Characterising repetitive behaviours in young boys with fragile X syndrome

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Abstract

Background Repetitive behaviours are frequently observed in individuals with intellectual disability (ID). The present study examined the profile, inter-correlations and predictive correlates of repetitive behaviours in boys with fragile X syndrome (FXS), the leading inherited cause of ID. Specific child characteristics examined as predictors included anxiety, nonverbal cognition and autism social–affective symptomatology.

Method Participants were 39 boys with FXS (aged 6–10 years). Repetitive behaviours were measured using the Repetitive Behavior Scale – Revised (RBS-R) – a 43-item caregiver-report measure normed on individuals with ID.

Results Restricted Interests and Sensory Motor behaviours were reported as most problematic for this sample of boys, whereas Self-injurious behaviours were less problematic. All subscales of the RBS-R were significantly inter-correlated. Nonverbal IQ was negatively related, whereas anxiety and social affective symptoms of autism spectrum disorder were positively related, to scores for Restricted Interests. Anxiety was also positively related to scores for Compulsive behaviours and Ritualistic Sameness behaviours.

Conclusions This study provides a preliminary description of repetitive behaviours in boys with FXS, which may form the groundwork for future research.

Keywords autism, behavioural phenotype, fragile X syndrome, repetitive behaviours

Introduction

Repetitive behaviours refer to a broad heterogeneous category of behaviours characterised by the repetition of unvarying movements (Edwards *et al.* 2012), rigidity and inappropriateness (Lewis & Kim 2009). Typically developing infants and young children commonly engage in repetitive behaviours and activities. In infancy, these behaviours take the form of banging, shaking, rocking and mouthing (Thelen 1981; Lifter 2000). Typically developing toddlers frequently display action patterns characterised by ordering objects, attachment to favourite objects and preferred routines for engaging in everyday activities. These types of ritualised behaviours, characterised by insistence on sameness and things being 'just right', commonly begin at about 14 months of age in typically developing children and decline by the age of 4 years (Evans *et al.* 1997; MacDonald *et al.* 2007). During this developmental period, these behaviours are presumed to be functional by scaffolding the precision and efficiency of motor movements (Thelen 1981), facilitating the development of mastery motivation and self-regulation (e.g. Kopp 1982;

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Jennings 2002) or serving as a mechanism to alleviate anxiety (Evans *et al.* 1997).

If repetitive behaviours persist later on in development, there can come a time when the presence of these behaviours begins to impede day-to-day functioning by creating a barrier to learning and social interaction (Leekam *et al.*, 2011). In fact, repetitive behaviours are frequently observed in a wide range of developmental [e.g. ID and developmental disabilities and autism spectrum disorder (ASD)] and psychiatric (e.g. schizophrenia and obsessive–compulsive disorder) conditions (e.g. Parkinson disease). Motor stereotypies occur more frequently in younger and more developmentally delayed individuals with autism, whereas preoccupations, restricted interests and obsessions are more often observed in individuals on the spectrum with higher language and cognitive abilities (Bishop *et al.* 2006; Richler *et al.* 2010).

Numerous behaviours are included in the broad umbrella of repetitive behaviour, including stereotypies, ritualistic behaviours, obsessive and compulsive behaviours, restricted interests, perseverations and self-injurious behaviours. Furthermore, the likelihood of specific behaviours varies across disorders (Moss *et al.* 2009). Numerous categorisation approaches have also been utilised in the investigation of repetitive behaviours. Some researchers have argued for the use of broad categorical classifications (e.g. motorically based behaviours and/or sensory behaviours and higher cognitively based behaviours), whereas others have argued that these broad categories may be too simplistic and mask more subtle, but important, differences in the topographies and functions of repetitive behaviours within and across disorders. For example, there are likely a variety of mechanisms (e.g. cognitive, communicative and anxiety) underlying the presence of repetitive behaviours, which impacts the management of these behaviours (Leekam *et al.*, 2011). That is, repetitive behaviours that serve as a method of alleviating anxiety in one child likely warrants a different management approach than repetitive behaviours that serve as a method of obtaining a preferred object.

The current study was designed to describe patterns of repetitive behaviours in children with fragile X syndrome (FXS), the leading inherited cause of ID (Crawford *et al.* 2001). Clinical reports suggest that repetitive behaviours are ubiquitous in boys with the full mutation of this disorder, although these behaviours have not been thoroughly described or characterised. Given that the full mutation of FXS in boys is also associated with high rates of ID, anxiety and ASD symptoms (Hagerman 2006; Harris *et al.* 2008; Hessl *et al.* 2009; Cordiero *et al.* 2011), the factors that drive the emergence of repetitive behaviours in FXS remain poorly understood. Clearly, there are many ways in which repetitive behaviours can be categorised in individuals with ID and development disabilities. Thus, it is important to acknowledge that any particular approach will affect the profile of the repetitive behaviours obtained.

Fragile X syndrome

It is estimated that 1 in 4000 boys and 1 in 6000 to 8000 girls are affected with FXS [Centers for Disease Control and Prevention (CDC) 2011]. FXS is caused by a mutation of the fragile X mental retardation 1 gene (*FMR1*; Verkerk *et al.* 1991) on the X chromosome, and this mutation interferes with the production of the fragile X mental retardation protein (Bell *et al.* 1991). The normal *FMR1* allele is comprised of 5–54 CGG repeats. Individuals with the 'full mutation' have expansions exceeding 200 repeats and typically display the FXS behavioural phenotype (Oostra & Willemsen 2003). Because it is an X-linked condition, FXS is more common in boys than girls, and boys are more severely affected given the protective presence of an unaffected X chromosome in girls (Crawford *et al.* 2001). Due to this difference in phenotypic expression, the current study focused only on boys with FXS.

Although there is variability in the expression of behavioural symptoms in boys with FXS, a specific behavioural phenotype is characteristically observed. Approximately 85% of boys with full mutation FXS have IQs less than 70 (Hagerman 2006; Hessl *et al.* 2009). The majority of boys with FXS also meet the criteria for an anxiety disorder, including social phobias, generalised anxiety and obsessive–compulsive disorder (Hessl *et al.* 2008; Cordiero *et al.* 2011; Hall *et al.* 2012). In addition, boys with FXS are likely to have delays, relative to age expectations, in multiple domains of language, including vocabulary, morphosyntax and the functional use of

conversational language for social communication (Abbeduto *et al.* 2007).

The limited evidence available suggests that the FXS phenotype is associated with increased risk for repetitive behaviours. Verbal perseveration is frequently described in boys with FXS and considered by some researchers to be a hallmark feature of the behavioural phenotype of this disorder (Sudhalter *et al.* 1990; Abbeduto *et al.* 2007; Roberts *et al.* 2008). Compared with other syndromes, researchers have found elevated levels of other types of repetitive behaviours in boys with FXS, including hand flapping, rocking and self-injury (Hagerman 2002).

Although repetitive behaviours have been reported in FXS at a global level, there is limited research characterising the relative rates of different types of repetitive behaviours in FXS or exploring the mechanisms that underlie their development. Such research is important given that different subcategories of repetitive behaviour may have different neurobiological underpinnings and different behavioural correlates, with these differences affecting the potential efficacy of different behavioural or pharmacological treatments. Recently, Wolff and colleagues (Wolff *et al.* 2012) used the Repetitive Behavior Scale – Revised (RBS-R; Bodfish *et al.* 2000) to examine the profile of repetitive behaviours present in a group of 27 preschool-aged boys with FXS. Results indicated that ratings were highest for stereotyped and sameness behaviours and the lowest for compulsive, ritualistic and self-injurious behaviours.

Utilising the Repetitive Behavior Questionnaire (RBQ), which shares some individual items with the RBS-R, Moss & colleagues (2009) examined the presence of repetitive behaviours across six groups of individuals with IDs including boys with FXS who ranged in age from 6 to 47 years. Participants with FXS were reported to have significantly more repetitive behaviours than at least two other disability groups in the categories of compulsive behaviour, insistence on sameness and repetitive speech. In terms of individual behaviour items, Moss & colleagues (2009) reported that boys with FXS scored significantly higher than at least two other ID groups in hand stereotypies, tidying up, lining up, preference for routine, just right behaviours and three types of verbal perseveration including

restricted conversation, repetitive phrases and echolalia.

Because Wolff *et al.* examined repetitive behaviours in a very young group of children and Moss *et al.* included boys with FXS who ranged in age from young childhood to adulthood, it is not yet clear whether the profile of repetitive behaviour in boys with FXS remains stable across development or if it differs based upon an individual's degree of delay. Furthermore, there remains much that we do not understand about the FXS behavioural phenotype, including the extent to which the different types of repetitive behaviours associated with FXS emerge from the same or different underlying mechanisms. The present study was designed to begin addressing these gaps by investigating the profile and potential predictors of repetitive behaviours in a group of school-aged boys with FXS.

Factors relating to repetitive behaviours

Recent studies have shown that 25–60% of individuals with FXS meet the criteria for ASD (e.g. Harris *et al.* 2008). Qualitatively, it is often the presence of repetitive behaviours that suggests overlap in the behavioural and neurobiological phenotypes of the two disorders (Kau *et al.* 2004; Baranek *et al.* 2005; Symons *et al.* 2010). However, there is growing evidence that the same behavioural symptoms in FXS and ASD may reflect different underlying mechanisms (Gallagher & Hallahan 2012; Wolff *et al.* 2012; McDuffie *et al.* 2015). This distinction is important given that behavioural and pharmacological treatments may fail to be effective across a range of disorders if underlying causes differ between disorders.

Indeed, Moss *et al.* (2009) found that, whereas individuals with FXS displayed the highest frequency and largest number of different topographies of repetitive behaviour relative to individuals with eight other low-incidence neurodevelopmental disorders, only one individual item from the Compulsive subscale of the RBQ (Moss & Oliver 2008) was correlated with ASD symptomatology scores as measured by the Autism Screening Questionnaire (Berument *et al.* 1999). This finding suggests that many repetitive behaviours commonly seen in FXS may not be associated with other symptoms of ASD. Consistent with this conclusion, other studies have

found many children with FXS present with compulsive or self-injurious behaviours but show no other symptoms associated with a diagnosis of ASD (Hall *et al.* 2008; Symons *et al.* 2003). Furthermore, Wolff *et al.* (2012) found that both boys with FXS and boys with FXS + ASD had fewer compulsive and ritualistic behaviours than did young boys with nonsyndromic ASD. Taken together, these studies suggest that repetitive behaviours in FXS and nonsyndromic ASD may differ in extent and type and that ASD symptomatology may not be the primary risk factor for the development of repetitive behaviours in FXS.

Thus, it is important to consider factors beyond ASD when investigating the mechanisms underlying repetitive behaviours in FXS. For example, cognitive delays (Kover *et al.* 2013; Sansone *et al.*, 2014) and anxiety (Cordiero *et al.* 2011; Talisa *et al.* 2014) may be important risk factors for the development of at least some types of repetitive behaviours (Miguel *et al.* 1997; Gabriels *et al.* 2005). In the case of FXS, therefore, it is possible that high rates of repetitive behaviours covary with lower levels of cognitive functioning as well as with higher levels of anxiety and are orthogonal to the social–affective impairments at the core of an ASD diagnosis. Taken together, these findings suggest that individuals with FXS present with multiple risk factors for the development of repetitive behaviours and that there is a need to determine the correlates of these behavioural symptoms as a first step towards identifying underlying neurobiological mechanisms.

Research questions

Given the cumulative impact of repetitive behaviours on participation in learning activities, acceptance by peers and family functioning (Boyd *et al.* 2012), and the implications for treatment, the goal of the current study was to develop a more nuanced description of repetitive behaviours in school-aged boys with the full mutation of FXS. To do this, we used the RBS-R to examine the profile, item-level scores, subscale inter-correlations and longitudinal correlates of repetitive behaviours. In particular, we were interested in examining whether nonverbal IQ, anxiety and social–affective symptoms of ASD were predictively associated with the later presence of repetitive

behaviours in this sample of children. The study addressed the following questions:

1. What is the profile of repetitive behaviours for boys with FXS?
2. What specific repetitive behaviours are most frequent for boys with FXS?
3. What are the inter-correlations among the categories of repetitive behaviours?
4. Which participant characteristics predict the various categories of repetitive behaviours later in development?

Method

Participants and setting

Participants were 39 boys with FXS who ranged in age from 6 to 10 years ($M = 7.41$ years) at the initial time point and who participated in a larger, longitudinal project on early word learning. Although other papers have been published from this larger project (McDuffie *et al.* 2012; McDuffie *et al.* 2013; Oakes *et al.* 2013; Kover *et al.* 2014; McDuffie *et al.* 2015; Thurman *et al.* 2014), none has focused on the questions of interest in the present study. Participants were recruited nationally using a variety of sources, including postings to internet listservs and websites, newspaper advertisements, flyers at parent meetings and a university research registry. Prior to participation, documentation confirming a diagnosis of the *FMR1* full mutation through molecular genetic testing was provided for each participant. In addition, diagnosis was confirmed during the study through molecular genetic testing of peripheral blood samples (although testing was not performed for three participants: two due to logistical reasons and one due to participant refusal of the blood draw). All participants met the following criteria: English as the native language, speech as the primary means of communication, no uncorrected sensory or physical impairments that would affect participation in the study, and no more than a mild hearing loss, all determined from caregiver report. Written consent was given by all caregivers prior to participation. Within the larger project, testing was implemented at two time points approximately 18 months apart. The Time 1 (T1) visit took place over three consecutive days and the Time 2 (T2) visit was completed in one

day. All sessions were conducted at a university clinic. All assessments were administered by trained examiners.

For inclusion in the present study, participants had relevant data available for both T1 and T2. At T1, participants were administered measures of nonverbal cognitive ability [i.e. Leiter International Performance Scale – Revised (Leiter-R; Roid & Miller 1997)], maladaptive behaviours [i.e. Anxiety, Depression, and Mood Scale (ADAMS; Esbensen *et al.* 2003)], and autism diagnostic assessments [i.e. Autism Diagnostic Observation Schedule (ADOS; Lord *et al.* 1999)]. Two participants in the current study were unable to complete the Leiter-R; for these two participants, floor scores on the Leiter-R at their chronological age level were used. Participant characteristics are presented in Table 1. The RBS-R (Bodfish *et al.* 2000) was administered at T2.

Measures

The RBS-R (Bodfish *et al.* 2000) is a 43-item caregiver-report measure normed on individuals with ID. Each item is scored on a 4-point Likert scale ranging from 0 (behaviour does not occur) to 3 (behaviour occurs and is a severe problem). Although there are many approaches to the measurement of repetitive behaviours in individuals with ID and

development disabilities (i.e. RBQ; Moss *et al.*, 2009), we utilised the RBS-R (Bodfish *et al.* 2000). The RBS-R has been widely used to characterise the presence of repetitive behaviours, particularly in individuals with autism symptomatology. Multiple studies have empirically evaluated the validity of the factor structure of the RBS-R (Lam & Aman 2007; Mirenda *et al.* 2010; Bishop *et al.* 2013; Harrop *et al.* 2014). Recently, Bishop & colleagues (2013) employed the largest sample to date in their examination of the RBS-R factor structure. Thus, we adopted the Bishop *et al.* (2013) 5-factor structure and item distribution in the current study. The five subscales included in the current study were as follows: Sensory Motor, Restricted Interests, Self-injury, Compulsive, and Ritualistic/Sameness. The RBS-R was administered as the T2 outcome measure.

The ADOS (Lord *et al.* 1999) is a semi-structured, direct assessment of communication, social interaction, play/imagination and repetitive behaviours used to evaluate ASD symptoms. The ADOS was administered during the T1 visit by an examiner trained to research reliability standards. Calibrated severity scores for the Social Affective domain of the ADOS (Hus *et al.* 2012) were used as a longitudinal predictor of repetitive behaviours at T2.

The Leiter-R (Roid & Miller 1997) Brief IQ screener (i.e. Figure Ground, Form Completion, Sequential Order and Repeated Patterns subscales) was collected at the T1 visit. These subtests measure visualisation and fluid reasoning kills and yield a nonverbal IQ score, age-equivalent score and growth score. The Leiter-R is administered in an entirely nonverbal manner and does not require any spoken or written output from the participant. The examiner uses pantomime and nonverbal cues to explain the task and participants respond by pointing or placing shapes or cards in a grid.

The ADAMS (Esbensen *et al.* 2003) is a 28-item caregiver-report measure. Five subscales are generated from the individual items: Manic/Hyperactive, Depressed Mood, Social Avoidance, General Anxiety, and Obsessive/Compulsive. The General Anxiety subscale of the ADAMS was used as the metric of anxiety for the current study. This scale was completed by caregivers during the T1 visit.

Table 1 Participant characteristics at time 1 (*n* = 39)

	Mean	SD
Chronological age[a]	7.41	2.03
Nonverbal IQ[b]	59.26	14.90
Anxiety[c]	5.52	3.26
Autism symptom severity[d]	5.90	2.11
	Frequency	
Caucasian	32	
Mothers with college degrees[e]	33	

[a]at T1;
[b]brief IQ scores from the Leiter-R;
[c]general Anxiety subscale from the ADAMS;
[d]from the ADOS (Gotham, Pickles, & Lord, 2009);
[e]missing for one participant.
Leiter-R, Leiter International Performance Scale – Revised; ADAMS, Anxiety, Depression, and Mood Scale; ADOS, Autism Diagnostic Observation Schedule.

Analysis plan

Mean subscale scores were used to address research questions 1, 3 and 4. Because the data violated the nonparametric assumption of normality, nonparametric analyses were used in the present project. A Friedman's analysis of variance was used to determine if repetitive behaviours differed as a function of the RBS-R subscale. This analysis was followed up with Wilcoxon rank sum tests to determine whether any between subscale differences were significant. We then descriptively examined caregiver ratings on the individual items within each subscale by graphing the percentage of caregivers who endorsed the presence of individual behaviours as being moderate to severe in nature. Finally, one-tailed Spearman rank correlations were used to evaluate the relations between the different subcategories of repetitive behaviours and to examine the predictive association between child characteristics at T1 and repetitive behaviours at T2. We predicted a negative association between T1 nonverbal IQ and T2 repetitive behaviours and positive correlations between anxiety and social affective symptoms of ASD at T1 and repetitive behaviours at T2.

Results

### Profile of repetitive behaviour as measured by the Repetitive Behavior Scale – Revised

Caregiver ratings significantly differed as a function of RBS-R subscale, $\chi^2 (4) = 55.67$, $P < 0.001$ (Fig. 1). Wilcoxon tests revealed that Restricted Interests were rated as significantly more of a problem than Self-injury, Compulsive or Ritualistic/Sameness behaviours ($Ps < 0.05$). In addition, Sensory Motor behaviours were rated as significantly more of a problem than were Self-injurious or Compulsive behaviours. No other significant differences were observed across subscales.

Item-level examination of repetitive behaviours

We followed up these subscale-level findings with an item-level examination of individual repetitive behaviours (Fig. 2; Table 2). Seven items were included within the Sensory Motor subscale. Of these items, hand/finger stereotypies and sensory difficulties were reported to be most problematic with approximately 49% and 36% of caregivers rating these behaviours as moderate to severe problems, respectively. In contrast, whole body and head stereotypies were reported to be the least problematic behaviours for boys with FXS, with approximately 8% and 0% of caregivers rating these behaviours as moderate to severe problems, respectively. Two items are included in the Restricted Interests subscale: fascination/preoccupation with one subject or activity and strongly attached to one specific object. These items were relatively comparable with approximately 44% and 39%, of caregivers rating these behaviours as moderate to severe problems, respectively. In terms of Self-injury, 15% of caregivers reported hitting self with a body part to be a moderate to severe problem in their sons with FXS. All other behaviours in the Self-injury subscale were seldom endorsed as a moderate or severe problem (<8%).

Of the 10 items within the Compulsive subscale, two behaviours emerged as problematic: 26% of caregivers reported completeness (e.g. must have
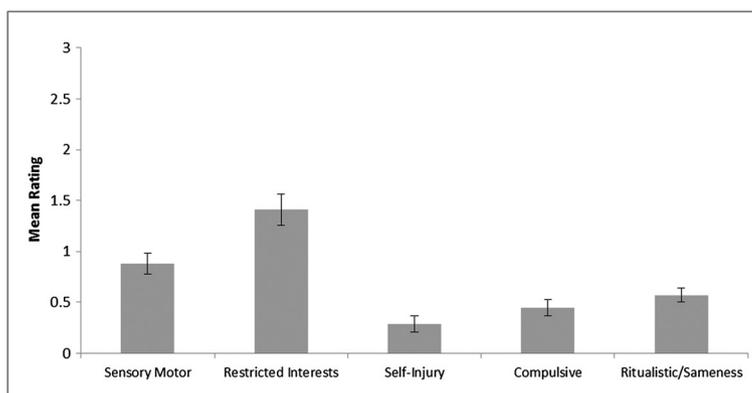
Figure 1 Mean rating scores for the five Repetitive Behavior Scale – Revised subscales.
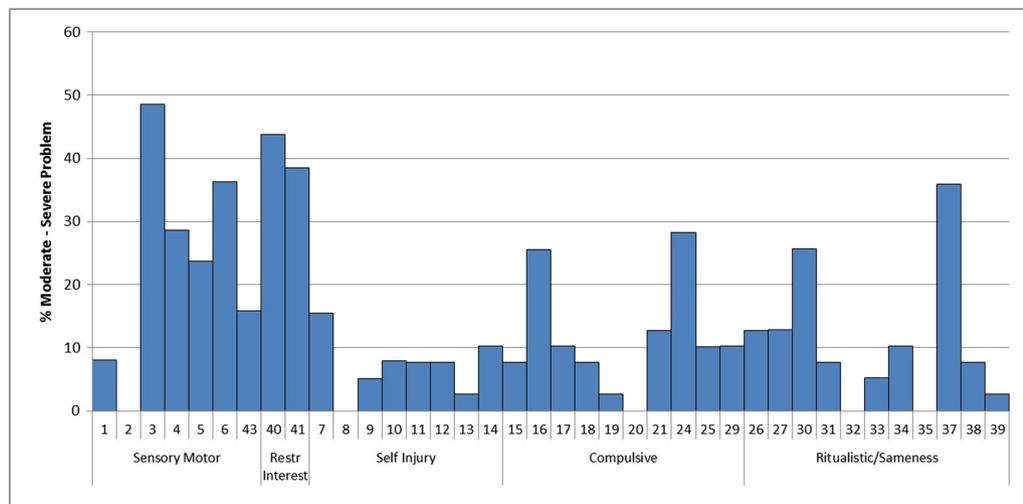
Figure 2 Percentage of caregivers reporting behaviours to be a moderate to severe problem.

doors opened or closed and takes all items out of a container or area) to be a moderate to severe problem and 28% of caregivers reported sleeping/bedtime rituals to be a moderate to severe problem. Finally, of the 11 items within the Ritualistic/Sameness subscale, 26% of caregivers reported visiting new places as a moderate to severe problem, and 36% of caregivers reported resisting changing activities/difficulties with transitions as a moderate to severe problem.

Inter-correlations across the Repetitive Behavior Scale – Revised subscales

Spearman correlation coefficients were used to examine associations between the five RBS-R subscales. These analyses indicated that all of the RBS-R subscales were significantly inter-correlated (Table 3).

Relations between T1 participant characteristics and repetitive behaviours at T2

Spearman correlations were also used to examine the extent to which nonverbal IQ, anxiety and ASD social–affective symptomatology at T1 were predictively correlated with the RBS-R subscales at T2 (Table 4). The ADAMS General Anxiety subscale was significantly and positively related to the RBS-R Restricted Interests ($P = 0.02$), Compulsive ($P = 0.02$) and Ritualistic/Sameness ($P = 0.003$) subscales. The Leiter-R Brief IQ was significantly and negatively

related to the RBS-R Restricted Interests subscale ($P = 0.03$). Finally, ASD social–affective symptomatology was significantly and positively associated with the RBS-R Restricted Interests subscale ($P = 0.03$).

Discussion

In this study, we sought to develop a more nuanced understanding of repetitive behaviours in school-age boys with FXS. To achieve this goal, we described the subscale-level and item-level profiles of repetitive behaviours reported by mothers and examined the inter-correlations among different categories of repetitive behaviours. Additionally, we evaluated several child characteristics as potential longitudinal predictors of different categories of repetitive behaviours. Insight into the presence and correlates of repetitive behaviours in FXS can help to further elucidate the behavioural phenotype of this neurodevelopmental disorder with the ultimate goal of identifying appropriate pharmacological and behavioural targets for intervention. Such insights are also conceptually useful in deriving theoretical models of repetitive behaviours in FXS that can then be compared with profiles and predictors for other neurodevelopmental disorders.

Using the RBS-R, a widely used informant report measure of repetitive behaviours, we found that some classes of repetitive behaviours were more

Table 2 Repetitive Behavior Scale – Revised (RBS-R) items and subscales according to Bishop *et al.*'s (2013) 5-factor structure

Subscale	Item
Sensory Motor	1. Whole body
	2. Head
	3. Hand/finger
	4. Locomotion
	5. Object usage
	6. Sensory
	43. Fascination, preoccupation with movement
Restricted Interest	40. Fascination, preoccupation with one subject or activity
	41. Strongly attached to one specific object
Self-injury	7. Hits self with body part
	8. Hits self against surface or object
	9. Hits self with object
	10. Bites self
	11. Pulls
	12. Rubs or scratches self
	13. Inserts finger or object
	14. Skin picking
Compulsive	15. Arranging/ordering
	16. Completeness
	17. Washing/cleaning
	18. Checking
	19. Counting
	20. Hoarding/saving
	21. Repeating
	24. Sleeping/bedtime
	25. Self-care (bathroom and dressing)
	29. Insists that things remain in the same place(s)
Ritualistic/ Sameness	26. Travel/transportation
	27. Play/leisure
	30. Objects to visiting new places
	31. Becomes upset it interrupted in what he/she is doing
	32. Insists on walking in a particular pattern
	33. Insists on sitting at the same place
	34. Dislikes changes in appearance or behaviour of the people around him/her
	35. Insists on using a particular door
	37. Resists changing activities; difficulty with transitions
	38. Insists on same routine, household, school or work schedule everyday
	39. Insists that specific things take place at specific times

Table 3 Concurrent associations across RBS-R subscale scores

	Restricted Interests	Self-injury	Compulsive	Ritualistic/ Sameness
Sensory Motor	r = 0.56*	r = 0.55**	r = 0.38*	r = 0.65**
Restricted Interests		r = 0.32*	r = 0.39**	r = 0.59**
Self-injury			r = 0.35*	r = 0.36*
Compulsive				r = 0.65**

**$P < 0.01$,
*$P < 0.05$, one-tailed
RBS-R, Repetitive Behavior Scale – Revised.

Table 4 Longitudinal associations between child characteristics at time 1 and RBS-R subscale scores 18 months later

	Nonverbal IQ[a]	Anxiety[b]	ADOS social–affective domain[c]
Sensory Motor	r = -0.05	r = 0.20	r = 0.05
Restricted Interests	r = -0.33*	r = 0.33*	r = 0.31*
Self-injury	r = 0.09	r = -0.01	r = 0.03
Compulsive	r = 0.13	r = 0.36*	r = 0.16
Ritualistic/ Sameness	r = 0.007	r = 0.44**	r = 0.05

**$P < 0.01$,
*$P < 0.05$, one-tailed;
[a]brief IQ scores from the Leiter-R;
[b]General Anxiety subscale from the ADAMS;
[c]calibrated severity score from the ADOS
RBS-R, Repetitive Behavior Scale – Revised; Leiter-R, Leiter International Performance Scale – Revised; ADAMS, Anxiety, Depression, and Mood Scale; ADOS, Autism Diagnostic Observation Schedule.

problematic than others for boys with FXS. Ritualistic/Sameness and Sensory Motor behaviours were frequently endorsed as problematic, whereas

Self-injury was the least commonly reported type of behaviour. This finding is consistent with the results reported for 3 to 5 year olds with FXS by Wolff & colleagues (2012) and suggests that the profile of repetitive behaviours remains stable in FXS from preschool through at least the middle school years.

When considering repetitive behaviours at the individual item level, the four behaviours most commonly reported by caregivers to be a moderate to

severe problem were found in the Sensory Motor and Restricted Interest categories. In the Sensory Motor category, almost half of caregivers reported hand/finger mannerisms (e.g. hand flapping) to be a moderate to severe problem and more than a third of caregivers reported sensory behaviours to be a moderate to severe problem. The two items (i.e. preoccupation with one subject or activity and strong attachment to one specific object) comprising the Restricted Interests category were reported as moderate to severe problems by more than a third of caregivers. The next most commonly reported behaviours were found in the categories of Compulsive and Ritualistic/Sameness behaviours. More than a third of caregivers reported difficulty with transitions as a moderate to severe problem and between a quarter and a third of caregivers reported sleeping/bedtime rituals, completeness (e.g. must have doors opened or closed) and objecting to visiting new places as moderate to severe problems. Once again, at the individual level, Self-injurious behaviours were reported to be least problematic subcategory endorsed in our sample.

It is interesting that self-injurious behaviours were least commonly endorsed as being problematic using the RBS-R. In the Bailey *et al.* (2008) survey completed by parents of 976 full mutation boys with FXS over the age of 6 years, 41% of parents reported self-injurious behaviour to be problematic for their children. It seems possible that self-injurious behaviours may emerge with age and become more problematic in adolescence and young adulthood, but the discrepancy between reports of self-injury using the RBS-R and the Bailey *et al.* (2008) parent survey should be noted. There are, however, several potential differences between the ways in which problem behaviours were classified/categorised between our study and the report of the parent survey by Bailey *et al.* (2008). First, the Bailey study queried self-injurious behaviours as a global category and did not report the percentage of parents who reported individual types of self-injurious behaviours as problematic. If we had added up the individual categories of self-injury reported in the current study, our findings are more comparable with theirs. Additionally, the current study reported only the percentage of children for whom self-injury was a moderate to severe problem. Nevertheless, the mean subscale score for the entire category of different self-

injurious behaviours in the current study was under 1, suggesting these were not seen as problems by parents for the most part.

In terms of the relations between the different types of repetitive behaviours, significant positive associations were observed between all subcategories of repetitive behaviours. The finding that repetitive behaviours seem to covary in FXS could suggest a common underlying mechanism that predisposes the emergence of several different topographies and types of repetitive behaviours. Alternatively, this finding could suggest that a great deal of overlap exists across the category structure of the RBS-R. Thus, it may be that an alternate factor structure would be more helpful in considering the ways in which repetitive behaviours are organised in FXS.

Regardless of the significant associations between all of the examined categories of repetitive behaviour, some authors may argue that self-injurious behaviours represent a distinct category of behaviours that is not accurately classified as a topography of repetitive behaviour. This perspective rests on the argument that self-injurious behaviours, unlike other categories of repetitive behaviours, are often maintained by environmental contingencies (Langthorne *et al.* 2011). However, other authors have suggested that, over time, behaviours that begin as stereotyped or repetitive may evolve into self-injurious behaviours as social reinforcement from the environment replaces the self-stimulating function of the original repetitive behaviour. According to this viewpoint, nonharmful levels of stereotypy may be maintained and shaped by environmental contingencies, potentially changing in function and topography into more problematic levels of self-injury (Kennedy 2002).

In order to gain insight into the participant characteristics that predict the various types of repetitive behaviours, longitudinal associations between nonverbal IQ, anxiety and social–affective symptoms of ASD and parent report of repetitive behaviours were examined. We found that multiple participant characteristics at T1 predicted scores on the Restricted Interest subscale measured 18 months later. As predicted, a negative association was observed between nonverbal IQ and Restricted Interests subscale of the RBS-R. Additionally, a positive association was observed between levels of anxiety and the severity of social affective symptoms of ASD with this same subscale of the RBS-R.

Finally, anxiety was also positively associated with scores on the Compulsive and Ritualistic/Sameness subscales at T2.

These predictive associations suggest that multiple types of repetitive behaviours may be driven by the presence of anxiety in boys with FXS. In particular, our data suggest that, for these young boys with FXS, high levels of anxiety are associated with increased difficulty with compulsive behaviours, restricted interests and ritualistic behaviours. It may be that these behaviours are serving as coping mechanisms to deal with heightened levels of anxiety; that is, when an individual is experiencing high levels of anxiety, engaging in repetitive behaviours (e.g. talking about a favourite topic of conversation and preoccupation with moving a favourite object in a repetitive or ritualistic fashion) may alleviate the physiological arousal associated with anxiety. As a result of engaging in these types of repetitive behaviours, the child may spend less time actively exploring or attending to the environment, thereby negatively impacting opportunities to learn from ongoing experiences. Our findings suggest that treating symptoms of anxiety may lead to the reduction of repetitive behaviours in FXS.

Limitations in nonverbal cognition and impairments in social communication were also observed to be predictively associated with a higher degree of restricted interests in young boys with FXS. Research indicates that more severe limitations in cognitive ability are a risk factor for high levels of repetitive behaviours (McClintock *et al.* 2003). Additionally, it would be reasonable to speculate that children who are preoccupied with strong and all-encompassing nonsocial interests would be less open to responding to the social bids of interactive partners and in learning from these social encounters. In addition, severity of ASD symptomatology is negatively associated with nonverbal IQ in FXS (Lewis *et al.* 2006). Thus, the relationship between social impairment as measured by the ADOS and restricted interests as measured by the RBS-R may be mediated by the shared variance of these child characteristics with nonverbal IQ. It should be mentioned that the negative association found between nonverbal IQ and restricted interests has not been reported for boys with nonsyndromic ASD who, on average, have higher levels of nonverbal cognitive ability than do same-aged boys with FXS (Bishop

et al. 2006; Szatmari *et al.* 2006). This finding suggests that, although restricted interests are a core symptom present in children with ASD regardless of their cognitive level, restricted interests in children with FXS may be, in part, the result of higher levels of cognitive impairment.

Limitations

As with all correlational studies, it is not possible to determine the direction of causality or to rule out the possibility that unmeasured variables explain the resultant patterns of associations. The relatively small sample precluded us from conducting a multiple regression analysis that could simultaneously evaluate the unique contribution of each potential predictor. Additionally, we did not administer the RBS-R at the initial T1 visit, which would have allowed us to examine changes in the level of repetitive behaviours over time and, additionally, to control for the level of repetitive behaviours at T1. In addition, as the present study did not include a comparison group of individuals with other neurodevelopmental disorders (e.g. ASD or Down syndrome), we are unable to determine the extent to which the observed pattern of findings is specific to FXS. Finally, as mentioned earlier, all participants in the current study were required to use speech as their primary means of communication. This inclusionary criterion for the current study, which required that participants use three word phrases on a daily basis, may have resulted in a sample that was not representative of the population of boys with FXS and may account for the lower levels and reduced severity of self-injurious behaviours in our sample.

Future directions

Taken as a whole, these results contribute to the literature examining profiles and predictors of repetitive behaviours in FXS, the leading inherited cause of ID. Future research should focus on identifying additional child and environmental characteristics that may have a causal relationship with repetitive behaviours. Candidate variables include executive functioning, attention, arousal, sensory processing and levels of fragile X mental retardation protein, the protein which is implicated in neurological functioning in FXS.

Research should also be directed towards examining whether these same or different variables influence the emergence of repetitive behaviours in children with nonsyndromic ASD and how profiles of affectedness differ between these two disorders. A direct between-group comparison utilising a sample of boys with nonsyndromic ASD (i.e. children who meet the criteria for an ASD diagnosis but for whom a diagnosis of the FXS full mutation has been ruled out) could provide insights into possible differences in the profile of repetitive behaviours. Additionally, such a comparison would inform our understanding of the strengths of association between child characteristics and the presence of repetitive behaviours, providing insights into similarities and differences in causal mechanisms. This line of research is especially pertinent given ongoing efforts to develop targeted pharmacological and behavioural treatments for individuals with neurodevelopmental disorders as it may not be the case that treatments designed to address repetitive behaviours in children with nonsyndromic ASD will be equally effective for children with FXS (Hall *et al.* 2010).

As mentioned previously, there are many approaches to the measurement of repetitive behaviours in individuals with ID and development disabilities. Researchers have used different measures that have been specifically developed to assess repetitive behaviour (RBS-R; Bodfish *et al.* 2000; RBQ; Moss *et al.* 2009) or have used subscales or items from tests developed for other purposes, such as autism diagnosis (i.e. ADI-R; Rutter *et al.* 2003). Although the present study provides preliminary insights into the presence of repetitive behaviours in FXS, comparing results of different assessments administered to the same sample of individuals with FXS would be a productive direction for future research. Additionally, other researchers have utilised one set of items/behavioural characteristics but have classified these items in different ways depending on factor analyses conducted for specific populations, particularly ASD (e.g. Bishop *et al.* 2013). It may be that the phenotypic characteristics associated with particular syndromes warrant different organisations of individual topographies of repetitive behaviours as a function of disorder. To date, no FXS-specific factor analyses have been conducted on any measure of repetitive behaviours.

Finally, measures of repetitive behaviours vary in terms of their focus on frequency of behaviours and severity of behaviours or may collapse both dimensions into a single rating scale. More work is needed to examine both frequency and severity of repetitive behaviours independently and the extent to which either of these factors interferes with day-to-day functioning.

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