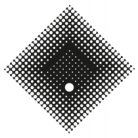
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Delineation of cross-domain associations between everyday executive function and adaptive behaviour in Down syndrome and Williams syndrome

Darren R. Hocking[1,2]✉, Elysse Byer[1] & Nancy Raitano Lee[3]

In genetic syndromes such as Down syndrome (DS) and Williams syndrome (WS), difficulties with executive functioning (EF) are a commonly reported feature and a key correlate of long-term success in everyday life. Despite a robust literature in children with these syndromes, it remains unclear how cross-syndrome characteristics of everyday EF relate to adaptive functioning and intelligence among adults with DS and WS, and if these relationships differ between these groups. This study aimed to characterise the profile of strengths and weaknesses in everyday EF using the Behaviour Rating Inventory of Executive Function-Adult Informant Version (BRIEF-A) in older adolescents and young adults with DS and WS. Associations between distinct EFs, adaptive/maladaptive functioning, and intellectual ability were also investigated. Results showed that the WS group displayed profound impairments in almost all BRIEF-A scales, with a large percentage of scores in the clinically significant range. Further, selective EFs (Inhibit, Organisation of Materials, Task Monitor) were able to discriminate between the two genetic syndromes. Contrary to previous research, in WS, Working Memory was linked to adaptive functioning and IQ. In DS, the Task-Monitor and Shift scales were unique predictors of externalising and internalising behaviours, respectively. These findings could have important implications for targeted cognitive interventions in these genetic syndromes.

In genetic syndromes associated with intellectual disability (ID) such as Williams syndrome (WS) and Down syndrome (DS), there are a range of difficulties in cognitive functioning and adaptive behaviour, which can have downstream effects on other domains and contribute to poor functional outcomes[1]. Although arising from different genetic abnormalities (WS: microdeletion of 25–28 genes on chromosome 7; DS: additional copy of chromosome 21), these neurodevelopmental disorders show some commonalities yet subtle differences at the cognitive and behavioural level. In DS, there are weaknesses in expressive language and verbal short-term/working memory relative to mental age expectations as well as a pattern of performance in which some visuospatial skills are commensurate with mental age expectations[2,3]. By contrast, WS is characterised by mild to moderate intellectual disability with relative strengths in language, verbal short-term memory and face processing accompanied by relative weaknesses in visuospatial construction, drawing, number processing and visual-motor functioning[4].

With regard to cognitive functioning, executive function (EF) consists of a variety of skills that are selectively impaired in both people with DS and WS relative to typically developing (TD) children and adults[5,6]. EF is an umbrella term for a set of top-down cognitive skills that enable an individual to concentrate when presented with novel, distracting, or conflicting task demands, and when automatic or instinctual processes would be insufficient[7]. It is generally accepted that three core EFs include the ability to deliberately suppress automatic responses and override internal or external distractions ('inhibition'), to shift between tasks ('shifting'), and to track incoming information to determine what is new or relevant to a task ('updating') in working memory[8,9]. These interrelated set of abilities form the basis for high-level cognitive functions such as reasoning, planning, problem solving and organisational skills[7].

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Research employing both performance-based measures of EF skills as well as informant-report measures of everyday EF difficulties among individuals with DS indicate that this group presents with difficulties in multiple domains, consistent with the limited neuroimaging data available documenting atypical frontal lobe morphometry[10] and connectivity[11] As reviewed in Lee, Maiman and Godfrey[12], studies employing performance-based EF measures provide consistent evidence for challenges in working memory and cognitive flexibility that exceed global learning difficulties in DS. The extant studies using informant report measures have consistently demonstrated that children with DS show selective impairments in EF, especially in the domains of working memory as well as planning/organisational skills[6,13]. By contrast, other studies have found evidence for relative strengths in emotional control and shifting[13], and inconsistent evidence for deficits in inhibitory control[51]. For example, using the parent report of the Behavior Rating Inventory of Executive Function (BRIEF) rating scales, Loveall et al.[6] examined the EF profile in a cross-sectional analysis of everyday EF in individuals with DS aged from 2 to 35 years. Although younger children from 2 to 5 years exhibited relative strengths in emotional control and shifting, the older children from 6 to 18 years showed relative weaknesses in shifting, planning/organisation, and working memory[6]. These findings indicate that selective EF components may worsen over time perhaps due to age-related changes in EF abilities and/or greater demands for age-appropriate behaviour in individuals with DS.

In people with WS, impairments in EF have been shown to be affected by significant deficits on visuospatial versus verbal tasks and include difficulty in inhibiting a prepotent response[14,53], set-shifting[15], and visuospatial working memory[16,17]. Importantly, deficits in response inhibition have been linked to reduced activation of frontostriatal circuits in adults with WS[52], which may explain difficulty in inhibition of inappropriate social behavior. With reference to higher-level EF, several studies using performance-based tasks have also demonstrated impairments in planning abilities in WS compared to DS and verbal mental-age matched TD controls[15,16]. Using informant-based measures of EF, several studies using the BRIEF (both Adult, BRIEF-A and Child, BRIEF-C versions) have reported selective weaknesses in working memory, planning and task monitoring, alongside relative strengths in behaviour and emotional regulation in children, adolescents, and young adults with WS[5,18,19].

With regard to cross-syndrome studies, one previous study found that adolescents and young adults with WS showed poorer performance on almost every scale (with a higher percentage in the clinically significant range) on the BRIEF-C when compared to spatial ability-matched individuals with DS and TD controls[18]. On performance-based EF tasks, some evidence suggests that impairments in selective EF components within the visuospatial domain appear to be more pronounced in children and adolescents with WS when compared to DS and mental age-matched TD controls[53]; however, another study found that children and adults with WS aged 10 to 34 years outperformed a comparison group with DS on inhibition, shifting, verbal memory, and nonword repetition[15]. These inconsistent findings may be a result of the combination of different age groups, the type of performance-based measures used, and/or differences in EFs within experimental settings compared to parent reports of behaviour in daily life.

Adaptive behaviour (AB) is another aspect of functioning with core impairments in people with DS and WS[20]. AB refers to the practical, conceptual, and social skills that are needed to meet age-appropriate demands in the environment. AB is a critical component in the diagnosis and evaluation of the severity of ID and determines the level of support required. The profile of AB in adults with DS is characterised by relative strengths in social skills with deficits in communication and practical skills[21]. However, studies across these two genetic syndromes have reported relationships between specific EFs and AB in children, adolescents, and young adults[5,13,19]. For example, working memory on the BRIEF-C has been found to be strongly associated with several domains of AB in children and adolescents with DS[13,22]. Yet, this relationship appears to vary with age, with another study showing that the EFs of inhibition and shifting were more strongly associated with selective domains of AB (Daily Living Skills, Socialisation) in older adolescents with DS[23].

Relations between distinct components of EF (e.g., emotional control) and maladaptive externalising behaviours (e.g., aggression, impulsivity) have also been found in young adults with WS[5]. Another study in a large sample of children and adolescents with WS showed that higher scores on behaviour and emotional regulation on the BRIEF were significantly correlated with most of the scales for adaptive and externalising behaviours[19]. However, there is a relative dearth of research on everyday EF and its relation to AB using cross-syndrome designs including both WS and DS, to tease apart convergences and divergences across EF profiles in these two genetic syndromes.

Another area of investigation relates to how each core EF is associated with intellectual functioning, however there is limited research in this area in people with DS and WS. Working memory has been identified as a core EF related to intelligence or logical thinking in children and adolescents with DS[24]. Contrastingly, other studies have reported that the EF of shifting was significantly correlated with Full Scale IQ in children and young adults with WS[5,19], but see Osorio et al.[25] for conflicting findings using performance-based EF tasks in WS.

Given these discrepant findings, it is important to characterise and compare distinct EF profiles across DS and WS so that potential mechanisms for success or failure on daily living tasks can be identified. The issue of the low correspondence between performance-based and rating scale measures of EF has been previously recognised in paediatric populations[26,27]. For example, common performance-based tests of EF may not properly represent the cognitive demands of real-world situations[28]. As research examining the development of EF in the general population suggests continued maturation of these skills during late adolescence and into early adulthood[29], studies during this developmental period are important for accurate characterisations of EF skills and their relations to adaptive behaviour in people with DS and WS. Further, among individuals with DS, research indicates that some aspects of cognition become increasingly deviant from age expectations over the course of development[12]. Given this developmental trajectory alongside research suggesting that executive dysfunction is an indicator of preclinical Alzheimer's dementia among older adults with DS[30], there is an even

greater need to characterise everyday EF skills among young adults with DS prior to possible onset of cognitive decline.

As research studies of everyday EF difficulties are limited in adolescents and young adults with DS and WS, the aim of the current study was therefore to delineate the pattern of relative strengths and weaknesses in EFs using the BRIEF-A rating scale in older adolescents and young adults with DS and WS. Another aim was to examine the relations between distinct components of EF and intellectual ability on a standardised measure of IQ across these two syndrome groups. The final aim was to explore the relationships between parent reported EFs as measured on the BRIEF-A and adaptive skills for everyday life across DS and WS. Given evidence of profound weaknesses in almost all EF domains in WS[18], it was predicted that the WS group would demonstrate a flat profile of EF impairments when compared to DS. We also hypothesised that the EF component of shifting will be more strongly related to IQ in WS[5,19], but no specific prediction will be made for the DS group given the lack of previous research. Regarding the relationships between EFs and adaptive behaviour, we hypothesised that working memory and behaviour/emotional control will be associated with adaptive skills in DS[13,22] and WS[5,19], respectively.

Method

Participants

The sample consisted of 32 adolescents and young adults with DS aged 15 to 35 years (M = 26.09, SD = 5.62), and 20 chronological age-matched participants with WS aged 16–39 years (M = 25.45, SD = 7.03). There were no significant differences in chronological age between the groups ($t(50) = 0.365$, $p = .717$). Participants were recruited as part of a baseline assessment across two studies (a feasibility study and a randomised controlled trial) examining the effects of an exercise intervention on executive function in DS. Convenience sampling was used to source participants from a stepped wedged trial of a community-based exercise program for young people with disability (ACTRN12617000766314), the FitSkills program (a fee-for service program at La Trobe University), Down Syndrome Victoria or a research database of the Developmental Neuromotor & Cognition Lab at La Trobe University. Most participants karyotype of DS was identified as trisomy of chromosome 21, others as translocation of chromosome 21, and one as mosaicism. Participants with WS were recruited through the Williams Syndrome Family Support Group (Victoria), the Williams Syndrome Association Australia, and an established research database at La Trobe University. WS diagnosis was confirmed by clinicians, as well as with fluorescent in situ hybridisation (FISH) testing for deletion of the elastin gene on chromosome 7.

Participants with DS were excluded from the sample if (1) they could not speak or understand English; (2) had previous participation in an exercise program within three months prior to recruitment that may interfere with the effects of the intervention; and (3) any acute or concurrent medical condition making the participant unfit to participate in exercise. Participants were screened for dementia and early cognitive decline using the NTG – Early Detection Screen for Dementia[31]. This ensured that cognitive decline would not impact performance on the measures of executive and adaptive functioning, and no participants showed any sign of dementia or early cognitive decline. Participants with WS were excluded from the study if (1) they could not speak fluent English; and (2) had visual defects (e.g., amblyopia, reduced visual acuity) and musculoskeletal problems (e.g., severe joint contractures).

The mental age and IQ of each of the DS participants was obtained by the Kaufman Brief Intelligence Test, Second Edition (KBIT-2[32]) and the Woodcock Johnson III Tests of Cognitive Abilities (WJ III COG[33]) was used for participants with WS. Full Scale IQ equivalent scores were lower in the DS group compared to the WS group ($t(45) = -5.27$, $p < .001$) (Table 1). The DS group had both lower verbal and non-verbal mental ages when compared to the WS group (verbal MA: $t(49) = -5.93$, $p < .001$; non-verbal MA: $t(45) = -5.41$, $p < .001$). The DS group also showed lower adaptive functioning on the VABS-II Adaptive Behaviour Composite relative to the WS group ($t(47) = -4.18$, $p < .001$). There were no differences in the distribution of males and females between the DS (17 female, 15 male) and WS (9 female, 11 males) groups.

Ethics approval for this study was obtained from the La Trobe Human Research Ethics Committee (HEC 18052) and Monash University Research Ethics Committee (2011_001134). Written informed consent was obtained from the parents/guardians of participants with DS aged 15–17 years, and written assent was obtained from participants who were not able to provide their own informed consent. An adapted version of the consent form for lower reading level was provided to participants to improve their understanding of the study's purpose and their participation rights. Participants were able to withdraw at any time and have their data removed from the study within 4 weeks of the completion of the data collection. All procedures were performed in accordance with the National Statement on Ethical Conduct in Human Research (NHMRC, 2018) and the declaration of Helinksi.

Materials

Behaviour rating inventory of executive function – adult version (BRIEF-A[34]) The BRIEF-A informant report was completed by parents/caregivers and used to examine everyday executive functioning in adults aged 18 to 90 years. The BRIEF-A consists of 75 items within 9 distinct scales and combine to form two indices. The Behaviour Regulation Index (BRI) includes the subscales of Inhibit, Shift, Emotional Control and Task Monitor. The Metacognition Index (MI) includes the subscales of Initiate, Working Memory, Plan/Organise, Organisation of Materials and Task Monitor. These indices produce chronological age-based T scores (M = 50, SD = 10), and a Global Executive Composite (GEC) provides an overall summary score. Given the BRIEF-A has been found to be a more valid measure of EF in adults with WS than the school-aged version of the BRIEF[5], the BRIEF-A was used in both adults with WS and DS. The BRIEF-A also has a high internal consistency, with alpha coefficients ranging from 0.80 to 0.98, as well as high test-re-test reliability[34]. Higher scores indicate greater difficulties in

	Participants ($N=52$)	
	DS ($n=32$)	WS ($n=20$)
Age (yr) Mean (*SD*)	26.09 (5.62)	25.45 (7.03)
Age range (yr)	15 to 35	16 to 39
Gender, female	17	9
Gender, male	15	11
KBIT – 2 – IQ standard score (*SD*)	46.42 (7.43)	
KBIT – 2 – IQ standard score range	40 to 71	
KBIT – 2 – Verbal MA (yr and month) Mean (*SD*)	6.45 (1.94)	
KBIT – 2 – Verbal MA range (yr and month)	4.00 to 10.40	
KBIT – 2 – Non-Verbal MA (yr and month) Mean (*SD*)	4.98 (1.04)	
KBIT – 2 – Non-Verbal MA range (yr and month)	4.00 to 9.09	
WJ III COG – IQ standard score (*SD*)		64.38 (12.03)
WJ III COG – IQ standard score range		32 to 89
WJ III COG – Verbal MA (yr and month) Mean (*SD*)		10.12 (2.45)
WJ III COG – Verbal MA range (yr and month)		6.08 to 15.75
WJ III COG – Non-Verbal MA (yr and month) Mean (*SD*)		7.28 (1.90)
WJ III COG – Non-Verbal MA range (yr and month)		5.50 to 11.50
VABS – Adaptive Behaviour Composite standard score, Mean (*SD*)	56.21 (15.11)	71.55 (7.58)
VABS – Adaptive Behaviour Composite standard score range	20.00 to 79.00	58.00 to 91.00
VABS – Maladaptive Behaviour Index V-score, Mean (*SD*)	17.88 (2.21)	16.30 (4.08)
VABS – Maladaptive Behaviour Index V-Score range	15.00 to 24.00	12.00 to 24.00

Table 1. Sample characteristics *Note*. KBIT-2 = Kaufman Brief Intelligence Test, Second Edition; WJ III COG = Woodcock-Johnson III Test of Cognitive Abilities; VABS-II = Vineland Adaptive Functioning Scales – 2nd edition

executive functioning, with scores at or above 65 indicating the presence of clinically significant executive dysfunction.

Behaviour rating inventory of executive function – child version (BRIEF-C[54]) The BRIEF-C (original version) is a parent report measure designed to assess EF of children ages 5 to 17 years. The BRIEF-C contains 86 items and 8 subscales, which combine to the same indices and the GEC as the BRIEF-A, producing aged-based T scores (M = 50, SD = 10). The BRIEF-C includes a subscale of Monitor, which measures the ability to evaluate one's own work and behaviour, but it does not include the Task Monitor (evaluating one's own problem solving) subscale included on the BRIEF-A. Given that only three participants in the DS group were given the BRIEF-C, scores for Monitor were not included in analyses pertaining to these subscales. The BRIEF-C evaluates EF skills in both the home and school environment using parent ratings on a Likert-type scale for behaviours exhibited by the child over the last 6 months. The BRIEF-C has high internal consistency (0.80–0.98) and test-retest reliability (0.82–0.88)[54]. BRIEF-C scores at or above 65 suggest clinically significant impairment in executive functioning.

Kaufman brief intelligence test – 2nd edition (KBIT-2[32]) The KBIT- 2 measures cognitive ability across ages 4 to 90 years and was only administered in the DS group. The KBIT-2 is a revision of the KBIT that intended to address the KBIT's weakness of reliance on verbal abilities[35]. The KBIT-2 uses the CHC theory of two types of intelligence to analyse crystallised (verbal) and fluid (non-verbal) intelligence through 3 matrices (verbal knowledge, matrices, riddles)[32]. The KBIT-2 has high test-retest reliability ($r=0.94$) and split-half reliability scores of 0.91 for nonverbal scales and 0.90 for verbal scales[32]. High correlations between the composite IQ scores of KBIT-2 and the Wechsler Abbreviated Scale of Intelligence demonstrate concurrent validity of the KBIT-2[36].

Woodcock-Johnson III tests of cognitive abilities, Australian adaptation—WJ III COG The WJ III COG is a standardised measure of intelligence designed for individuals aged 2 to 90 years and was only administered in the WS group. The WJ III COG is based on the Cattell-Horn-Carroll (CHC) theory proposing two types of intelligence: fluid (G*f*) and crystallised (Gc) intelligence[37]. The WJ III COG comprises seven broad abilities including Long-Term Retrieval (visual-auditory learning), Short-Term Memory (numbers reversed), Processing Speed (visual matching), Auditory Processing (sound blending), Visual-Spatial Thinking (spatial relations), Comprehension-Knowledge (verbal comprehension), and Fluid Reasoning (concept formation). The WJ III COG provides an overall General Intellectual Ability (GIA) or single g factor, which is analogous to the Full-Scale IQ (FSIQ) of the Wechsler Scale of Intelligence. The raw scores on the WJ III COG can be converted to standard scores (M = 100, SD = 15) based on the age of the individual. Lower scores are indicative of greater cognitive deficits. WJ III COG is psychometrically sound with reliability coefficients above 0.80, and median reliabilities for each cluster are typically at 0.90 or higher[38].

Vineland adaptive behaviour scales – 2nd edition (VABS-II[39]) The VABS-II is a measure of adaptive function with the parent/caregiver ratings used in the current study. The VABS-II measures adaptive functioning in four domain composites (communication, daily living skills, socialisation, and motor skills), and 11 subdomains. The domain composites combine to create an adaptive behaviour composite, while the raw scores of the subdomains are converted into standard scores. Additionally, externalising and internalising behaviours are combined to create the maladaptive behaviour composite. These include externalising behaviours such as aggressive outbursts, defiance, impulsivity, or self-harm, and internalising behaviours such as excessive worrying, avoidance, fearfulness, or moodiness. Lower domain scores indicate greater impairments in adaptive functioning. Test-retest reliability was found to be high, ranging between 0.74 and 0.98 for the maladaptive behaviour subscales and index, and between 0.76 and 0.92 across the remaining domains[39].

Procedure

Participants with DS attended a neuropsychological assessment at the baseline testing session of a pilot study and a randomised controlled trial of a community-based exercise program to improve executive function in individuals with DS during the period of 2018 to 2020[40]. The measures were completed in one assessment session, which lasted between 90 and 120 min. The assessment session was conducted at the Developmental Neuromotor and Cognition Lab at La Trobe University, and other locations chosen by the participants such as community libraries, schools, or the participant's home. To avoid fatigue, breaks were offered to participants between measures, and they were informed of their right to withdraw from the assessment session at any time. The first measure completed was the KBIT-2. Participants sat at a table across from the examiner. During the neuropsychological assessment, parents/guardians of the participants completed informant measures of the BRIEF-A and the VABS-II. The WS group were tested as part of a larger study on dual-task gait interference in DS and WS[41], which included a broad battery of performance-based neuropsychological tests. For both DS and WS groups, the informant measures were either completed on a table separate from the participant or completed at home and returned via a reply-paid envelope. Participants were reimbursed with a $30 gift card for their time and effort after completing the assessment session.

Data analysis

Power analysis was conducted using G*Power 3.1.9.7[42] and indicated a sample size of 84 (for correlational analysis) was needed to achieve an adequate power level of 80% with a medium effect size (d = 0.5). This study was therefore underpowered with a sample size of 52 in the DS and WS groups. Thus, significance was set at 0.05 for all analyses to minimise the rate of Type II error, but statistical significance was interpreted relative to effect sizes (r2, rho2, η2p; 0.01 = small, 0.09 = medium, 0.25 = large)[43]. In the case of results with smaller effect sizes and probability coefficients closer to the set alpha level, results were interpreted with caution[44].

Missing cases were identified from frequencies and a missing values analysis was conducted to determine missing cases completely at random and missing cases were excluded pairwise during analyses. Normality of all variables were checked using the Shapiro-Wilk test, as well as histograms, boxplots, normal Q-Q plots, skewness, and kurtosis. Univariate outliers were winsorized at above or below the 95th and 5th percentile, respectively. The assumptions of normality, linearity and homoscedasticity of residuals were met by way of normal P-P plots and scatterplots.

To examine group differences across BRIEF-A scales, clinical indexes and GEC, a series of independent samples t-tests were conducted, and followed up with Analysis of Covariance (ANCOVA) with IQ as the covariate. To explore whether the pattern of EF performance was distinctive across DS and WS, Discriminant Function Analysis was conducted to determine how the relationships among BRIEF-A clinical scales differentiated the groups. To establish the combinatory value of each EF scale, canonical variate correlations (i.e., zero-order correlations with a discriminant function representing substantive contributions) and standardised discriminant coefficients (i.e., partial correlations with a discriminant function representing unique contributions) with values ≥ 0.3 were examined.

To examine associations between BRIEF-A clinical scales and IQ or adaptive functioning, Pearson's product moment correlations were conducted in the case of normal distributions of each variable, or Spearman's Rank Correlation Coefficients where non-normal distributions were identified. We used these initial analyses to select the specific scales of the BRIEF-A to examine in more detail using linear multiple regression. We carried out separate hierarchical linear regressions with chronological age and IQ at the first step, and BRIEF-A scales identified as moderately correlated ($r > .40$) were entered at the second step for predicting adaptive or maladaptive functioning (internalising and externalising behaviours) in DS and WS groups. The assumptions of singularity and multicollinearity were met ($r < .7$), and inspection of residual scatterplots indicated assumptions of normality, linearity, homoscedasticity, and independence of residuals were also met. Cook's distances were less than one and values of the standardized residuals were between −3 and 3. An alpha level was set at $p < .05$ for all analyses.

Results

Profile of strengths and weaknesses in everyday EF in DS and WS

In relation to our first objective, the results showed a much higher percentage of T scores above the clinical cut-off indicating clinically significant executive dysfunction (Inhibit, Initiate, Plan/Organise, Task-Monitor, Metacognition index, Global Executive Composite) in the WS group when compared to the DS group (Table 2). This showed that the WS group had poorer executive functioning across several BRIEF-A clinical scales including Inhibit, Plan/Organise, Task Monitor, Organisation of Materials, and Working Memory, relative to the DS group. The WS group also showed greater executive dysfunction on the Behavior Regulation Index, Metacognition

	Down syndrome		Williams syndrome		
	Mean (*SD*) Range	% in clinically significant range	Mean (*SD*) Range	% in clinically significant range	*t*(df), *p d*
Inhibit	47.90 (11.56) 2–68	6.68%	57.68 (10.58) 39–76	31.58%	-2.98(47), **0.005**, − 0.87
Shift	60.43 (11.80) 38–87	43.33%	63.32 (11.39) 43–84	52.63%	− 0.844(47), 0.403, − 0.25
Emotional Control	50.30 (12.74) 7–79	10%	57.26 (12.07) 40–81	26.32%	-1.90(47), 0.063, − 0.56
Behaviour Regulation Index	53.13 (10.00) 38–83	13.33%	59.53 (11.52) 42–83	21.05%	-1.99(47), **.045**, − 0.60
Initiate	53.87 (15.22) 6–81	16.67%	61.74 (10.05) 42–80	47.37%	-1.99(47), 0.052, − 0.58
Working Memory	58.10 (15.28) 6–95	30%	66.79 (12.00) 41–86	47.37%	-2.01(47), **0.041**, − 0.62
Plan/Organise	58.00 (8.85) 40–77	26.67%	66.26 (11.96) 40–88	52.63%	-2.78(47), **0.008**, − 0.81
Organisation of materials	51.53 (11.88) 37–74	20%	63.53 (8.83) 45–75	57.89%	-3.78(47), < **0.001**, − 0.81
Task Monitor	56.70 (11.01) 41–88	23.33%	67.22 (15.19) 41–93	61.11%	-2.78(45), **0.008**, − 0.78
Metacognition	55.33 (14.58) 5–86	20%	65.63 (10.78) 46–83	50%	-2.65(47), **0.011**, − 0.78
Global Executive Composite	55.53 (11.31) 39–88		61.80 (10.73) 44–83	35%	-1.96(47), **0.028**, − 0.56

Table 2. T-scores for the BRIEF-A scales and percentages of scores in the clinically significant range for DS and WS groups. # Three participants in the DS group were administered the BRIEF-C, and hence scores were not available for the Task Monitor clinical scale, which is reflected in lower degrees of freedom.

	Function 1
BRIEF Inhibit	**0.928**
BRIEF Organisation of Materials	**0.653**
BRIEF Task Monitor	**0.648**
BRIEF Shift	**0.498**
BRIEF Initiate	**0.482**
BRIEF Emotional Control	0.288
BRIEF Working Memory	0.282
BRIEF Plan/Organise	0.128

Table 3. Standardised canonical discriminant function coefficients.

Index and Global Executive Composite when compared to the DS group (see Table 2). Notably, the pattern of results did not substantially change when adjusting for group differences in IQ using ANCOVA.

To establish whether the distinct EF components predicted DS and WS group membership based on the pattern of performance, a Discriminant Function Analysis was conducted on the BRIEF-A clinical scale scores. One function was identified, and correctly discriminated the groups (L = 0.568, X^2 (9) = 22.36, $p = .008$), explaining 53.1% percent of the variance (canonical $R^2 = 0.657$). Table 3 provides a summary of the highest standardised discriminant coefficients for the BRIEF-A subscales in descending order. This shows that this function was substantiated largely by Inhibit, Organisation of Materials and Task Monitor scales in discriminating between DS and WS groups.

Relationships between everyday EF and IQ across DS and WS

Considering our second objective, the results showed that FSIQ on the WJ III COG was negatively correlated with the BRIEF-A Working Memory scale, ($r = -.568$, $p = .022$) (see Fig. 1). This shows that lower IQ was associated with poorer working memory in the WS group. There were no significant correlations between Total IQ on the KBIT-2 and any of the BRIEF-A clinical scales, indexes, or composite scores in the DS group (Table 4).

Associations between adaptive functioning, maladaptive behaviour, and everyday EF across DS and WS

Regarding our third hypothesis, there was a strong negative correlation between BRIEF-A Working Memory and the VABS-II Adaptive Behaviour Composite in the WS group ($r = -.649$, $p < .01$). The BRIEF-A Plan/Organise and Metacognition Index also showed moderate negative associations with the Adaptive Behaviour Composite in WS (Plan/Organise: $r = -.463$, $p = .046$; Metacognition: $r = -.480$, $p = .038$). In the DS group, there were

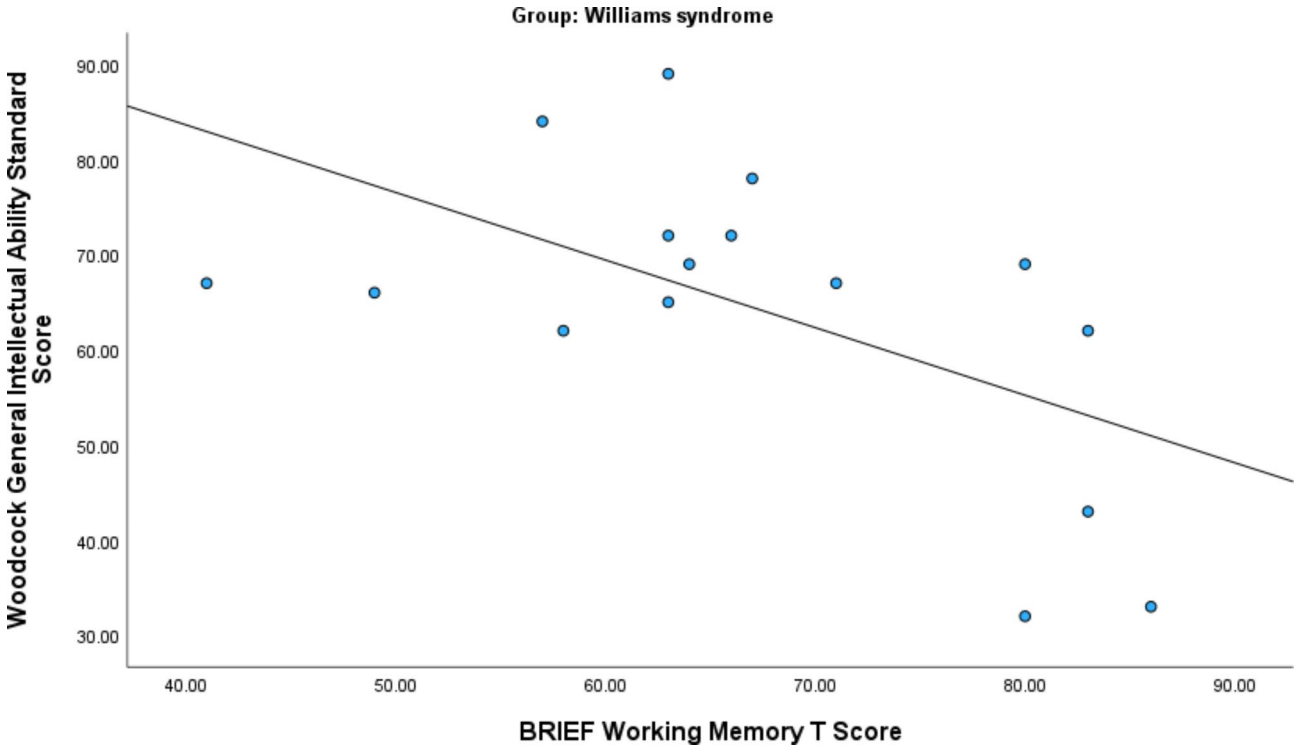

Fig. 1. Scatterplot illustrating the correlation between IQ and BRIEF-A Working Memory score in the WS group.

	KBIT-2 IQ standard store (DS)	WJ III COG standard score (WS)
	r (p)	*r (p)*
Inhibit	−0.103 ($p = .596$)	−0.353 ($p = .180$)
Shift	−0.042 ($p = .830$)	−0.381 ($p = .145$)
Emotional Control	0.007 ($p = .971$)	−0.209 ($p = .438$)
Behaviour Regulation Index	−0.048 ($p = .806$)	−0.287 ($p = .281$)
Initiate	−0.083 ($p = .667$)	−0.391 ($p = .135$)
Working Memory	−0.165 ($p = .393$)	**−0.568* ($p = .022$)**
Plan/Organise	−0.232 ($p = .225$)	−0.304 ($p = .252$)
Organisation of Materials	−0.081 ($p = .675$)	0.033 ($p = .904$)
Task Monitor	−0.178 ($p = .355$)	−0.305 ($p = .268$)
Metacognition Index	−0.068 ($p = .728$)	−0.397 ($p = .128$)
Global Executive Composite	−0.040 ($p = .836$)	−0.220 ($p = .207$)

Table 4. Correlations between IQ standard scores and BRIEF-A scales, indexes and Global Executive Composite score. Note: r = Pearson's correlation coefficient, ** $p < .01$, * $p < .05$. KBIT-2 = Kaufman Brief Intelligence Test, Second Edition; WJ III COG = Woodcock-Johnson III Test of Cognitive Abilities.

moderate negative correlations between the VABS-II Adaptive Behaviour Composite and the BRIEF-A subscales, Shift ($r = -.393$, $p = .035$), Task Monitor ($r = -.456$, $p = .017$), and Initiate ($r = -.405$, $p = .029$) (see Table 5).

Next, we explored the relationships between the BRIEF-A scores and internalising or externalising behaviours from the Maladaptive Behaviour Index. In the DS group, this analysis showed moderate positive correlations between the BRIEF-A Behaviour Rating Index and both internalising ($r = .462$, $p = .012$), and externalising behaviours (rs = .514, $p < .01$). There was also a moderately strong positive correlation between BRIEF-A Shift and internalising behaviours ($r = .596$, $p < .01$) (see Fig. 2A). For externalising behaviours, a moderate positive correlation was observed with the BRIEF-A Emotional Control (rs = .527, $p = .003$) and Task Monitor (rs = .573, $p = .002$) scales (Fig. 2B). There were no significant correlations between any BRIEF-A scores and internalising or externalising behaviours in the WS group.

Table 6 presents the results of multiple linear regression to examine the contribution of BRIEF-A clinical scales as predictors of internalising/externalising behaviour in the DS group. The variables identified as a

	Inhibit	Shift	Emotional Control	Task Monitor	Behaviour Regulation Index	Initiate	Working Memory	Plan/Organise	Organisation of Materials	Metacognition	Global Executive Composite
Adaptive Behaviour Composite											
DS (*r*)	−0.016	**−0.393***	−0.346	**−0.456***	−0.296	**−0.405***	−0.304	−0.307	−0.200	−0.267	−0.270
WS (*r*)	−0.329	−0.196	−0.275	−0.289	−0.313	−0.313	**−0.649****	**−0.463***	−0.092	**−0.480***	−0.171
Internalising Behaviour											
DS (*r*)	0.081	**0.596****	**0.461***	0.325	**0.462***	0.316	0.288	0.186	0.200	0.301	0.226
WS (*r*)	−0.133	0.287	0.021	0.025	0.042	0.209	−0.234	0.096	0.298	0.021	−0.281
Externalising Behaviour											
DS (r_s)	**0.460***	0.323	**0.423***	**0.573****	**0.514****	0.329	**379***	0.250	0.323	0.325	**0.383***
WS (*r*)	−0.300	0.133	0.025	−0.297	−0.093	0.098	−0.025	−0.109	−0.020	−0.250	−0.013

Table 5. Correlations between BRIEF-A scales, indexes, overall composite, and VABS-II adaptive, internalising/externalising behaviours in DS and WS. *Note*: ** $p < .01$, * $p < .05$, Spearman Rho (r_s) used for Externalising Behaviour correlations in DS group.

moderate to large association in the correlational analysis were included in the regression model. In Step 1, neither age nor IQ were related to internalising or externalising behaviours. In Step 2, the BRIEF-A Task Monitor scale was a significant predictor of externalising behaviours ($\beta = 0.696$, $p < .001$), while the BRIEF-A Shift scale was the strongest predictor of internalising behaviours ($\beta = 0.574$, $p = .005$), which accounted for 42.6% and 35.5% of the variance, respectively.

Discussion

Although there is a large body of literature characterising everyday EF skills in children with DS and WS, research on this topic among adults with these genetic syndromes is scant as are comparisons of the two groups on informant report measures of EF skills. Thus, the current study addressed this gap in the literature by comparing the profile of relative strengths and weaknesses on everyday EFs, and relationships with IQ and adaptive functioning, in adolesents and young adults with DS and WS. In line with our first objective, the current results were consistent with the hypothesis that the WS group would display a flat profile of weaknesses across multiple EFs, with a larger percentage of scores in the clinically significant range relative to DS. Further, these results corroborate previous reports of selective EFs (Inhibition, Organisation of Materials) that appear to differentiate between individuals with WS and DS[18]. Regarding the relation between each core EF and intellectual ability, the finding that working memory was associated with variation in IQ in WS was not consistent with our hypothesis. However, in the DS group, selective EFs (Shift, Task Monitor) were associated with internalising and externalising behaviours, respectively. These findings may have important implications for detection of everyday EF difficulties as an early sensitive marker for onset of cognitive decline in older adults with DS.

The results of the current study revealed that the average degree of difficulty with specific areas of EF in the WS group was consistent with previous studies using the BRIEF-2 parent or BRIEF-A informant report[5,19]. Further, there was a substantially increased percentage of individuals with WS meeting the criteria for clinically significant executive dysfunction, with relative weaknesses in Task Monitor (61%), Organisation of Materials (58%), Initiate (47%) and Working Memory (47%) scales. In contrast, the DS group showed relative weaknesses in BRIEF-A Shift (43%), Working Memory (30%), and Plan/Organise (27%) scales, which is consistent with previous studies using the BRIEF-C in children and adolescents with DS[6], but not with other studies that found relative strengths in shifting in younger children with DS[13]. One explanation for the discrepancy between these findings and those of Daunhauer et al.[13] may relate to the older adolescents and adults included in the current study while preschool aged children were included in the latter study. Thus, the items on the BRIEF adult versus preschool versions would be different and determine how parents report on EFs for their child.

To further explore specific EF components differentiating between DS and WS, a discriminant function analysis was conducted and revealed that Inhibit, Organisation of Materials, and Task Monitor scales were the highest in discriminating between the two genetic syndromes. The results are partly consistent with a previous study that identified Organisation of Materials as the most highly loading factor in discriminating adolescents with DS from WS and TD controls[18]. However, our results suggest that inhibition and task-monitoring appear also to be sensitive at discriminating between WS and DS. These findings could have important implications for interventions that target EF strengths (DS: inhibition, emotional control; WS: task-monitoring) to build upon areas of relative weakness and improve daily living skills across these genetic syndromes.

In relation to the hypothesis of a significant relationship between flexibility in changing set and intelligence in WS, the current results did not support this prediction. Specifically, the results of the current study revealed that the BRIEF-A Working Memory scale was significantly related to general intellectual ability in the WS group. This finding sits at odds with previous studies[5,19], but is consistent with a prior study that used performance-based assessments of EF in children and adolescents with WS[25]. These inconsistencies might relate to the difference in measures of overall intellectual ability used across these studies: the Differential Abilities Scales-II[19], Weschler Preschool and Primary Scale of Intelligence[25], and the WJ III COG[5]. Additionally, while some studies had a wide age range of children and adolescents with WS[19,25], the current study used a sample of older adolescents

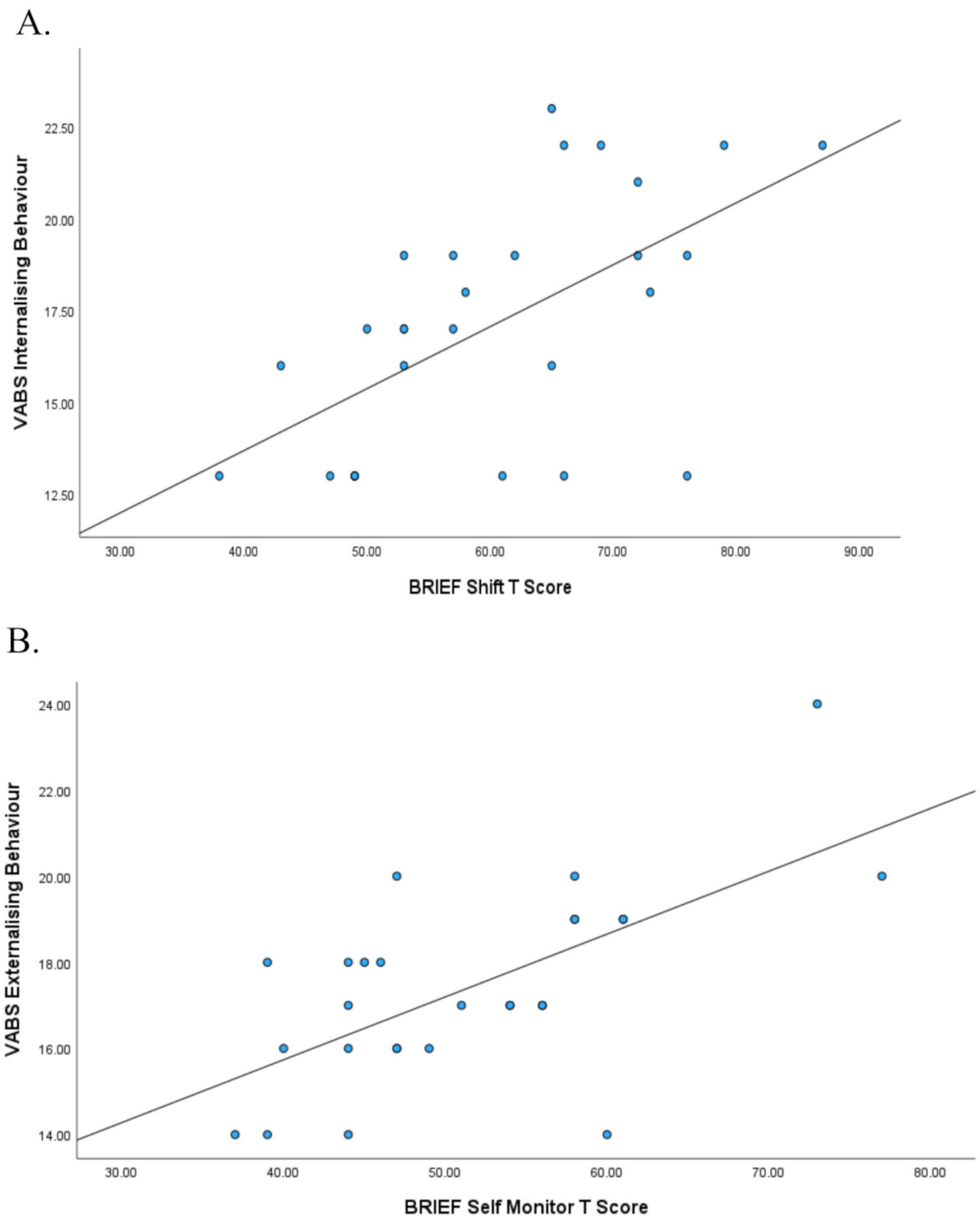

Fig. 2. Scatterplots illustrating the correlations between BRIEF-A clinical scales and internalising/externalising behaviour on VABS-II for the DS group.

	Internalising behaviours				*Externalising behaviours*			
Predictor	***B***	***SE B***	***β***	***sr²***	***B***	***SE B***	***β***	***sr²***
Age	0.079	0.084	0.196	0.038	0.058	0.102	0.119	0.014
IQ	−0.018	0.060	−0.064	−0.065	0.009	0.061	0.032	0.001
Inhibit[1]	0.080	0.121	0.080	0.072	0.022	0.117	0.022	0.019
Shift[2]	0.171	0.045	0.596**	0.355	1.241	0.528	0.258	0.241
Monitor[3]	-	-	-	-	0.158	0.039	0.696**	0.426
Emotional[4]	0.101	0.075	0.300	0.071				
R^2 (adjusted R^2)	0.462 (0.365)				0.436 (0.359)			
F	4.731**				5.663**			
ΔR^2	0.462				0.420			
F for ΔR^2			4.731**		16.375**			

Table 6. Multiple regression analyses for BRIEF-A scales predicting internalising and externalising behaviours in the DS group. *$p < .05$. **$p < .01$, [1]BRIEF-A Inhibit; [2]BRIEF-A Shift; [3]BRIEF-A Task Monitor; [4]BRIEF-A Emotional Control.

and adults with WS and DS and employed different measures of IQ across the two groups (KBIT-2, WJ III COG). This may provide an explanation of the current finding of a lack of association between specific EF scales and overall intellectual ability in the DS group, which differs from previous studies using performance-based measures where a significant relationship between verbal working memory and IQ was revealed in children and adolescents with DS[24].

Regarding the relationships between specific EFs and AB domains, we hypothesised an association between working memory and AB in adolescents and young adults with DS. On the contrary, the current findings showed a strong negative correlation between BRIEF-A Working Memory and AB in the WS group, which is not consistent with previous studies in children and adults with WS[5,19]. Interestingly, however this relationship in WS is consistent with several previous studies showing that working memory is related to AB across a wide age range in DS[13,22,23]. In the DS group, there were several associations between multiple EFs (Shift, Initiate, Task Monitor) and AB, but no support for the importance of working memory. One explanation for this inconsistency might be that studies showing this relationship included school-aged children with DS (age range: 6–17 years), whereas the current study examined a wider age range of adolescents and young adults with DS. Thus, it is possible that with increasing age different EF abilities are needed to meet age-appropriate demands in the environment in people with DS.

Although not one of our main objectives, we explored relationships between core EFs and internalising/externalising behaviour from the Maladaptive Behaviour Index on the VABS-II. In the DS group, our results showed several significant correlations between BRIEF-A clinical scales (Inhibit, Emotional Control, Task Monitor) and externalising behaviours. These findings are consistent with previous research in children and adolescents with DS, where BRIEF Emotional Control was the strongest predictor of maladaptive behaviours including rule breaking, and externalising and aggressive behaviour[45]. Further, there were unique associations with specific EFs when examining internalising and externalising behaviours, separately. In the DS group, the BRIEF-A Shift scale significantly predicted more internalising behaviours, while the BRIEF-A Task-Monitor scale was a significant predictor of greater externalising behaviours. This is consistent with research in typically developing children where attention set-shifting has been linked to internalising symptoms[46], suggesting similar mechanisms in people with DS. Thus, higher levels of internalising symptoms could impair attentional control, thereby resulting in EF decrements in the ability to shift attention, or alternatively difficulties in set-shifting might constrain the ability to adapt behaviour to regulate emotional responses under stressful or challenging events. Our findings suggest the relationships between distinct EFs, and maladaptive behaviours extends to older adolescents and young adults with DS.

Our findings may have important implications for adolescents and young adults with WS and DS. The significantly elevated EF impairments in the WS group are consistent with frontal lobe impairments, which may underlie the distinct hypersociability observed across a wide age range in WS[47]. Together with evidence that EF impairments are also associated with the presence of elevated anxiety in people with WS[48], the current findings could inform interventions targeting selective EFs to improve socio-emotional functioning in this population comparable to the benefits shown in typically developing children[49]. Moreover, the current relationships between core EFs and maladaptive behaviours in the DS group may have important implications for early detection of executive dysfunction prior to developing cognitive decline associated with Alzheimer's disease (AD). People with DS are known to have a high risk of manifesting clinical features of AD in middle age, increasing from 25 to 75% between the ages of 30 to those over 60 years. Previous research has indicated that early symptoms of AD in people with DS is marked by executive dysfunction and changes in personality and behaviour, but not in deterioration in episodic memory[30,50,56]. Further, impairments on measures of EF but not adaptive functioning are a distinctive feature of adults with DS (over 30 years of age) who show early cognitive deterioration compared to those without cognitive decline[51]. Hence, the current relationships between distinct EFs and internalising/externalising behaviours in DS suggest that informant reports could provide an early indicator of cognitive decline and increased risk of onset of AD in this population.

There are several limitations to be considered in our study. First, there were small sample sizes that might reduce statistical power to detect group differences. Second, we used different standardised measures of intelligence across DS and WS, and thus, it was not possible to determine the specificity of associations between EF and IQ. Third, the reliance on behavioural measures of EF might open the possibility of response bias or common methods bias. Fourth, the cross-sectional and correlational nature of this study does not directly support any causal role of EFs influencing IQ and adaptive/maladaptive functioning, and it is possible a third unknown factor might be involved. Finally, the current study used a wide age range of adolescents and young adults with DS and WS, and therefore any conclusions should be tempered about potential relationships between EF and maladaptive behaviour in middle aged adults with DS at-risk for cognitive decline. Future longitudinal studies should explore the association between everyday EF, maladaptive behaviours and age using a longitudinal design in an older DS cohort with and without cognitive decline.

There are several strengths of our study including a cross-syndrome design using a well-established and valid measure of real-world EF to explore the relationships between core EFs, intellectual ability and AB across these genetic syndromes. Rather than providing the inherent cues and structure of performance-based assessments of EF, informant-based ratings of daily aspects of EF increase ecological validity in people with intellectual disability. Another strength of our study relates to the identification of syndrome-specific differences in EF profiles in young adults with DS and WS, which extends the previous studies that have predominately focused on children and adolescents with these genetic syndromes.

In conclusion, we found syndrome-specific differences consistent with a profile of more profound weaknesses across multiple components of EF in adolescents and young adults with WS, and selective EFs appeared to discriminate people with WS from those with DS. Contrary to previous studies using the BRIEF, the current findings showed that working memory is a component of EF most closely related to intellectual ability and AB in WS. Further, in the DS group, the significant relationships between selective EFs and internalising/externalising behaviours could have important implications for identifying informant-based cognitive changes that signal the early onset of deterioration in AD. These distinctive EF profiles across DS and WS warrant concerted efforts in developing targeted cognitive interventions that build upon cross-domain interactions for improving a range of real-world outcomes for affected individuals.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

D.H.: Conception, design and execution and wrote first draft of manuscript, analysis and interpretation of re-

sults and final review and editing; E.B.: Partial execution of research project; statistical analysis; co-writing the manuscript. N.RL: Critical review of the manuscript, revisions on draft of manuscript; All authors reviewed the manuscript and approved the final version.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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