American Journal on Intellectual and Developmental Disabilities

The executive function account of repetitive behavior: Evidence from Rubinstein-Taybi syndrome

--Manuscript Draft--

Manuscript Number:	AJIDD-D-20-00052R1
Article Type:	Research Report
Keywords:	executive function; repetitive behaviour; Rubinstein-Taybi syndrome; genetic syndromes; repetitive questioning
Corresponding Author:	Jane Waite Aston University Birmingham, UNITED KINGDOM
First Author:	Jane Waite
Order of Authors:	Jane Waite
	Sarah Beck
	Laurie Powis
	Chris Oliver
Manuscript Region of Origin:	UNITED KINGDOM
Abstract:	Background. In this study, we focus on Rubinstein-Taybi syndrome (RTS) to explore the relationship between executive function deficits and repetitive behaviors. Methods. Thirty individuals with RTS completed direct assessments of inhibition, working memory and set-shifting. Informants completed repetitive behavior and executive function questionnaires. Results. Repetitive questions were associated with poorer inhibition and working memory. Stereotypy was associated with poorer inhibition. Adherence to routines was associated with poorer set-shifting, but only on the parental report measure. No other associations were evident. Conclusions. There is evidence of an association between specific repetitive behaviors and executive functioning in RTS, suggesting executive dysfunction may underpin behavioral difference in RTS. The findings point towards specific associations that are of interest for further research across populations in which repetitive behaviors are present.

Abstract

Background. In this study, we focus on Rubinstein-Taybi syndrome (RTS) to explore the relationship between executive function deficits and repetitive behaviors. *Methods.* Thirty individuals with RTS completed direct assessments of inhibition, working memory and set-shifting. Informants completed repetitive behavior and executive function questionnaires. *Results.* Repetitive questions were associated with poorer inhibition and working memory. Stereotypy was associated with poorer inhibition. Adherence to routines was associated with poorer set-shifting, but only on the parental report measure. No other associations were evident. *Conclusions.* There is evidence of an association between specific repetitive behaviors and executive functioning in RTS, suggesting executive dysfunction may underpin behavioral difference in RTS. The findings point towards specific associations that are of interest for further research across populations in which repetitive behaviors are present.

Key words

Executive function, repetitive behavior, Rubinstein-Taybi syndrome, genetic syndromes, repetitive questioning

The executive function account of repetitive behavior: Evidence from Rubinstein-Taybi syndrome

Repetitive behavior is an umbrella term for a broad class of invariant, high frequency behaviors, which appear inappropriate for the environmental context (Turner, 1997). A behavior with these characteristics will be classed as repetitive irrespective of how qualitatively distinct it appears from other behaviors that share these characteristics. For example, a specific stereotyped motor movement (e.g. hand flapping) and adherence to routines are both identified as repetitive behaviors (Moss et al., 2009).

The profile of repetitive behaviors has been the focus of recent research. Factor analytical studies in Autism Spectrum Disorder (ASD) have described clusters of lower-order sensory /motor behaviors and higher-order insistence on sameness behaviors (Szatmari et al., 2006). Research across rare genetic syndromes associated with intellectual disability (ID), utilizing a measure designed for this population, has identified high variability in syndrome related profiles of repetitive behaviors (Repetitive Behaviour Questionnaire; Moss et al., 2009; Waite et al., 2015; Royston et al., 2018). In certain genetic syndromes the form of repetitive behaviors and the frequency at which they occur appears similar to ASD (e.g. fragile-X syndrome). In other syndromes such as Prader-Willi, Williams, Angelman, Cri du Chat, Cornelia de Lange, Smith-Magenis and Rubinstein-Taybi syndromes there is within and between group variability with overall differences to the ASD profile (Moss et al., 2009; Royston et al., 2018; Waite et al., 2015). In addition, highly specific repetitive behaviors occur in some syndromes, such as the self-hug noted in Smith-Magenis syndrome and attachment to specific objects in Cri du Chat syndrome (Cornish and Pigram, 1996; Dykens et al. 1997). A fine-grained approach to studying these behaviors is warranted as the variation within and across syndromes suggests differing causal mechanisms (Moss et al., 2009).

Several theories have been proposed to explain the occurrence of repetitive behaviors in ID; the majority of which originate from the ASD literature. These theories suggest that repetitive behaviors: decrease anxiety by lowering demands and filtering environmental stimulation (Rodgers et al., 2012), reduce or increase arousal (Dantzer, 1986; Hutt & Hutt, 1965), provide perceptual reinforcement (Lovaas et al., 1987), result from compromized mentalising ability (Baron-Cohen, 1989; Jones et al., 2018), result from detailed-focused cognitive style or weak central coherence (Chen et al., 2009), or arise due to executive function or attentional deficits (Miller et al., 2015; Faja & Darling, 2018; Ravizza et al., 2013; Turner, 1997, 1999; Mosconi et al., 2009; Yerys et al., 2009; South et al., 2007, D'Cruz et al, 2013; Lopez et al., 2005).

While evidence for these proposed theories has been identified in ASD populations, there has been limited application of these theories within genetic syndromes associated with ID, despite repetitive behaviors being prevalent in these populations. Further understanding the mechanisms underlying repetitive behaviors has the potential to inform interventions in populations, as well as the broader ID community, which is relevant when repetitive behaviors are severe or frequent enough that they interfere significantly with an individual's quality of life. Within syndrome groups characterized by uneven repetitive behavior profiles, such as Rubinstein-Taybi syndrome, it may also be possible to examine how specific mechanisms may contribute to specific repetitive behaviors, which may lead to theoretical insights into the origins of these behaviors. In this study we focus on the executive function account of repetitive behavior with Rubinstein Taybi syndrome (RTS) as the syndrome of interest.

The executive function account of repetitive behavior proposes that executive dysfunction might lead an individual to perseverate on a behavior (e.g. if behavior was underpinned by compromized inhibition) or to become ‘stuck’ on a behavior, if set-shifting was compromized (Turner, 1997). There is also some evidence that poor verbal memory span may lead to repetitive questions (Cullen et al., 2005). This theory was selected due to its potential to contribute to understanding of the uneven profile of repetitive behaviors within and across syndromes. Given that executive function is not a unitary construct, deficits in specific executive functions could drive the increase in frequency of a single, or group of qualitatively similar, repetitive behaviors in a given group (Turner, 1997).

There is evidence to support the association between executive functions and repetitive behaviors across a range of populations apart from ASD, including Alzheimer’s disease (Cullen et al., 2005), typical development (Tregay et al., 2009; Evans et al. 2004), obsessive compulsive disorder (Samuels et al., 2018; Synder et al., 2015) and genetic syndromes associated with ASD (e.g. Woodcock et al., 2009); although the evidence is often inconsistent (e.g. in ASD see Rapp & Vollmer, 2005). Studies utilising a fine-grained approach rather than aggregating repetitive behaviors, have typically found associations between executive functions and specific repetitive behaviors. For example, Mosconi et al., (2009) found that inhibitory control impairments were associated with higher-order compulsive behaviors in ASD and Turner (1997) who found that impaired set-shifting was associated with greater insistence on sameness in ASD.

In rare genetic syndromes a pathway from set-shifting difficulties to adherence to routines has been described in Prader-Willi syndrome, with identification of potential underlying neural mechanisms (Woodcock et al., 2009). This research grew out of an initial observation of an association between set-shifting, adherence to routines and repetitive questioning specifically. The findings of this initial study were later replicated with a series of observational and experimental studies. The current study is the first step in examining these potential mechanisms utilising direct assessments of executive function in Rubinstein-Taybi syndrome, a rare genetic syndrome that is characterized by an uneven profile of repetitive behavior (Waite et al., 2015). The uneven profile of repetitive behavior in RTS also provides an opportunity to examine the associations between specific repetitive behaviors and specific executive function difficulties, further elucidating mechanistic pathways.

Rubinstein-Taybi syndrome occurs in 1 in 100,000-125,000 births and is caused by deletions, microdeletions and mutations in the Cyclic-AMP-Regulated Enhancer Binding (CREB) Binding Protein (CREBBP) and ‘E1A Binding Protein’ (p300). The syndrome is characterized by a moderate ID, although a broad range of ability is noted (Hennekam, 2006). Group comparisons have indicated that certain repetitive behaviors occur as frequently in RTS as ASD, whereas other repetitive behaviors occur at significantly lower rates; indicating an uneven profile of repetitive behavior in RTS (Waite et al., 2015; Waite, 2012).

In a large sample of over eighty children and adults with RTS, the repetitive behaviors that were reported to occur once or more than once a day in over >40% of individuals with RTS, and at a comparable frequency to in ASD, were body, hand and object stereotypies, repetitive questioning and adherence to routines (Waite et al., 2015; Waite, 2012). These behaviors also occurred more frequently in RTS than in Down syndrome (Waite et al., 2015). This profile is consistent with previous literature, in which rocking, spinning, hand flapping, ‘stubbornness’ and repetitive speech have been documented in RTS (Stevens at al., 1990; Hennekam, 2006; Boer et al., 1999). In the current study, the possible associations between executive functions and repetitive behaviors were explored by focusing on the most phenotypic repetitive behaviors in RTS (stereotypy, routines & questions) as these are the most clinically significant.

In summary, Rubinstein-Taybi syndrome (RTS) is an understudied rare disorder group where there is a high frequency of specific repetitive behaviors. Understanding the causal mechanisms underlying these behaviors may lead to improved support for individuals with RTS and other genetic syndrome and ID groups who engage in these behaviors. Furthermore, the uneven profile of repetitive behavior observed in this syndrome may be associated with specific executive function difficulties (Waite et al., 2015). Examining these associations is the aim of the paper. While there is some inconsistency across populations as to the exact nature of the association between specific repetitive behaviors and executive functions, a fine-grained analysis of these associations may have merit for understanding the aetiology of repetitive behaviors. A fine-grained analysis will avoid masking associations by aggregating behaviors into composite scores that might not provide an accurate representation of how behaviors cluster together in these rare genetically determined syndromes. As the evidence for a link between set-shifting and adherence to routines is more consistent, we hypothesize that this will be replicated in RTS (Woodcock et al., 2009; Turner, 1997).

Materials and Methods

Participants

Rubinstein-Taybi syndrome. Thirty-two individuals with RTS were recruited to the study initially (16 males; mean chronological age: 18.42 years; range: 3.83 – 44.42) through an existing database held by the [redacted] and via the UK Rubinstein-Taybi Syndrome support group. Inclusion criteria were that the person was mobile and had a confirmed diagnosis of RTS from either a paediatrician, clinical geneticist or other appropriate medical practitioner. Participants had physical features consistent with an RTS diagnosis (e.g. broad thumbs, downslanted palpebral fissures, low-hanging columella). Two participants were excluded because a questionnaire pack was not returned/missing data and measures were not appropriate for an individual's cognitive and adaptive functioning.

Thirty participants remained in the sample. Chronological age for the group was 17.97; range: 3.75-44.42 years. The mean developmental age equivalent score on the direct cognitive assessments (Mullen Scales of Early Learning or Wechsler Abbreviated Scales of Intelligence) was 4.98 years; range: 1.25-12.23 years. Mean age equivalent receptive language score on the indirect informant report measure of adaptive functioning (Vineland Adaptive Behavior Scales- 2nd Ed; VABS) was 4.36, 1.42-11 years.

Participants completed a cognitive assessment and direct executive function tasks (see Table 1). Of the 30 participants, all attempted the simplest inhibition task (Buckets Conflict Task), however, this was the only task that seven participants were able to complete, due to their lower ability level. One additional participant did not complete the Black-White Stroop and Dimensional Card Sort Tasks due to poor engagement. The number of participants completing each assessment are summarized in Table 1. To maximize sample size all partial datasets were included. Parents completed questionnaire measures about their child documenting ability, repetitive behavior and executive functioning

--------------------------------------Insert Table 1 about here--

Measures

Measure of general cognitive functioning. Participants completed the Mullen Scales of Early Learning (MSEL; Mullen, 1995), a cognitive assessment capturing abilities from birth to 5yrs 8ms. Participants at ceiling on the Mullen Scales completed the Wechsler Abbreviated Scaled of Intelligence (WASI; Wechsler, 1999), suitable for individuals aged 6 to 89 years. A developmental age equivalent score for each participant was derived from the raw score tables of the MSEL by averaging the receptive language, expressive language, visual reception and fine motor age equivalents (Richler et al., 2007, Waite et al., 2016). Similarly, developmental age equivalent scores were extracted for each of the WASI sub-domains and an average taken. The MSEL age equivalent was utilized for 22 participants (N = 22; MSEL Mean MA: 3.8 years, Range: 1.2-5.7 years). WASI age equivalents were utilized for eight participants who were at ceiling on the MSEL (N = 8; WASI Mean MA: 8.23, 5.9-12.23 years).

Parents of individuals with RTS also completed the Vineland Adaptive Behavior Scales-II (VABS) and the age equivalent score for the receptive language domain was included in this study as an alternative proxy measure of intellectual functioning. This individual subscale was utilized because the scores were less likely to be influenced by the physical or behavioral phenotype in RTS (e.g. poor expressive language or daily living skills due to physical development, heightened social motivation influencing play and leisure scores). The Vineland receptive language and MSEL-WASI age equivalent scores were positively associated ($R = .76$, $p < .001$).

Executive Function Tasks. The executive function (EF) tasks were adapted from the typically developing literature and are part of a battery of EF tasks compiled for individuals with ID: The Battery of Executive Function for Intellectual Disabilities (BEF-ID; Waite, 2012). Heald (2010) administered the battery to a group of 262 typically developing children aged 3 to 7.5 years and reported that the measures showed good internal validity (Cronbach's alpha >.80% for all tests) and convergent/divergent validity.

These tasks were administered as part of a broader study investigating the development of EF in RTS. Of the tasks in the BEF-ID, three conflict inhibition tasks were selected for the current analysis: Buckets, Bear-Dragon and Black-White Stroop. These tasks were included because previous research, and pilot data from typically developing children, indicate these tasks increase in difficulty incrementally and are developmentally sensitive (Carlson, 2005; Garon et al., 2008). There were three versions of the Dimensional Change Card Sort (DCCS) included in the BEF-ID. However, only the standard version is included in this analysis because this is the most extensively validated. A working memory task measuring phonological span (Animal Span task) was included in the analysis because verbal working memory has been implicated in repetitive behavior (Cullen et al., 2005) and because verbal working memory has been shown to be poorer in RTS relative to typically developing children (Waite et al., 2016). Therefore, working memory was an important variable to consider as a causal mechanism in repetitive behavior, as well as a potential covariate.

Inhibition Tasks

Buckets Conflict Task (adapted from the Reverse Categorisation; Carlson et al., 2004). A red bucket and a blue bucket, and 14 coloured balls (seven red, seven blue) were used. Participants were asked to identify a red and a blue ball and the buckets to ensure they could label these correctly. Participants were then asked to sort the blue balls into the red bucket and the red balls into the blue bucket during twelve pseudo-randomized trials of red (R) and blue (B) balls (B, R, B, R, R, B, B, R, B, R, R, B). The sorting rule was demonstrated, followed by two practice trials with feedback. The rules were repeated after six balls had been sorted. The maximum score on this task was 12 points. After the experimental trials, all participants were asked to sort the balls correctly into the matching buckets (e.g. blue balls into the blue bucket) 'to help the experimenter put the balls way', to check that participants could match. Unlike Carlson et al. (2004), colour was chosen as the sorting dimension rather than size because a pilot study with children had indicated that colour was more salient [redacted]

Bear-Dragon (Reed et al., 1984). Participants were asked to complete nine actions to check they could execute them e.g. "touch your head." They were then introduced to a bear puppet and a dragon puppet and instructed to do the actions commanded by the bear but not those commanded by the dragon. There were two practice trials after which feedback was given. Participants proceeded to the experimental trials irrespective of performance on practice trials. However, the experimenter asked a check question, "who don't we listen to?" to check the participant had understood the inhibition rule. There were sixteen predetermined pseudorandomized bear (B) and dragon (D) trials (B, D, B, B, D, D, B, D, B, D, B, D, D, B, D). The experimenter reminded participants of the rules after eight trials. The rule-check question "who don't we listen to?" was repeated at the end to ensure task comprehension was maintained throughout the task. The dragon trials were coded with a maximum score of eight. Typically developing children completing this task commonly pass or fail this task (e.g., a binary distribution is typical) (Carlson et al., 2005).

Visual Black-White Stroop (Adapted from Simpson & Riggs, 2005). A black (B) and a white (W) card (20cm x 20cm) were mounted horizontally on a 40 x 60 cm board. Participants were asked to identify the black and white card to check comprehension. In the experimental phase, participants were required to point to the black card when the experimenter said 'white' and to the white card when the experimenter said 'black'. Two practice trials (one for a "white" card, and one for a "black" card) were followed by feedback. There were 16 predetermined pseudorandomized experimental trials (B, W, B, W, W, B, B, W, B, W, W, B, W, B, B, W). Feedback was not given after individual trials, but the rules were repeated after eight trials. The maximum score was 16. To reduce expressive language demands, participants responded by pointing rather than providing a verbal response like in the original task described by Simpson and Riggs (2005).

Working memory task

Verbal Animal Span (Bull et al., 2004). In the Verbal Animal Span the experimenter read out a string of monosyllabic animal names and the participant was asked to repeat them. The strings increased one word in length every three trials. The task was discontinued if a participant made an error in three consecutive trials. A version of a pairs coding scheme was used (Fudala et al., 1974). For example, if the sequence was cat, horse, bird, dog and the response given was correct the paired score was 3 (i.e. cat–horse, horse–bird and bird–dog).

Set-Shifting Tasks

Dimensional Change Card Sort Task (Standard Version; Zelazo, 2006). Two were target cards were used: a red boat and a blue rabbit that were mounted above two sorting trays. A further six cards depicted red rabbits (R) and six depicted blue boats (B). Participants were asked to sort the cards by *colour*. Participants watched a demonstration and had one practice trial (sorting a red rabbit card), followed by feedback. Participants then sorted six cards and no feedback was provided. After six trials participants were asked to change to sorting the cards by *shape*. The participant sorted another six cards and no feedback was given. The cards were presented to the participant in a predetermined pseudo-randomized order (Pre-switch: R, R, B, R, B, R; Post-Switch: R, R, B, R, B, B). The total score was the number of cards sorted correctly in the post-switch phase (maximum score = 6). The task was terminated after the pre-switch phase if the participant failed to attain set because they made a sorting error.

Parental Questionnaire Measures.

Repetitive Behavior Questionnaire (RBQ; Moss et al., 2009). The RBQ as developed by Moss et al. (2009) is an informant questionnaire that measures operationally defined repetitive behaviors. Items are presented alongside a five-point Likert scale that is used to measure the average occurrence of behavior during the last month (ranging from never (0) to more than once a day (4)). The RBQ has good item-level inter-rater reliability (75% > .60) and test-retest reliability (range: .61-.93) at item level. In the current study, analyses were conducted at item level for stereotypy, adherence to routines and repetitive questioning items. A higher score on this measure indicates more occurrences of repetitive behavior.

Behavior Rating Inventory of Executive Function – Preschooler Version (BRIEF-P; Gioia et al., 2003). The BRIEF-P is a 63-item informant questionnaire of the behavioral manifestations of EF impairment in typically developing children aged 2-5.11 years. The measure utilizes a three-point Likert scale format (never, sometimes and often). A higher score on this assessment indicates greater executive dysfunction. The measure has good internal consistency (.80-.95) and test-retest reliability (.78- .90). Convergent and discriminant validity have been demonstrated with other rating scales e.g. Child Behavior Checklist (Gioia et al., 2003). Although this measure is designed for children aged 2-5.11 years it has been utilized with children and adults with ID (Daunhauer et al., 2014; Lee et al., 2011; Pritchard et al., 2015), and the items align closely with the developmental age of individuals with ID (e.g. Daunhauer et al., 2014; Lee et al., 2011). As 76.67% of the RTS sample had a developmental age of < 6 years, based on cognitive testing, the items on the BRIEF-P were deemed more developmentally appropriate for use across the group than items in alternative versions that were available at the time of testing, developed for older children and adults (i.e. BRIEF and BRIEF-A).

While most participants fell within the developmental age range for this measure, all but two participants in the current study had a CA > 5.11 years, and hence fell outside of the BRIEF-P chronological age range. Pritchard et al. (2015) used exploratory factor analysis to evaluate the psychometric properties of the BRIEF-P out of age range in a large genetic syndrome sample (Down syndrome; N = 188; Mage: 6.99 years; range: 3-13 years). The analysis provided support that the BRIEF-P measured similar constructs in youth with Down syndrome as in pre-schoolers, which suggests the BRIEF-P may have utility in older individuals with other rare genetic disorders.

In the current study, three clinical scales from the BRIEF-P were selected for the current analysis to align with the direct assessment measures: Inhibition, Set-Shifting and Working Memory. To increase confidence in the validity of the use of the BRIEF-P, a conservative approach to application of this measure was adopted, whereby, a) items were only included in each subscale if there was preliminary evidence in RTS that they loaded onto the relevant EF construct, b) and Cronbach's Alphas for each subscale were examined to confirm internal consistency. The process of determining the factor loadings for items is described below.

BRIEF-P Factor Loadings

To examine factor loadings, BRIEF-P data were made available from a larger sample of 51 individuals with RTS (Mage: 21.67, range: 6-53; 30 males) from an ongoing cross syndrome study conducted by [blinded for review]. All participants in the sample were recruited from the RTS-UK Syndrome Support Group and had a confirmed diagnosis from a professional (e.g., paediatrician, clinical geneticist). Participants' were not able (N = 8; 15.7%), partly able (N = 33, 65.7%) or able (N = 10; 19.6%) based on their self-help score on the Wessex Questionnaire (WQ; Palmer & Jenkins, 1982). Exploratory Factor Analysis was conducted utilising Principal Axis Factoring (PAF). As inspection of the scree plot indicated a change in trajectory after the third point, PAF was conducted with a fixed number of factors (factors = 3). Direct Oblimin rotation was applied due to the oblique nature of the data and small coefficients (< .40) were suppressed as factor analysis is more robust with smaller samples when factor loadings are greater (de Winter, Dodou & Wieringa, 2009). The factor loadings are displayed in Table 2. Overall, the factors were aligned substantially with those from the original scale, although with a smaller subset of items, providing preliminary support for the integrity of the BRIEF-P with this population. The working memory loadings consisted of 9 items (8 working memory items and 1 inhibition; 53% of the original working memory items); the shifting loadings consisted of 12 items (all 10 shift items from the original measure, 1 inhibition item and 1 working memory item); and the inhibition loadings consisted of 12 items (9 inhibition, 2 working memory, 1 shift; 56% of the original inhibition items). Items that were consistent with the original subscales and loaded at >.4 were summed into conservative abbreviated subscales for subsequent analyses (highlighted in grey in Table 2).

--Insert Table 2 about here------------------------------------

BRIEF-P Cronbach's Alphas

The Cronbach's alphas for the three abbreviated BRIEF-P subscales were calculated for the current sample reported on in this study (N = 30). These are displayed in Table 3 for a) all participants b) the subset of 8 individuals who were at ceiling on the MSEL, placing their developmental age outside the range of the BRIEF-P. The subscales had good to excellent internal consistency (range: .85-91).

--Insert Table 3 about here------------------------------------

BRIEF-P subscale raw scores were used in the correlational analyses. While it was not possible to calculate t-scores, the use of the raw scores was preferred given associations between age and total EF difficulties could be then examined as part of the analysis, which is consistent with the approach taken in the direct assessment analysis.

Statistical Analysis

All participants passed the integrity checks for the inhibition tasks and DCCS pre-switch trials, which indicated that the tasks were likely working as intended; therefore, all data were included. However, inspection of MSEL age equivalents, indicated that the two least able participants, who only completed the Buckets task, had a MA significantly below < 2 years (MA equalled 14.50 and 19 months respectively) despite being able to match the coloured balls correctly during the integrity check for this task. The Buckets task was adapted from a task that is typically used with children from 2 years, therefore, analyses for the Buckets task was repeated with these participants removed to reduce potential floor effects (see footnote of Table 4). Spearman's Rho correlations were used to explore associations between all variables due to the small N and non-parametric nature of the data. Two-tailed tests were used. A preliminary analysis of the inter-correlations between repetitive behaviors indicated that hand stereotypy was highly correlated with object and body stereotypy (see Table 5). Due to these patterns of associations, the stereotypy items were combined into a single subscale: The Stereotypy Subscale as reported by Moss et al. (2009). Following Spearman correlations between all variables, partial correlations were conducted to explore associations while controlling for mental age, inhibition and/or working memory (two-tailed). The alpha level was set at p <.01 due to multiple tests. However, in Table 4, p-values at <.005 and <.001 are highlighted to aid interpretation.

---Insert Table 4 about here------------------------------------

---Insert Table 5 about here------------------------------------

Results

Descriptive Statistics

Descriptive statistics for variables of interest are displayed in Table 1. As anticipated, a large proportion of the sample engaged in object (35%), hand (53%), and body (70%) stereotypy once or more than once a day. Repetitive questioning (71%) and adherence to routines (50%) were also frequently reported.

Associations with age.

Associations between chronological age (CA) and EF measures, and mental age (MA) and EF measures are displayed in Table 4. There was a moderate positive association between CA associated and performance on the Buckets task, R = .56, p = .001, and a moderate negative association between CA and the Inhibition Subscale of the BRIEF-P, R = -.52, p = .004. The Buckets task, Bear-Dragon and Animal Span tasks were significantly associated with MA (Mullen/WASI), with better performance on these tasks being moderately to strongly associated with higher MA, Rs = .70, .80, .71; *ps* < .001 respectively. The Buckets task was moderately associated with the VABS Receptive Language Scale, R = .70, p < .001. In addition to the correlations for EFs displayed in Table 4, there was a moderate negative association between repetitive questioning and MA (Mullen/WASI), R = -.70, p < .001. No other associations between repetitive behavior, MA, VABS Receptive Language Scale and CA reached significance.

Associations between repetitive behavior and executive functions.

Spearman's associations between repetitive behaviors, all EF tasks (working memory, switching and inhibition) and parental report of behavioral markers of executive dysfunction (BRIEF-P) are displayed in Table 4. Strong significant associations were found between more frequent repetitive questioning and lower inhibition scores on the Bear-Dragon task (R = -.85, p < .001). There was a significant association between the BRIEF-P Inhibit Subscale and repetitive questioning (R = .55, p = .006), replicating the direct assessment findings (BRIEF-

P) where poorer inhibition was associated with more frequent repetitive questioning. Scores indicating greater executive dysfunction on the direct working memory task (Animal Span) and BRIEF-P Working Memory Subscale were also associated with more frequent repetitive questioning ($R = -.65$, $p < .001$; $R = .60$, $p = .002$ respectively).

----*insert Figure 1 about here*---

More frequent stereotyped behavior was moderately associated with greater difficulties on the BRIEF-P inhibitory control subscale ($R = .48$, $p = .007$). Finally, BRIEF-P scores indicating poorer set-shifting were associated with higher scores on an adherence to routine item ($R = .68$, $p < .001$). However, these associations were not replicated with the direct assessments of inhibition and set-shifting.

Partial Correlations between direct assessments.

Given that MA (MSEL/WASI) was strongly associated with repetitive questioning and performance on the Bear-Dragon and Animal Span tasks (see Table 4), the association between the tasks and repetitive questioning may have been driven by MA. Partial correlations indicated that the association between the Bear-Dragon task and repetitive questioning remained significant after controlling for MA, $R = -.59$, $p = .004$. The association between working memory and repetitive questioning was no longer significant once MA was controlled for, $R = -.24$, $p = .28$. Finally, further analysis revealed that there was a positive association between the Bear-Dragon task and the Animal Span, $R = .64$, $p = .001$, and the BRIEF-P inhibition and working memory subscales ($R = .73$, $p < .001$) so further partial correlations were conducted to explore the contribution of working memory to the association between inhibition and repetitive questioning. Partial correlations for the direct assessments indicated that the negative association between inhibition and repetitive questioning remained significant when verbal working memory was controlled for, $R = -.60$, $p = .004$, however, no significant associations remained for the BRIEF-P inhibition scale and repetitive questions, or the BRIEF-P working memory scale and repetitive questions, when working memory and inhibition were controlled for respectively. A diagram indicating the strong association between the Bear-Dragon task and the repetitive questioning item is displayed in Figure 1.

Analysis Using Conservative Set-Shifting Calculation.

Greater adherence to routines on the RBQ was associated with poorer set-shifting ability measured by the BRIEF-P. However, as these are both questionnaire measures it was possible that the results were due to common method variance. A conservative set-shift score was calculated for the BRIEF-P including items that did not address adherence to routines (remaining items 40, 50 and 25). The result remained significant, $R = .50$, $p = .003$.

Discussion

In this study we explored associations between repetitive behaviors noted as part of the behavioral phenotype of RTS, and components of EF, measured by direct assessments and informant report. We utilized a measure of repetitive behavior developed specifically for people with rare genetic syndromes (RBQ; Moss et al., 2009). The purpose of this study was to inform understanding of factors that may give rise to repetitive behavior in RTS, but also to provide further evidence of associations between these constructs, which may have relevance to other populations in which repetitive behaviors occur. RTS is an interesting syndrome to examine these associations because it is characterized by high prevalence of particular repetitive behaviors, including behaviors such as repetitive questioning, allowing for associations between specific repetitive behaviors and specific EFs to be explored. Given previous literature, it was predicted that scores indicative of poorer EF on the direct assessments and informant assessments, would be associated with more frequent occurrences of repetitive behavior, beyond that explained by developmental age.

We found that specific repetitive behaviors may be associated with specific EF difficulties in RTS. However, the inconsistency in the findings across the direct EF assessments and a proportion of non-significant findings means that the current study only provides limited evidence that aligns with the executive dysfunction theory. Despite this, the analysis yielded a pattern of results that are of interest for further studies that should seek to replicate and extend these findings.

Fewer occurrences of repetitive questioning were associated with better performance on a direct measure of inhibition and a direct measure of verbal working memory. While this pattern was only found with one of the inhibition tasks (Bear-Dragon), these findings are strengthened by a similar pattern of associations emerging between repetitive questioning the informant report subscales of EF, despite the informant subscales not correlating with mental age. Mental age was associated with repetitive questioning and the direct assessments of EF. However, when mental age was included in a partial correlation, the association between the direct measure of inhibition and repetitive questioning remained, while the relationship between the verbal working memory and repetitive questioning did not. Furthermore, the association between inhibition and repetitive questioning remained significant when verbal working memory was controlled for, which suggests that inhibition difficulties could contribute to repetitive questioning.

To our knowledge, a specific relationship between inhibition and repetitive questioning has not been reported in the literature. However, inhibition has been linked to repetitive behavior more generally (e.g. Lopez et al., 2005), and dysexecutive syndrome has been associated with repetitive speech (Alderman & Ward, 1991). If an individual has difficulty inhibiting a previously adaptive behavior once it has been initiated, they may continue to perseverate with this behavior. Alternatively, an individual may be unable to stop the activation of prepotent responses in response to environmental cues. In this circumstance, questioning could be triggered by an external cue (e.g. seeing a parent).

While a strong association was found between inhibition and repetitive questioning when controlling for working memory, it will be important to replicate these results. The Bear-Dragon task contains a working memory, as well as an inhibition, component, because the participant must remember rules. The participants in our sample passed the integrity check questions that were asked to ensure that the participants remembered the rules throughout the tasks. However, there is still a possibility that while the participant actively completed the task, they had forgotten the rules until the researcher's questions prompted the participants to recall them. Obtaining a 'pure' measure of an EF such as inhibition is challenging, even when statistically controlling for working memory (Miyake, 2000).

In addition, there was a clear split between participants passing (maximum score) and failing the Bear-Dragon task (e.g., scoring zero), this binary pattern of scores replicates what has been observed in typically developing populations where this task has been extensively researched (Carlson et al., 2005). The performance of typically developing children has indicated that this pattern of scores is likely to be due to biological and contextual maturation driving EF development, rather than the individual's understanding of the task rules (Carlson et al., 2005).

While this study found an association between inhibition and repetitive behaviors, it may be that a third variable, such as anxiety, may mediate this relationship. For example, executive dysfunction has been linked to higher trait anxiety in the typically developing population (Ursache & Raver, 2014) and in individuals with rare genetic syndromes, such as Williams syndrome (Ng-Cordell et al., 2018). In ASD, repetitive behaviors are postulated as the mechanism by which individuals who experience anxiety execute control over their environment to reduce anxiety (Rodgers et al., 2012). Thus, in this model, repetitive behavior is a symptom of anxiety. Studies examining anxiety in people with RTS have indicated that while children with RTS have been found to have lower levels of anxiety than a developmentally age matched comparison group, studies that have included older individuals have found increased levels of anxiety (Crawford et al., 2017; Galéra et al., 2009; Yagihashi et al., 2012). Further research should examine the role of anxiety in explaining associations observed in this study. As anxiety and repetitive behavior have been associated with Autism Spectrum Disorder (Rodgers et al., 2012), future research should examine how the presence of autism in RTS may influence the results. While this study did not include a measure of autism symptomatology, prevalence estimates of autism in RTS have been reported to range between 31-77.4%. However, further research examining autism, repetitive behavior and anxiety in RTS should move beyond global screening measures used in existing studies as these may inflate autism estimates by failing to account for a potential dissociation of the dyad of impairments in RTS in the literature (Waite et al., 2015).

As noted previously, associations between repetitive questioning and inhibition were only found with one of the direct assessments, the Bear-Dragon task. This might be explained by differences between the Bear-Dragon task and the other inhibition tasks because, unlike the other tasks, the Bear-Dragon task requires participants to withhold responses on some trials; it is a go no-go task. The task also requires more elaborate gross motor responses and has a greater social element as the participant engages more intensely with the researcher. Thus, the relationship between this task and repetitive questioning might be explained by one of these additional task elements.

The social element to the Bear-Dragon task is of particular interest given that preserved, or even heightened, social motivation has been noted in RTS (Moss et al., 2016; Stevens et al., 1990), and individuals with RTS are often described as lacking in stranger awareness. A distinction has been drawn between EF tasks with a 'hot' affective/motivational component and 'cool' EF tasks that do not contain an affective component (Zelazo & Müller, 2002). One possibility is that the Bear-Dragon is particularly difficult for people with RTS because it interacts with the RTS social phenotype, heightening the task's motivational component. If individuals with RTS have difficulty inhibiting repetitive questions in salient (hot) social situations, the Bear-Dragon task may be most sensitive to this. It will be interesting to conduct further research with versions of the Go No-Go task that are delivered in a social and non-social format.

A further relationship was found between stereotypy and the informant measure of inhibition, replicating previous studies (Turner, 1997). Despite previous research that has linked set-shifting difficulties and adherence to routine in Prader-Willi syndrome (Woodcock et al., 2009a, 2009b), no relationships were found between the direct set-shifting task and adherence to routine in RTS. However, on the indirect parent report measure, weaker shifting ability was strongly associated with greater adherence to routines. One concern was that the association between adherence to routines and shifting on the parental report measures may be a product of the similarity of the items across the two questionnaire measures. However, further analysis using a more conservative shift subscale (overlapping items removed) was conducted and the results remained consistent. These associations emerged even though there were no significant associations between the mental age and the informant measure. The absence of significant associations is further evidence that mental age is unlikely to account for associations between EF and repetitive behavior in RTS.

As previously noted, the association between the shifting and adherence to routine has been described in Prader-Willi syndrome (Woodcock et al, 2009a, 2009b). It has been found that some individuals with this syndrome have a deficit in set-shifting that reduces the ability to move attention flexibly and cope with unexpected changes. It has been argued that this set-shifting deficit makes sudden changes aversive for people with Prader-Willi syndrome and that this can lead to temper outbursts (Woodcock et al., 2009b). Further research could consider whether a similar process is operating in RTS by observing how individuals respond to changes in routine, drawing on the methodology used in Prader-Willi to map the pathway from cognition to behavior.

This study has some limitations including the number of correlations that were conducted, which increases the likelihood of making a type I error. Despite finding significant associations between EF and repetitive behaviors, these results do not provide enough evidence to support a causal link between these constructs, nor can these correlations be used to specify the direction of causation if a link did exist. These associations could have occurred because repetitive behavior impacts on EF development or performance on EF tasks, or because another unmeasured variable (e.g. anxiety) is driving the association. The results are also limited by sample size as the trends in the data suggest further associations may reach significance if more participants were included in the analysis. Despite this, the sample is large given the rarity of RTS and the study provides a starting point for further investigation into these associations.

Conclusions

Previous research has indicated that repetitive behaviors, particularly repetitive questioning, adherence to routines and stereotyped motor movements occur frequently in RTS (Waite et al., 2015). This study is the first to explore potential mechanisms of these behaviors in RTS using direct assessments and is one of the few studies to examine these behaviors at a fine-grained level of description. While these analyses cannot infer causality, findings indicate that poor inhibitory control may be implicated in the development or maintenance of repetitive questions. Mixed evidence is found for an overarching executive dysfunction account of repetitive behavior, which reinforces the importance of examining behaviors at a fine-grained level. Furthermore, these findings will inform the development of models of repetitive behavior in other populations and may inform clinical interventions to help reduce high intensity or frequent behaviors that impact quality of life.

List of Abbreviations:

BEF-ID: Executive Function for Intellectual Disabilities

EF: Executive Function

MSEL: Mullen Scales of Early Learning

RTS: Rubinstein-Taybi Syndrome

WASI: Wechsler Abbreviated Scaled of Intelligence – Second Edition

Compliance with Ethical Standards:

This study was approved by the NHS Coventry and Warwickshire Research Ethics Committee. All participants consented to participation in this study and written consent was provided by the person with RTS and/or their parents and, when appropriate, a personal consultee was sought for adults with RTS over the age of 16 years. The authors have no financial or other interests related to the research in this manuscript.

References

Alderman, N., & Ward, A. (1991). Behavioral treatment of the dysexecutive syndrome: Reduction of repetitive speech using response cost and cognitive overlearning. *Neuropsychological Rehabilitation*, *1*(1), 65-80.

Baron-Cohen, S. (1989). Do autistic children have obsessions and compulsions?. *British Journal of Clinical Psychology*, *28*(3), 193-200.

Boer, H., Langton, J., & Clarke, D. (1999). Development and Behavior in Genetic Syndromes: Rubinstein-Taybi Syndrome. *Journal of Applied Research in Intellectual Disabilities*, *12*(4), 302-307.

Bull R., Espy K.A., & Senn T.E. (2004). A comparison of performance on the Towers of London and Hanoi in young children. *Journal of Child Psychology and Psychiatry*, 45, 743-754.

Carlson, S. M. (2005). Developmentally sensitive measures of executive function in preschool children. *Developmental Neuropsychology, 28*(2), 595–616.

Carlson, S. M., Mandell, D., & Williams, L. (2004). Executive function and theory of mind: Stability and prediction from ages 2 to 3. *Developmental psychology, 4,* 1105–1122.

Carlson, S. M., *&* Moses, L. J. (*2001*). Individual differences in inhibitory control and children's theory of mind. *Child Development*, *72*(4), 1032-1053.

Chen et al., (2009)

Cornish, K. M., & Pigram, J. (1996). Developmental and behavioral characteristics of Cri du Chat syndrome. *Archives of disease in childhood*, *75*, 448-450.

Crawford, H., Waite, J., & Oliver, C. (2017). Diverse Profiles of Anxiety Related Disorders in Fragile X, Cornelia de Lange and Rubinstein–Taybi Syndromes. *Journal of autism and developmental disorders*, *47*(12), 3728-3740.

Cullen, B., Coen, R. F., Lynch, C. A., Cunningham, C. J., Coakley, D., Robertson, I. H., et al. (2005). Repetitive behavior in Alzheimer's disease: Description, correlates and functions. *International Journal of Geriatric Psychiatry*, *20*(7), 686-693.

Dantzer, R. (1986). Behavioral, physiological and functional aspects of stereotyped behavior: a review and a re-interpretation. *Journal of Animal Science*, *62*(6), 1776-1786.

Daunhauer, L. A., Fidler, D. J., Hahn, L., Will, E., Lee, N. R., & Hepburn, S. (2014). Profiles of everyday executive functioning in young children with Down syndrome. *American journal on intellectual and developmental disabilities*, *119*(4), 303-318.

D'Cruz, A. M., Ragozzino, M. E., Mosconi, M. W., Shrestha, S., Cook, E. H., & Sweeney, J. A. (2013). Reduced behavioral flexibility in autism spectrum disorders. *Neuropsychology*, *27*(2), 152.

de Winter*, J. C., Dodou*, D., & Wieringa, P. A. (2009). Exploratory factor analysis with small sample sizes. *Multivariate behavioral research*, *44*(2), 147-181.

Dykens, E. M., Finucane, B. M., & Gayley, C. (1997). Brief report: cognitive and behavioral profiles in persons with Smith-Magenis syndrome. *Journal of Autism and Developmental Disorders*, *27*(2), 203-211.

Evans, D.W., Lewis, M.D., & Iobst, E. (2004). The role of the orbitofrontal cortex in normally developing compulsive-like behaviors and obsessive-compulsive disorder. *Brain and Cognition*, *55*, 220-234.

Faja, S., & Nelson Darling, L. (2018). Variation in restricted and repetitive behaviors and interests relates to inhibitory control and shifting in children with autism spectrum disorder. *Autism*, 1362361318804192.

Fudala, J. B., Kunze, L. V., & Ross, J. D. (1974). *Auditory pointing test manual*. San Rafael: Academic Therapy Publications.

Galéra, C., Taupiac, E., Fraisse, S., Naudion, S., Toussaint, E., Rooryck-Thambo, C., ... & Bouvard, M. P. (2009). Socio-behavioral characteristics of children with Rubinstein-Taybi syndrome. *Journal of autism and developmental disorders*, *39*(9), 1252-1260.

Garon, N., Bryson, S. E., & Smith, I. M. (2008). Executive function in 16ehaviour16ers: a review using an integrative framework. *Psychological bulletin*, *134*(1), 31.

Gioia, G. A., Andrews Epsy, K., & Isquith, P. K. (2003). *BRIEF-P: Behavior Rating Inventory of Executive Function– Preschool Version, professional manual*. Lutz, FL: Psychological Assessment Resources.

Heald, M., (2010). Executive function in typically developing preschool and school age children. (Unpublished masters thesis). University of Birmingham, Birmingham, UK.

Hennekam, R. C. (2006). Rubinstein-Taybi Syndrome. *European Journal of Human Genetics*, *14*, 981–985.

Hutt, C., & Hutt, S. J. (1965). Effects of environmental complexity on stereotyped behaviors of children. *Animal Behavior*, *13*(1), 1-4.

Jones, C. R., Simonoff, E., Baird, G., Pickles, A., Marsden, A. J., Tregay, J., ... & Charman, T. (2018). The association between theory of mind, executive function, and the symptoms of autism spectrum disorder. *Autism Research*, *11*(1), 95-109.

Lee, N. R., Fidler, D. J., Blakeley-Smith, A., Daunhauer, L., Robinson, C., & Hepburn, S. L. (2011). Caregiver report of executive functioning in a population-based sample of young children with Down syndrome. *American journal on intellectual and developmental disabilities*, *116*, 290-304.

Lopez, B. R., Lincoln, A. J., Ozonoff, S., & Lai, Z. (2005). Examining the relationship between executive functions and restricted, repetitive symptoms of Autistic Disorder. *Journal of Autism and Developmental Disorders*, *35*, 445-460.

Lovaas, I., Newsom, C., & Hickman, C. (1987). Self-stimulatory behavior and perceptual reinforcement. *Journal of Applied Behavior Analysis*, *20*(1), 45-68.

Miller, H. L., Ragozzino, M. E., Cook, E. H., Sweeney, J. A., & Mosconi, M. W. (2015). Cognitive set shifting deficits and their relationship to repetitive behaviors in autism spectrum disorder. *Journal of autism and developmental disorders*, *45*(3), 805-815.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41,*49-100.

Mosconi, M. W., Kay, M., D'cruz, A. M., Seidenfeld, A., Guter, S., Stanford, L. D., & Sweeney, J. A. (2009). Impaired inhibitory control is associated with higher-order repetitive behaviors in autism spectrum disorders. *Psychological medicine*, *39*(9), 1559-1566.

Moss, J., Oliver, C., Arron, K., Burbidge, C., & Berg, K. (2009). The prevalence and phenomenology of repetitive behavior in genetic syndromes. *Journal of Autism and Developmental Disorders, 39,* 572-588.

Moss, J., Nelson, L., Powis, L., Richards, C., Waite, J., & Oliver, C. (2016). A comparative study of sociability and selective mutism in autism spectrum disorder, Angelman, Cri du Chat, Cornelia de Lange, Fragile X and Rubinstein-Taybi syndromes. *American Journal on Intellectual and Developmental Disabilities*, *121*, 465-486.

Mullen, E. M. (1995). *Mullen Scales of Early Learning*: *AGS Edition*. Circle Pines, MN: American Guidance Service.

Ng-Cordell, E., Hanley, M., Kelly, A., & Riby, D. M. (2018). Anxiety in Williams Syndrome: The Role of Social Behavior, Executive Functions and Change Over Time. *Journal of autism and developmental disorders*, *48*(3), 796-808.

Palmer, J., & Jenkins, J. (1982). The 'Wessex' behaviour rating system for mentally handicapped people: Reliability study. *The British Journal of Mental Subnormality*, *28*(55), 88-96.

Pritchard, A. E., Kalback, S., McCurdy, M., & Capone, G. T. (2015). Executive functions among youth with Down Syndrome and co-existing neurobehavioral disorders. *Journal of Intellectual Disability Research*, *59*(12), 1130-1141.

Rapp, J. T., & Vollmer, T. R. (2005). Stereotypy I: A review of behavioral assessment and treatment. *Research in developmental disabilities*, *26*(6), 527-547.

Ravizza, S. M., Solomon, M., Ivry, R. B., & Carter, C. S. (2013). Restricted and repetitive behaviors in autism spectrum disorders: the relationship of attention and motor deficits. *Development and psychopathology*, *25*(3), 773-784.

Reed, M., Pien, D. L., & Rothbart, M. K. (1984). Inhibitory self-control in preschool children. *Merrill-Palmer Quarterly*, *30*, 131–147.

Richler, J., Bishop, S. L., Kleinke, J. R., & Lord, C. (2007). Restricted and repetitive behaviors in young children with autism spectrum disorders. *Journal of autism and developmental disorders*, *37*(1), 73-85.

Rodgers, J., Glod, M., Connolly, B., & McConachie, H. (2012). The relationship between anxiety and repetitive behaviors in autism spectrum disorder. *Journal of autism and developmental disorders*, *42*(11), 2404-2409.

Royston, R., Oliver, C., Moss, J., Adams, D., Berg, K., Burbidge, C., ... & Waite, J. (2018). Brief report: repetitive behavior profiles in Williams syndrome: cross syndrome comparisons with Prader–Willi and Down syndromes. *Journal of autism and developmental disorders*, *48*(1), 326-331.

Samuels, J., Bienvenu, O. J., Krasnow, J., Wang, Y., Grados, M. A., Cullen, B., ... & Rasmussen, S. A. (2018). Self-reported executive function and hoarding in adults with obsessive-compulsive disorder. *Comprehensive psychiatry*, *81*, 53-59.

Simpson, A., & Riggs, K. J. (2005). Inhibitory and working memory demands of the day-night task in children. *British Journal of Developmental Psychology*, *23*, 471-486.

Snyder, H. R., Kaiser, R. H., Warren, S. L., & Heller, W. (2015). Obsessive-compulsive disorder is associated with broad impairments in executive function: A meta-analysis. *Clinical Psychological Science*, *3*(2), 301-330.

South, M., Ozonoff, S., & Mcmahon, W. M. (2007). The relationship between executive functioning, central coherence, and repetitive behaviors in the high-functioning autism spectrum. *Autism*, *11*(5), 437-451.

Sparrow, S., Cicchetti, D., & Balla, D. (2005). Vineland Adaptive Behavior Scales (2nd ed.). Minneapolis, MN: Pearson Assessment.

Stevens, C. A., Carey, J. C., & Blackburn, B. L. (1990). Rubinstein-Taybi syndrome: A natural history study. *American Journal of Medical Genetics*, *37*, 30-37.

Szatmari, P., Georgiades, S., Bryson, S., Zwaigenbaum, L., Roberts, W., Mahoney, W., ... & Tuff, L. (2006). Investigating the structure of the restricted, repetitive behaviors and interests domain of autism. *Journal of Child Psychology and Psychiatry*, *47*(6), 582-590.

Tregay, J., Gilmour, J., & Charman, T. (2009). Childhood rituals and executive functions. *British Journal of Developmental Psychology*, *27*(2), 283-296.

Turner, M. A. (1997). Towards an executive dysfunction account of repetitive behavior in Autism. In: Russell J. (ed.), *Autism as an Executive Disorder*. Oxford: Oxford University Press; p. 57–100.

Turner, M. A. (1999). Annotation: Repetitive Behavior in Autism: A review of psychological research. *Journal of Child Psychology and Psychiatry, 40*, 839–49.

Ursache, A., & Raver, C. C. (2014). Trait and state anxiety: Relations to executive functioning in an at-risk sample. *Cognition & emotion*, *28*(5), 845-855.

Waite., J. (2012). *The behavioral and cognitive phenotype of Rubinstein-Taybi syndrome.* (Unpublished doctoral dissertation). University of Birmingham, Birmingham, UK.

Waite, J., Beck, S. R., Heald, M., Powis, L., Oliver, C. (2016). Dissociation of Cross-Sectional Trajectories for Verbal and Visuo-Spatial Working Memory Development in Rubinstein-Taybi Syndrome. *Journal of Autism and Developmental Disorders*, *46*, 2064-2071.

Waite, J., Moss, J., Beck, S. R., Richards, C., Nelson, L., Arron, K., Berg, K., Oliver, C. (2015). Repetitive Behavior in Rubinstein–Taybi Syndrome: Parallels with Autism Spectrum Phenomenology. *Journal of Autism and Developmental Disorders*, *45*, 1238-1253.

Weschler, D. (1999). *Wechsler abbreviated scale of intelligence*. San Antonio, TX: Psychological Corporation.

Woodcock, K. A., Oliver, C., Humphreys, G. W. (2009). Associations between repetitive questioning, resistance to change, temper outbursts and anxiety in Prader-Willi and Fragile-X syndromes. *Journal of Intellectual Disability Research, 53*, 265-278.

Woodcock, K. A., Oliver, C., Humphreys, G., W. (2009). Task switching deficits and repetitive behavior in genetic neurodevelopmental disorders: Data from children with Prader-Willi syndrome chromosome 15 q11-q13 deletion and boys with Fragile-X syndrome. *Cognitive Neuropsychology*, 26, 172-194.

Yagihashi, T., Kosaki, K., Okamoto, N., Mizuno, S., Kurosawa, K., Takahashi, T., ... & Kosaki, R. (2012). Age‐dependent change in behavioral feature in Rubinstein‐Taybi syndrome. *Congenital anomalies*, *52*(2), 82-86.

Yerys, B. E., Wallace, G. L., Harrison, B., Celano, M. J., Giedd, J., Kenworthy, L. E. (2009). Set-shifting in children with autism spectrum disorders. *Autism, 13,* 523-538.

Zelazo, P. D. (2006). The Dimensional Change Card Sort (DCCS): A method of assessing executive function in children. *Nature Protocols*, *1,* 297-301.

Zelazo, P. D., & Müller, U. (2002). Executive functions in typical and atypical development. In U. Goswami (Ed.), *Handbook of childhood cognitive development* (pp. 445–469). Oxford, UK: Blackwell.

Table 1.

Descriptive statistics for executive function battery and BRIEF-P subscales.

	N	Mean (SD)	Range	% of sample once or more than once a day
RBQ: Body Stereotypy	30	2.73 (1.57)	0-4	70
RBQ: Hand Stereotypy	30	2.03 (1.81)	0-4	53
RBQ: Object Stereotypy	30	1.62 (1.73)	0-4	35
RBQ: Adherence to Routine	30	1.93 (1.72)	0-4	50
RBQ: Repetitive Questioning[a]	24	2.71 (1.81)	0-4	71
Inhibition: Buckets Task	30	7.67 (4.15)	0-12	
Inhibition: Bear-Dragon	23	3.61 (3.71)	0-8	
Inhibition: Black-White Stoop	22	10.73 (4.15)	0-16	
Working Memory: Verbal Animal Span	23	10.17 (5.69)	3-38	
Set-Shifting DCCS	22	6.36 (5.27)	0-12	
Abbreviated BRIEF-P: Inhibition	30	16.70 (4.78)	9-27	
Abbreviated BRIEF-P: Working Memory	30	15.97 (3.53)	7-21	
Abbreviated BRIEF-P: Set-Shifting	30	16.67 (5.04)	10-26	

[a] Verbal participants only
[b] *Note*. N is higher for the Animal Span than previously reported in [blinded for review] and descriptive statistics differ. This is due to the inclusion of three more able individuals in the current analysis. These individuals were excluded from the previous analysis to isolate a portion of a cross-sectional trajectory that overlapped with typically developing comparison data.
Note. N varies across tasks due to engagement of participants with the battery and the ability of participants to understand the instructions.

Table 2. Factor loadings for the BRIEF-P subscale in Rubinstein-Taybi syndrome

BRIEF-P Item	**Factor Loadings** **Working Memory**	**Shifting**	**Inhibition**
Q42. Has trouble finishing tasks (such as games, puzzles or other activities)	.809		
Q61. Has a short attention span.	.690		
Q37. Forgets what he/she is doing in middle of activity.	.633		
Q58. Gets easily sidetracked during activities.	.609		
Q27. Has trouble with activities or tasks that have more than one step.	.559		
Q51. Has trouble getting started on activities or tasks even after instructed.	.457	-.410	
Q12. Has trouble concentrating on games, puzzles, activities.	.436		
Q17. Repeats same mistakes over and over even after help is given.	.431		
Q32. Needs help from adult to stay on task.	.409		
Q10. Has trouble adjusting to new people.		-.836	
Q20. Takes a long time to feel comfortable in new places or situations (such as visiting distant relatives or new friends).		-.772	
Q45. Resists change of routine, foods, places etc.		-.711	
Q15. Is upset by a change in plans or routine (for example, order of daily activities, adding last minute errands to schedule, change in driving route to shop)		-.644	
Q40. Has trouble joining in at unfamiliar social events (such as birthday parties, picnics, holiday gatherings)		-.617	
Q25. Is bothered by loud noises, bright lights or certain smells.		-.586	
Q5. Becomes upset with new situations.		-.577	
Q30. Is disturbed by changes in the environment (such as new furniture, things in room moved around or new clothes).		-.570	
Q35. Has trouble changing activities.		-.508	
Q50. Acts overwhelmed overstimulated in crowded situations		-.503	-.480
Q38. Does not realise certain actions bother others		-.498	
Q18. Acts wilder, sillier than others in group (such as, birthday parties, class at school/college, family gatherings).			.767
Q62. Behaves carelessly or recklessly in situations where he/she could be hurt (such as playground, swimming pool).			.756
Q60. Becomes too silly.			.727
Q48. Talks or plays too loudly.			.700
Q43. Gets out of control more than peers.			.693
Q22. Makes silly mistakes on things he/she can do.			.691
Q52. Acts too wild or out of control.			.668
Q59. Has trouble remembering something even after a brief period of time.			.553
Q54. Has trouble putting the brakes on his/her actions even after being asked.			.502
Q28. Is impulsive.			.429
Q63. Is unaware when he/she performs a task right or wrong.			.405

Table 3.
Internal consistency of the BRIEF-P subscales in Rubinstein-Taybi syndrome

Subscale	**Cronbach Alpha for Current RTS Group (N = 30)**	**Cronbach Alpha for participants at ceiling on MSEL (N = 8) (MA)**
Abbreviated Inhibition	.80	.86
Abbreviated Working Memory	.87	.88
Abbreviated Shifting	.91	.86

Table 4. Correlations between age, repetitive behaviors and EF assessments.

		Age			Repetitive Behaviors		
		CA	VABS (Receptive Language)	MA (Mullen /WASI)	Questions	Stereotypy	Routines
Direct EF Assessments	Buckets Task *(inhibition)*	.56*	.70***	.80***	-.23	-.35	.15
	Bear-Dragon *(inhibition)*	.20	.32	.70***	-.85***	-.26	-.07
	Black-White Stroop *(inhibition)*	-.08	.13	.38	-.25	.18	-.14
	DCCS *(set-shifting)*	.29	.43	.41	-.12	-.30	-.07
	Animal Span *(verbal working memory)*	.33	.41	.71***	-.65***	-.25	.12
Informant Assessment (N =30)	BRIEF-P Inhibition	-.52**	-.45	-.42	.55 *[a]	.48*[a]	.27
	BRIEF-P Working Memory	-.37	-.29	-.46	.60**	.55**	.13
	BRIEF-P Set-Shifting	-.03	-.09	.06	.22.	.42	.68 ***[b]

* $p < .01$; ** $p < .005$; *** $p < .001$ (two-tailed)

[a] $p = .006$ and $p = .007$

[b] Result remained significant when items pertaining to routine were removed from the set-shifting scale ($R = .51$, $p = .004$).

Note. Abbreviated BRIEF-P subscales are reported in Table 5 analysis (as described in Methods). The analyses were repeated with the original BRIEF-P subscales and the findings remained consistent (i.e., all significant results remained significant and no further significant findings emerged).

Note. Buckets task analysis was repeated with two participants removed due to age equivalent scores < 2 years. Results remained consistent.

Note. Repetitive questions item only answered by verbal participants (N = 24).

Table 5.
Inter-correlations between repetitive behavior items

	Body Stereotypy	Hand Stereotypy	Repetitive Questions	Routines
Object stereotypy	0.31	.582**	0.46	0.22
Body stereotypy		.616***	0.24	0.05
Hand stereotypy			0.18	0.30
Repetitive Questions				0.19

*** <.001 ** <.005 * <.01 (two-tailed)

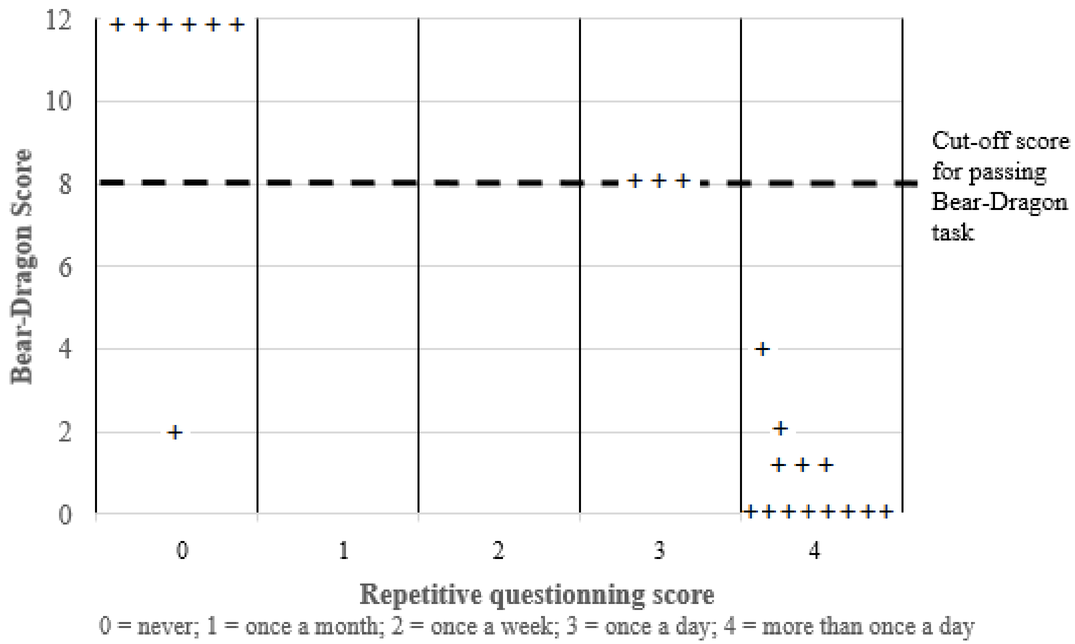

Figure 1. The number of participants who passed the Bear-Dragon task and their corresponding repetitive questioning status. Each + represents one person. A score of 8 or above represents passing this task.

Note. The binary distribution of scores on this task is consistent with what is often observed in typically developing children, whereby children tend to either fail or pass. In typical development, there is generally a shift in performance around 3-4 years of age on this task (Carlson, 2005).