attenuated behaviour and disordered movement. Routine screening for attenuated behaviour [autistic catatonia] should be considered in those with CdLS and FXS, particularly for those who exhibit high levels of RRB. Such initiatives would allow for a more pro-active approach in providing information and support to individuals, families and staff carers.

The current study provides a valuable initial insight into the prevalence of attenuated behaviour within CdLS and FXS, but further research using larger samples and participants with other genetic syndromes is required to confirm the status of RRB as a cross-syndrome risk marker. Meeting the ASD cut-off on the SCQ was not significantly associated with showing attenuated behaviour, but the SCQ is not a diagnostic assessment *per se*. Future studies should ideally utilise a diagnostic instrument such as the Autism Diagnostic Observation Schedule-Second

Edition (Lord *et al.* 2012). Across ASD, CdLS and FXS, there is a need to elucidate the specific neurological and/or psychological mechanisms underlying attenuated behaviour. Such research will have implications for approaches to intervention and management.

Conclusions

The current study investigated the issue of ASD-related attenuated behaviour in people with CdLS and FXS, and the predictive value of other ASD characteristics in differentiating between those with and without later attenuated behaviour in each of these groups. The results indicated that attenuated behaviour was present in a minority of individuals with CdLS and FXS, with associated movement problems being seen in the majority of individuals. Across both groups, RRB emerged as a significant predictor of attenuated behaviour 4 years later, highlighting the importance of RRB as a possible cross-syndrome risk marker for attenuated behaviour.

The results of the current study present a further challenge for clinicians to identify syndrome-specific needs that may have a direct impact on community access and to prioritise preventative action and support for families. Further research is required to identify other characteristics that could be used to inform a preventative screening approach to attenuated behaviour. Research into the mechanisms underlying these difficulties is also required in order to provide effective interventions.

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