Executive function, repetitive behaviour and restricted interests in neurodevelopmental disorders

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Abstract

Background: Individuals with genetic syndromes show unique profiles of repetitive behaviours and restricted interests (RRBs). The executive dysfunction account of RRBs suggests that in autistic (AUT) individuals executive function impairments underpin RRBs, but not communication and social interaction autistic characteristics. Aims: To 1) describe profiles of behavioural manifestations of executive function (EF behaviours) and 2) explore the relationship between EF behaviours and autistic traits across individuals with Cornelia de Lange (CdLS), fragile X (FXS) and Rubinstein-Taybi syndromes (RTS), and AUT individuals. Method: Carers completed the Behavior Rating Inventory of Executive Function – Preschool Version and the Social Communication Questionnaire. Data reporting on 25 individuals with CdLS (Mage=18.60, SD=8.94), 25 with FXS (Mage=18.48, SD=8.80), 25 with RTS (Mage=18.60, SD=8.65) and 25 AUT individuals (Mage=18.52, SD=8.65) matched on chronological age and adaptive ability were included in analyses. Results: All groups showed impairments across EF behaviours compared to two-to-three-year-old typically developing normative samples with no differences between groups. Different EF behaviours predicted RRBs in the syndrome groups with no associations found in the AUT group. Conclusions: Syndrome related differences should be considered when developing targeted interventions that focus on EF behaviours and/or RRBs in these groups.

Keywords: Executive function, repetitive behaviours and restricted interests, autism, genetic syndromes

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What this paper adds?

This is one of few studies that compares profiles of EF processes across individuals with different genetic syndromes and autistic individuals. To our knowledge, this is also the first study to explore the relationship between EF processes and repetitive and restricted interests (RRBs) in individuals with CdLS, FXS and RTS. Investigating behavioural manifestations of executive function provide an ecologically valid assessment that meaningfully describes clinically relevant EF difficulties in response to daily life. These findings support the fractionation hypothesis of autistic traits, and that executive dysfunction may underpin RRBs in these syndrome groups, highlighting a potential factor for intervention in these groups. The variability in relationships between different EF processes and RRB across syndromes demonstrates the importance of investigating the different patterns of relationships between cognitive and behavioural phenotypes at a refined level and these differences should be considered in intervention planning.

1. Introduction

The term 'executive function' (EF) refers to top-down cognitive processes that control and regulate behaviour. Core EF processes include working memory (short-term memory capacity), inhibition (the control of automatic responses) and shifting (the ability to switch between mental processes). These core abilities contribute to higher order EF functions such as planning/organisation i.e., the ability to evaluate and select the sequence of actions to achieve a goal (Miyake, Friedman, Emerson, Witzki & Howerter, 2000). EF processes contribute to other cognitive processes such as emotion regulation (Marceau, Kelly & Solowij, 2018; Calkins & Marcovitch, 2010; Xiu, Wu, Chang & Zhou, 2018) and verbal fluency (Shao, Janse, Visser & Meyer, 2014; Henry, Messer & Nash, 2015) and are associated with a range of outcomes, including better physical and mental health, success in school and work, and better quality of life (Diamond, 2013).

Impairments in EF processes may account for repetitive behaviour and restricted interests (RRBs), a core diagnostic characteristic of autism; (Turner, 1998). While RRBs may enable autistic individuals to self-regulate in stressful environments, and manage overarousal and extreme emotions (Kapp et al., 2019, Rodgers, Glod, Connolly & McConachie, 2012; Turner, 1998), they may also contribute to the onset and maintenance of anxiety (Rodgers, Riby, Janes, Connolly & McConachie, 2012; Turner 1998) and may impede children from exploring their environment and reduce opportunities for learning (Pierce & Courchesne, 2001; Bodfish, Symons, Parker & Lewis, 2000). Understanding the mechanisms that underpin RRBs may help develop focused interventions.

The theory of executive dysfunction in autism suggests that EF impairments lead to autistic people becoming 'locked in' to one set of cognitions or behaviours due to an inability to inhibit these responses and shift to novel responses (Turner, 1999; Demetriou et al., 2018). Autistic individuals with and without an intellectual disability show impairments across a

range of executive function domains throughout development (Turner, 1998; Demetriou et al., 2018; Reed, Watts & Truzoli, 2011) and poorer cognitive flexibility, working memory and response inhibition are associated with and predict greater levels of RRBs (Lopez., Lincoln., Ozonoff, S., & Lai, 2005; Demetriou, DeMayo & Guastella, 2019; Reed et al., 2011). According to the fractionation hypothesis of autism, EF impairments are considered to underpin RRBs and not social communication traits that are also characteristics of autism (Happé & Ronald, 2008). This assertion might be examined by study of EF and autistic traits in genetic syndromes with differing profiles of autism characteristics.

Genetic syndromes associated with intellectual disability such as fragile X (FXS), Cornelia de Lange (CdLS) and Rubinstein-Taybi syndromes (RTS) (Oliver, Arron, Sloneem & Hall, 2008; Boyle & Kaufmann, 2010; Hennekam, 2006) show differences in autistic traits. While all groups show a high prevalence of RRBs (Moss, Oliver, Arron, Burbidge & Berg, 2009; Hall, Lightbody & Reiss, 2008; Grados, Alvi & Srivastava, 2017; Oliver et al., 2008; Waite et al., 2015; Boer, Langton & Clarke, 2010), individuals with CdLS and FXS also evidence social and communication autistic traits (Oliver, Berg, Moss, Arron & Burbidge, 2011). Fine-grained comparison reveals different strengths and weaknesses in social interaction skills and behaviours that differ from those seen in non-syndromic autism. Whereas individuals with FXS evidence a milder presentation of social and communication autistic traits, individuals with CdLS show a unique profile characterised by communication impairments and selective mutism (Moss et al., 2013; Moss, Oliver, Nelson, Richards & Hall, 2013b; Abbeduto, McDuffie & Thurman, 2014). These groups also differ in the profiles of RRBs. Individuals with FXS show a heightened prevalence across a range of RRBs such as hand stereotypies, lining up objects, restricted conversation, preference for routine and echolalia, while RRBs in individuals with CdLS are characterised by tidying and lining up behaviours, despite these groups having similarly high scores on the Autism Screening

Questionnaire (Moss et al., 2009). In RTS, frequent repetitive questions, body stereotypies and adherence to routines are common, whereas restricted conversation, repetitive phrase and echolalia are less pronounced (Waite et al., 2015). These differences highlight the need for detailed comparisons in cognitive and behavioural phenotypes between groups that show superficially similar behaviours and afford the opportunity to examine the correlates of different RRBs.

These groups also evidence impaired EF processes that, arguably, underpin their RRBs. Individuals with FXS show broad impairments in working memory, shifting, inhibition and planning relative to mental age. Whilst few studies have investigated performance between EF domains within individuals with FXS, comparison between studies indicates that working memory may be a weakness in boys with FXS but later become a strength in adulthood (Schmitt et al., 2019 for a review). Individuals with CdLS and RTS may also show unique profiles of EF impairments. Individuals with RTS show delayed development of both verbal and visuo-spatial working memory span deficits relative to mental age, but although verbal working memory is positively associated with mental age, visuo-spatial working memory is not, indicating a dissociation between abilities (Waite, 2012). Individuals with CdLS show greater impairments in shifting, inhibition and working memory compared to individuals with Down syndrome comparable on developmental age. In addition, working memory impairments may increase with age in this group (Reid, Moss, Nelson, Groves & Oliver, 2017).

Cross-syndrome comparisons can determine whether individual syndrome groups evidence distinct profiles of EF impairments (Hodapp & Dykens, 2001). Johnson (2015) compared profiles of performance on direct EF assessments of verbal and visuo-spatial working memory, inhibition and shifting between individuals with CdLS, FXS and RTS. Whereas individuals with FXS and RTS showed difficulties across these EF domains relative

to their receptive language, those with CdLS only showed deficits in verbal memory and shifting. These groups also showed different associations between performance on EF tasks and chronological age, which may indicate differing developmental trajectories between different EF domains across syndromes. Characterising syndrome associated EF profiles provides the foundation for the development of better targeted interventions and support planning for a group (Johnson, 2015). However, few studies have compared profiles of EF processes across genetic syndromes matched on ability to determine whether these groups show greater or lesser impairments compared to other syndromes and autistic individuals (Schmitt et al., 2019).

In this study, we extended the work by Johnson (2015) by using the Behaviour Rating Inventory of Executive Function – Preschool Edition (BRIEF-P) (Gioia, Espy and Isquith, 2005) to measure informant reported behavioural manifestations of EF processes (EF behaviours) across individuals with CdLS, FXS and RTS. We used the preschool edition (appropriate for two years to five years, 11 months) to evaluate behaviours that were appropriate and achievable for individuals with an intellectual disability. A strength of informant EF measures is that they assess the ability for an individual to independently choose and use EF processes when pursuing a goal in typical situations. These ratings provide a more ecologically valid assessment that, arguably, more meaningfully describes clinically relevant EF difficulties in response to daily life, compared to EF performance-based assessments that assess the speed and accuracy of specific EF skills in response to superficial and decontextualized stimuli (Isquith, Crawford, Espy & Gioia, 2005; Toplak et al., 2013; Zelazo & Carlson, 2012).

We also investigated the relationship between EF behaviours and autistic traits, with a particular focus on RRBs in these groups. Both children with FXS and Prader-Willi syndromes show attention switching difficulties, which are associated with aversion to

changes in routine and then followed by repetitive questioning in both groups (Woodcock, Oliver & Humphreys, 2009a; 2009b). In contrast, repetitive questioning observed in people with RTS was associated with verbal memory impairments (Waite et al., 2015). Identifying syndrome associated EF-behaviour relationships helps determine when interventions need to be tailored for a particular syndrome and what RRBs would be expected to change as a result of improvement of a specific EF skill.

Executive dysfunction is considered to underpin RRBs but not social and communication difficulties in autistic people (Turner, 1998; Happé & Ronald, 2008). We aimed to describe the profile of EF behaviours and their associations with RRBs in individuals with CdLS, FXS and RTS, syndrome groups that are characterised by unique profiles of autistic traits (Moss et al., 2013; Moss et al., 2013b; Abbeduto et al., 2014) and impaired performance on direct EF assessments (Schmitt, 2019; Reid et al., 2017; Waite, 2012). As these groups are characterised by differing profiles of autistic traits (Oliver et al., 2011; Moss et al., 2013), we included a comparison group of autistic (AUT) individuals. We aimed to 1) compare profiles of EF behaviours in individuals with CdLS, FXS, RTS and AUT matched on chronological age and adaptive ability between one another and to typically developing (TD) cohorts detailed in the BRIEF-P manual, to establish whether the CdLS, FXS, RTS and AUT participant groups have atypical EF related behaviours and 2) to evaluate the relationship between EF behaviours and autistic traits between the four groups whilst controlling for adaptive abilities. We hypothesise that AUT individuals and individuals with CdLS, FXS and RTS will show more EF behavioural difficulties compared to TD children (Demetriou et al., 2018; Waite et al., 2015; Reid et al., 2017). Due to their unique profiles of repetitive behaviours (Moss et al., 2013; Demitrou et al., 2018), we also hypothesise that individuals with CdLS, FXS and RTS and AUT individuals will show different profiles of EF behaviours. Given previous evidence of syndrome associated EF-

behaviour relationships (Woodcock et al., 2009ab; Waite et al., 2015), we hypothesise that syndrome groups will show different patterns of associations between EF behaviours and RRBs and associated EF behaviours will predict RRBs. Given the fractionation hypothesis of AUT (Happé & Ronald, 2008) we predict that EF behaviours will not be associated with communication and reciprocal interaction skills in any of the groups.

2. Method

2.1 Recruitment

Parents/carers of 941 AUT individuals, and individuals with Cornelia de Lange (CdLS), Rubinstein-Taybi (RTS) and Fragile X (FXS) syndromes were contacted through a database held at the [anonymised for review] compiled through recruitment via relevant syndrome support groups. Due to gender differences in behavioural phenotypes in individuals with FXS, including profiles of executive function (Schmitt et al., 2019) and developmental trajectories of repetitive behaviours (Reisinger, Shaffer, Tartaglia, Berry-Kravis & Erickson, 2020), only males with FXS were recruited.

2.2 Participants

Carers of 351 individuals returned completed questionnaires (37.3% return rate). Participants were excluded if: 1) on the Wessex Scale (Kushlick, Blunden & Cox, 1973) they were scored as not verbal and/or not mobile or if they had a self-help score of five or below (to ensure that any deficit in EF behaviours were due to a lack of that specific skill and not because their overall ability was too low to be able to engage in these behaviours), 2) they did not have a confirmed diagnosis from an appropriate professional, 3) had completed less than 75% of the questionnaire survey or 4) did not meet the cut-off score for autism spectrum disorder on the Social Communication Questionnaire (Rutter et al., 2003; AUT group only). We matched the FXS and RTS groups against the CdLS group. 74 out of 106 participants with CdLS were excluded based on the exclusion criteria outlined above. 25 out of the

remaining 32 participants with CdLS were able to be matched by hand to participants with FXS, RTS and AUT groups individually first by chronological age (+/- two years) and then self-help scores (+/- a score of two). Table 1 shows demographics of each group (age range five to 47 years). AUT individuals showed higher scores on the social communication questionnaire (Rutter et al., 2003) *social communication* and *reciprocal social interaction* subscale compared to the CdLS and RTS groups, but no differences were found in the *restricted interests/repetitive behaviour* subscale between the four groups.

(table 1 here)

2.3 Measures and Procedures

Parents/carers of prospective participants were sent a questionnaire pack, consent form and prepaid return envelope. Several questionnaires were included in the pack which are not reported here. A demographic questionnaire regarding chronological age, gender, verbal ability, mobility and details of diagnosis. The *self-help skills* subscale of the Wessex Scale (Kushlick, Blunden & Cox, 1973) was used as a proxy of level of adaptive ability. The lifetime version of the Social Communication Questionnaire (SCQ) (Rutter et al., 2003) was used to assess autistic traits. It has three subscales: social communication, restricted interests/repetitive behaviours and reciprocal social interaction (*RRBs*).

The Behaviour Rating Inventory of Executive Function- Preschool Version (BRIEF-P) (Gioia et al., 2005) measures everyday behavioural manifestations of executive function (EF behaviours) in pre-school aged children aged two years to 5 years, 11 months. The BRIEF-P has five subscales; *Inhibit, Shift, Working Memory, Emotional Control* and *Plan/Organize.* A higher score on a subscale indicates greater difficulty. Normative data from TD two- to three-year olds, outlined in the BRIEF-P Professional Manual, were used to provide a benchmark for comparison of behaviours that are appropriate for the typical mental

age of individuals with the RTS, CdLS, FXS and AUT groups (Ellis, Oliver, Stefanidou, Apperly & Moss, 2020).

2.4 Data analysis

Participant's chronological age and scores on all subscales of the BRIEF-P and SCQ subscales were normally distributed in all groups. *Self-help* scores were not normally distributed in three out of four participant groups and were transformed using Log10 transformation to a normal distribution. Differences between the participant groups on the BRIEF-P were investigated using one way-ANOVAs and t-tests. Associations between the BRIEF-P and SCQ subscales were explored using partial correlations (controlling for self-help skills). Predictive values of the BRIEF-P subscales on SCQ subscale scores between participants groups were calculated using linear regression analyses. Comparisons with normative data (means and standard deviations) from the BRIEF-P Manual was conducted using Welch's unpaired t-test procedure. Due to multiple comparisons and correlations an adjusted alpha level of $p<.01$ was employed.

3. Results

To investigate whether level of adaptive ability may account for BRIEF-P subscale scores in any of the participant groups, Pearson correlations (see table 2) between Wessex self-help scores and each BRIEF-P subscale scores for each group generated no significant associations, except for a moderate negative association between *Shift* and *Self-Help* scores in the FXS group ($r=-.59$, $p<.01$).

(table 2 here)

3.1 Comparing profiles of EF behaviours between AUT, CdLS, FXS, RTS and TD boys and girls.

Table 3 shows the mean subscale scores on each BRIEF-P subscale for each group and the normative sample of TD boys and girls outlined in the BRIEF-P manual. Independent

samples t-tests between each of the four participant groups (CdLS, FXS, RTS and AUT), and the normative samples of TD boys and girls indicated that the TD normative samples scored significantly lower than all three clinical groups. A one-way ANOVA between the clinical groups indicated no significant group differences on any of the five subscales between group, although the difference on the *Inhibit* subscale approached significance (p=.02). Bonferroni post hoc tests revealed that the CdLS group had lower *Inhibit* scores compared to the AUT group (t=-2.91, p<.01).

(Table 3 here)

3.2 The relationship between EF behaviours and autistic traits in CdLS, FXS, RTS and AUT.

Table 4 shows partial correlation coefficients controlling for overall adaptive ability between BRIEF-P subscale scores and SCQ subscale scores per group. In the AUT group, no significant correlations were found between any of the BRIEF-P and SCQ subscale scores. There was a strong positive correlation between the *RRBs* subscale of the SCQ and the *Inhibit* subscale in the CdLS group and between *Working Memory* and *RRBs* in the RTS group. In the FXS group all BRIEF-P subscales showed a significant correlation with SCQ *RRBs* subscale scores, except for the *Plan/Organization* subscale.

(Table 4 here)

Table 5 shows the predictive values of the BRIEF-P subscales that correlated with *RRBs* SCQ scores per group. The Inhibit subscale of the BRIEF-P explained 55% of the variance in the *RRBs* in the CdLS group. In the RTS group, the Working Memory BRIEF-P subscale explained 49% of the variance in RRBs. In the FXS group, 4 out of 5 BRIEF-P subscales contributed to the variance in *RRBs* scores, at similar levels of between 27-36% predicted for each subscale.

(Table 5 here)

4. Discussion

This is the first study to directly compare profiles of EF behaviours and examine the association between EF behaviours and autistic traits in individuals with CdLS, FXS and RTS. This study included participant groups matched on chronological age and adaptive ability, with good sample sizes for rare population research. The first aim was to compare profiles of EF behaviours of individuals with CdLS, FXS, RTS and AUT between one another and to normative data from two-to-three-year-old TD children. Consistent with previous reports (Reid et al., 2017; Waite et al., 2015; Schmitt et al., 2019; Johnson, 2015) all syndrome groups showed high levels of executive dysfunction similar to AUT individuals. However, no differences were found between syndrome groups on any BRIEF-P subscale. Adaptive behaviour was not associated with EF subscale scores, except for the Shift subscale in the FXS group, suggesting that executive dysfunction is not typically related to overall level of adaptive ability.

The second aim was to compare the associations between EF behaviours and autistic traits between individuals with CdLS, FXS, RTS and AUT individuals, while controlling for adaptive ability. BRIEF-P subscale scores did not correlate with either the *Communication* or *Reciprocal Social Interaction* SCQ subscales in any of the groups. These findings support the fractionation hypothesis of autistic traits i.e., impaired social interaction and communication skills, and RRBs may have distinct causes from one another (Brunsdon & Happé, 2014). Interestingly, while there were no significant group differences with regard to the profile of EF behaviours across all four groups, the nature of association between EF behaviours and RRBs differed between groups. Whereas in those with FXS RRBs appear to be associated with EF processes broadly (Inhibit, Working Memory, Shift, Emotional Control), in those with CdLS the association between EF and RRBs appears specific to Inhibition skills, and to Working Memory skills in those with RTS. These findings demonstrate the importance of

investigating behavioural and cognitive phenotypes in different syndromes and the pattern of their association within groups at a refined level.

EF behaviour subscales significantly predicted RRBs in the same pattern as the correlation analysis results. The proportion of variance that was accounted for by EF subdomains varied between genetic syndromes. Whereas behaviours indicative of inhibition skills accounted for about half of the variance of RRBs reported in the CdLS group (55%), as did working memory skills in the RTS group (49%), a range of EF behaviours each account for around a third of the variance of reported RRBs (27-36%). These findings indicate that improvements in specific EF behaviours may be a non-invasive way of improving RRBs in individuals with these syndromes. However, not all of the variance was explained by EF behaviours in any of the syndrome groups. This points to other factors, other than EF impairment, contributing to the occurrence of RRBs between syndrome groups (Lopez et al., 2005), such as response to anxiety and different cognitive processes (Oakes et al., 2016; Ray-Subramanian & Ellis, 2012).

Surprisingly, the AUT group did not show any significant correlations between the SCQ and BRIEF-P subscales. Except for a few studies (e.g., Reed et al., 2011) most research investigating the relationship between EF and RRBs has only included autistic individuals without intellectual disability (see Demetriou et al., 2018 for a review of studies). These findings may suggest that the nature of the association between EF and RRBs may differ between those with and without intellectual disability. However, previous studies that utilised the BRIEF instead of direct assessments also did not find any associations between BRIEF subscale scores and RRBs in pre-schoolers and school-aged autistic children without intellectual disability (Boyd, McBee, Holtzclas, Baranek & Bodfish, 2009; Smithson et al., 2013). A review of twenty studies using both clinical and performance-based assessments of EF across clinical and non-clinical groups shows only 24% of relevant correlations were

statistically significant and the overall median correlation was .19. The authors suggested that these findings may indicate that parent report measures and performance-based measures may assess different EF constructs and subsequently show different patterns of associations with behaviours (Eycke & Dewey, 2015; Toplak, West & Stanovich, 2013). Whereas EF performance-based assessments assess efficiency of the available processes in isolation (algorithmic cognitive level), informant-based measures may also assess the ability to apply EF processes when pursuing a goal in a typical daily situation (reflective level) (Toplak et al., 2013). These differences in measures may be why the unique profile of spared (visuo-spatial working, inhibition) and impaired (verbal working memory, shifting) EF abilities previously observed in CdLS (Johnson, 2015) was not observed in the current study. Consequently, both BRIEF-P and performance-based findings should be considered alongside one another when considering intervention (Topak et al., 2013).

Performance- and informant-based assessments may also be dissociable by whether they evaluate 'hot' or 'cool' EF as goal-oriented EF behaviours assessed by informant measures are likely to have more emotional and motivational salience whereas there are few obvious rewards or punishers in performance-based tasks (Zelazo & Carlson, 2012). Previously in the BRIEF, inhibition and emotional control have been considered to be more likely applied in emotionally significant situations ("hot EF") whereas working memory, shift and planning/organisation have been considered more likely to occur in neutral contexts ("cool EF") (Gioia, Isquith, Retzlaff & Epsy, 2002). However, EF is "malleable" dependent on context (Zelazo & Calrson, 2012) and certain situations may be more emotionally salient to some syndromes compared to others. For example, greater levels of anxiety are associated with poorer working memory, shifting and planning (Moran, 2016; Lukasik, Waris, Soveri, Lehtonen & Laine, 2019; Ajilchi & Nejati, 2017) and mood can influence performance on these skills as well (Figueira et al., 2017, 2018; Phillips, Bull, Adams & Fraser, 2002).

Individuals with FXS show heightened anxiety in response to changes in routine (Woodcock et al., 2009) and in social situations (Crawford et al., 2020; Crawford., Waite & Oliver, 2017). As these situations are often inevitable, these individuals frequently experience high levels of anxiety in daily life that may contribute to greater reported EF impairments in the BRIEF and heightened occurrence of RRBs to help self-regulate. Outlining the emotional salience of contexts and its influence on EF and RRBs within each syndrome may be essential in developing refined and successful interventions across these groups.

One problem when measuring executive function that should be considered, whether directly or by questionnaire, is that different EF subscales are associated with one another. However, whilst these abilities are correlated and have some commonalities, they are still considered separable (Miyake et al., 2000). This is supported by evidence showing different relationships between specific EF processes and behaviours (Sabat, Arango, Tassé & Tenorio, 2020; Stautz, Pechey, Couturer, Dreary & Marteau, 2016), skills (Cragg et al., 2017; Costa et al., 2017), neuropsychological tests (Friedman et al., 2006), biomarkers (Wilkinson et al., 2017) and genes (Barnes, Dean, Nandam, O'Connell & Bellgrove, 2011) and findings from the current study indicating that different EF behaviours are differentially associated with RRBs between groups. The BRIEF-P may lack sensitivity to detect differences in EF deficits in individuals with intellectual disability matched on level of ability. This possibility warrants further investigation using direct assessments of EF and ability.

Females with FXS were not included due to differences in IQ (Baker et al., 2019), and behavioural and cognitive phenotypes (Schmitt et al., 2019). Despite emerging research providing evidence of EF impairment (Schmitt et al., 2019; Tamm, Menon, Johnston, Hessl & Reiss, 2002; Keysor & Mazzocco, 2002) and RRBs (Reisinger et al., 2020) in these individuals, females with FXS remain an under-researched group. In addition, subtle differences in the development and profile of autistic traits and cognitive mechanisms that

contribute to behavioural phentoypes between individuals with FXS with and without comorbid autism have been reported (Abbeduto, McDuffie & Thurman, 2014; Abbeduto et al., 2019). Future studies are warranted to refine the similarities and differences in profiles of EF behaviours and its relationships with RRBs between males and females with FXS both with and without comorbid autism, to determine whether within-group differences in those with FXS require further refined EF and RRB intervention strategies (Schmitt et al., 2019).

Finally, we did not collect information on the types of genetic causes within each syndrome group. Emerging evidence indicates that the six different variants which act on the cohesion complex and cause CdLS (Kline et al., 2018) are related to different profiles and trajectories of physical, cognitive, and behavioural phenotypes (Mannini et al., 2013), including a positive association between chronological age and insistence of sameness scores on the RBQ only found in those with NIPBL mutations (Moss et al., 2017). Different types of mutations on the same gene have identified further within-group differences in both people with CdLS (NIPBL gene, Ajmone et al., 2021) and RTS (CREBBP gene; Schorry et al., 2008). Further work should delineate how these fine-grained genetic differences influence EF and RRBs profiles in sufficiently powered studies of people with CdLS or RTS. FXS is caused by >200 repeats of cyosine-guanine-guanine (CGG) on the X chromosome, which represses fragile X mental retardation protein (FMRP) expression (Bardoni, Schenck & Mandel, 2001). Interestingly, it is deficient FMRP and not the number of CGG repeats that has a dose-dependent relationship with EF abilities, indicating that FMRP may act as more important neurobiological marker of cognitive variability than genetic variation in those with FXS (Schmitt et al., 2019).

5. Conclusions

The fractionation hypothesis proposes that executive dysfunction underpins RRBs but not social and communication skills in autistic people (Happé & Ronald, 2008). We explored

this theory in three genetic syndromes, CdLS, FXS and RTS, associated with distinct profiles of autistic traits (Moss et al., 2013; Moss et al., 2013b; Abbeduto et al., 2014) and impairments on direct EF assessments (Schmitt, 2019; Reid et al., 2017; Waite, 2012). Although the profiles of informant reported behavioural manifestations of EF processes in CdLS, FXS, RTS and AUT were not found to be significantly different, the relationships with RRBs varied between syndromes. These results provide useful information about the aetiology of RRBs in CdLS, FXS and RTS which could have important clinical implications for intervention planning. The AUT group did not show relationships between BRIEF-P and SCQ profiles, which may reflect that the BRIEF-P assesses different EF constructs to performance-based measures (Toplak et al., 2013). Further investigation of the EF profiles in these syndrome groups using direct assessments to supplement BRIEF-P scores, as well as the environmental influence on EF, is necessary to gain a more complete picture of EF and its relationship with RRBs in CdLS, FXS and RTS.

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Table 1

Comparing demographic information across participant groups.

		CdLS (n=25)	FXS (n=25)	RTS (n=25)	ASD (n=25)	F (X^2)	df	*P*	Post Hoc
Age in years	Mean (SD)	18.60 (8.94)	18.48 (8.80)	18.60 (9.06)	18.52 (8.65)	.001	3	1.00	
Self-help score[1]		7.04 (1.24)	7.24 (1.20)	7.04 (1.14)	7.78 (1.29)	2.06	3	.11	
Communication SCQ score		5.10 (2.45)	6.47 (2.56)	4.73 (2.30)	9.01 (2.11)	14.32	3	**<.001**	ASD>CdLS, RTS
Reciprocal Social Interaction SCQ score		5.19 (3.04)	6.98 (2.89)	5.57 (3.11)	8.24 (3.21)	7.45	3	**<.001**	ASD>CdLS, RTS
Repetitive Behaviour SCQ score		3.45 (2.12)	4.44 (2.30)	4.00 (2.43)	5.06 (1.66)	2.54	3	.061	
Gender	% Male	36	100[2]	56	84	(25.83)	3	**<.001**	FXS>CdlS, RTS

[1] According to Wessex Scales (Kushlick et al., 1973)

[2] Only males with FXS recruited due to differences in cognitive and behavioural phenotypes between males and females

Table 2.
Pearson correlations between Wessex self-help scores and BRIEF-P subscales in CdLS, RTS, FXS and ASD.

	Wessex Self Help Score			
	CdLS (n=24)	RTS (n=25)	FXS (n=25)	ASD (n=25)
Inhibition	-.096	-.215	-.318	-.253
Shifting	.276	-.357	-.592**	.074
Emotional control	.102	-.001	-.450	.084
Working memory	-.228	-.114	-.394	-.115
Planning/organisation	-.080	-.013	-.413	.009

**indicates significance at the *p*=.01 level

Table 3

The mean scores on the BRIEF-P subscale scores, standard deviations, statistical analyses and post hoc analyses across participant groups and TD normative sample means and standard deviations for comparison.

		Group C	F	R	A						
		CdLS (n=25)	**FXS (n=25)**	**RTS (n=25)**	**ASD (n=25)**	**F**	**df**	***p***	**TDBoys* (n=113)**	**TDGirls* (n=105)**	**t-test analysis**
Inhibition	Mean	31.17	34.96	33.32	37.10	3.385	3	.021	25.04	22.33	TDBoys, TDGirls
	(SD)	(8.00)	(6.71)	(5.89)	(6.06)				(5.61)	(4.77)	<(C,F,R,A)**
Shift	Mean	22.63	22.60	20.28	23.18	1.46	3	.230	15.00	14.18	TDBoys, TD Girl
	(SD)	(7.16)	(4.68)	(4.82)	(4.27)				(4.06)	(3.32)	<(C,F,R,A)**
Working Memory	Mean	35.02	37.92	35.50	37.70	.995	3	.399	24.18	22.50	TDBoys, TDGirls,
	(SD)	(8.52)	(7.12)	(5.56)	(7.93)				(5.02)	(4.73)	<(C,F,R,A)**
Emotional control	Mean	21.25	20.76	20.36	23.12	1.564	3	.203	16.00	15.45	TDBoys, TDGirls
	(SD)	(5.29)	(4.85)	(5.25)	(4.04)				(4.06)	(3.97)	<(C,F,R,A)**
Planning/ organization	Mean	19.96	20.56	20.84	22.64	2.042	3	.113	15.81	14.67	TDBoys, TDGirls
	(SD)	(4.94)	(3.74)	(3.22	(4.00)				(3.26)	(3.05)	<(C,F,R,A)**

*Normative samples taken from BRIEF-P Professional Manual; samples aged 2-3 years

**Indicates significance at p<.001 level

Table 4

Partial correlations (controlling for self-help skills) between BRIEF- and SCQ subscales in CdLS, FXS, RTS and AUT

	CdLS (n=25)	RTS (n=23)	FXS (n=25)	AUT (n=25)
	Communication on the SCQ subscale			
Inhibit	.25	.10	.03	-.05
Shift	.05	.08	.01	-.09
Emotional Control	-.02	-.09	.07	-.09
Working Memory	.31	.10	-.04	-.03
Planning/Organization	.33	-.04	.07	.05
	Reciprocal social interaction on the SCQ subscale			
Inhibit	-.01	.04	.00	.36
Shift	.48	.01	.39	.30
Emotional Control	.16	-.22	.00	.40
Working Memory	.12	.19	.14	.32
Planning/Organization	.09	.28	.36	.07
	Repetitive Behaviours on the SCQ subscale			
Inhibit	.57**	.40	.57**	.30
Shift	.20	.39	.58**	.23
Emotional Control	.40	.21	.55**	.26
Working Memory	.23	.68**	.54**	.20
Planning/Organization	.28	.51	.49	.20

**Indicates significance at the $p = .01$ level

Table 5

Linear regression equations for the CdLS, RTS and FXS groups between SCQ RRB and the

	F	df	*p*	R^2
		CdLS		
Inhibit	26.08	1, 22	<.001**	.55
		RTS		
Working Memory	22.27	1, 23	<.001**	.49
		FXS		
Working Memory	7.66	1, 22	.012*	.27
Inhibit	11.78	1, 21	.002**	.36
Shift	10.76	1,22	.003**	.33
Emotional Control	9.98	1,22	.005**	.31

EF function subscales of the BRIEF-P