A 12-week exercise programme has a positive effect on everyday executive function in young people with Down syndrome: a pilot non-randomised controlled trial

JIDR Journal of Intellectual Disability Research
Published on behalf of mencap and in association with IASSID

Journal of Intellectual Disability Research doi: 10.1111/jir.12979

VOLUME 66 PART 12 pp 924–938 DECEMBER 2022

A 12-week exercise programme has a positive effect on everyday executive function in young people with Down syndrome: a pilot non-randomised controlled trial

N. Shields,[1] N. Mizzi,[2] K. Buhlert-Smith,[1] A. Strydom,[3] L. Prendergast[4] & D. R. Hocking[2,5]

1 *Department of Physiotherapy, Podiatry and Prosthetics and Orthotics, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Australia*

2 *Developmental Neuromotor & Cognition Lab, School of Psychology and Public Health, La Trobe University, Melbourne, Australia*

3 *Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, Psychology & Neuroscience, Kings College London, London, UK*

4 *Department of Mathematics and Statistics, La Trobe University, Melbourne, Australia*

5 *Centre for Mental Health, Swinburne University of Technology, Melbourne, Australia*

Abstract

Background Exercise has the potential to reduce cognitive decline in people with Down syndrome by maximising their cognitive function. The aim of the study was to determine the effect of regular exercise on cognitive functioning in young people with Down syndrome.

Method People with Down syndrome were eligible if aged between 13 and 35 years and enrolled to participate in an exercise programme (called *FitSkills*). The intervention was a 12-week community-based exercise programme completed with a student mentor. Outcomes were assessed before (week 0) and immediately after (week 13) the intervention. Executive functioning (planning, response inhibition, attention shifting) was assessed using Tower of London, Sustained Attention to Response Task, CANTAB Intra-extra Dimensional Set Shift Test, Cognitive Scale for Down Syndrome, and Behaviour Rating Inventory of Executive Function (BRIEF). Working memory was assessed using the CANTAB Paired Associates Learning task, and information processing speed was assessed using the Motor Screening Task. Outcomes were analysed using ANCOVA with the baseline measure as the covariate.

Results Twenty participants (9 women; mean age 23.6 ± 6.6 years) enrolled. Between-group differences, in favour of the experimental group, were found for the global executive composite score of the BRIEF (mean difference −4.77 units, 95% CI −9.30 to −0.25). There were no between group differences for any other outcome measured.

Conclusion Participation in a 12-week exercise programme was effective in improving everyday executive functions in young people with Down syndrome. These preliminary findings need to be confirmed in future randomised controlled trials of community-based exercise with larger sample sizes.

Correspondence: Prof Nora Shields, Department of Physiotherapy, Podiatry and Prosthetics and Orthotics, School of Allied Health, Human Services and Sport, La Trobe University, Melbourne, Victoria 3086, Australia (e-mail: n.shields@latrobe.edu.au).

Keywords community, executive function, intellectual disability, peer mentor, physical activity, working memory

Background

Early cognitive decline is a major problem for 5.8 million people with Down syndrome living worldwide (Ballard *et al.* 2016). Up to 80% of adults with Down syndrome experience cognitive decline and at a much younger age than the general population. Specifically, adults with Down syndrome are affected by cognitive deficits (Basten *et al.* 2018) including language skills, processing speed, attention, visuospatial abilities, and reduced abilities in executive functions (Tungate & Conners 2021). Executive functions are top-down mental processes that enable an individual to concentrate when presented with novel, distracting, or conflicting task demands, and when automatic or instinctual processes would be insufficient (Diamond 2013). These 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 ('working memory'). Although executive functions are commonly divided into these three subdomains, this set of abilities form the basis for higher-order cognitive processes such as planning, which is an area of specific weakness for individuals with Down syndrome (Lee *et al.* 2015). These deficits can impact everyday living by reducing daily activity performance, limiting opportunities to participate in the community, and make people with Down syndrome more dependent on others.

Improved life expectancy means an increasing number of people with Down syndrome are at risk of cognitive decline. This poses a challenge for services who support people with Down syndrome. There is no cure for cognitive decline, and it is unclear if drug therapies help (Livingstone *et al.* 2015). A Lancet commission on dementia (Livingston *et al.* 2020) called for public health programmes and tailored interventions to increase physical activity, particularly for groups at high risk of cognitive decline. This is based on research indicating getting people to change their lifestyle early in life, such as exercising more, could prevent or delay up to 40% of dementias in the general population, even in those with genetic risk (Lourida *et al.* 2019). Cross-sectional and longitudinal studies show people with Down syndrome who exercise have better executive functioning and memory than those who do not exercise (Fleming *et al.* 2021; Pape *et al.* 2021). Young adulthood is when the brain reaches peak health and is an ideal time to maximise cognitive function. The transition from adolescence to young adulthood is a crucial period for shaping long-term physical activity behaviours because it coincides with a time of natural decline in physical activity (Shields *et al.* 2009) and reduced access to formal services that support participation.

Exercise interventions have the potential to improve executive functioning in people with Down syndrome. Preliminary trials, with small sample sizes, have reported mixed effects of exercising at home or in laboratory settings on executive function in those with Down syndrome. Two small trials (Ptomey *et al.* 2018; Perrot *et al.* 2021) (n = 12 and 27) reported no effect on executive function after 12 weeks of exercise in either younger (mean age 28 years) or older adults (mean age 50 years) with Down syndrome. However, a third trial (mean age 19 years) (Ringenbach *et al.* 2016) (n = 33) reported 8 weeks of assisted cycling, where a mechanical motor turned the pedals of a stationary bicycle at a cadence 80% faster than self-selected speed, resulted in improved planning (Holzapfel *et al.* 2016), inhibition (Ringenbach *et al.* 2016), working memory (Holzapfel *et al.* 2016) and reaction time (Ringenbach *et al.* 2016), but not short-term memory (Holzapfel *et al.* 2016) compared with voluntary cycling at a self-selected speed. Having Down syndrome and difficulties with executive functions can make it harder to exercise. People with Down syndrome typically do not participate in recommended levels of exercise (Phillips & Holland 2011) due to physiological, environmental, social, and attitudinal barriers related to their disability (Mahy *et al.* 2010; Barr & Shields 2011), including the need for social support (Mahy *et al.* 2010). These barriers, however, can be successfully navigated in community gym settings using a mentor model of exercise (Shields & Taylor 2010, Shields *et al.* 2013, Shields & Taylor 2015, Shields *et al.* 2022).

A limitation of previous studies is the exercise programmes tested are not readily available in the community and require specialist equipment or specialist supervision. Further, previous studies have investigated the effect of performance-based measures as executive function outcomes, so it is unknown if there is an effect on everyday executive functioning.

This is important as direct performance-based assessments may not be representative of the multidimensional nature of real-world impairments in executive functions in people with Down syndrome. Given the importance of executive functions for everyday life, the beneficial effects of community-based exercise as an intervention to maximise executive function warrants further investigation. Therefore, this study aimed to determine the effect of exercise in a community setting with a non-specialist support person on direct and informant reports of executive functioning in young adults with Down syndrome.

Methods

Research design

We completed a non-randomised controlled trial using a convenience sample. Ethics approval was obtained from the La Trobe University Human Ethics committee. Written informed consent was sought from the next of kin (parent or guardian) of adolescents with Down syndrome aged 13 to 17 years. To respect the developing capacity of these young people to be involved in decisions about their participation, they were involved in discussions about the study, were provided with an information sheet written in easy to read language, and were invited to give written consent to take part based on their parents' recommendation. Young adults with Down syndrome aged 18 to 35 years provided their own written informed consent if they usually provided their own consent (e.g. if they are their own legal guardian). For those young adults with Down syndrome who did not usually provide their own consent, their legal guardian (usually their parent) provided written informed consent.

Participants

Adolescents and young adults with Down syndrome were eligible if they (1) were aged 13 to 35 years; (2) expressed interest in taking part in either a clinical trial of community-based exercise for young people with disability (ACTRN12617000766314) or a fee-for service exercise programme called *FitSkills* during 2018 or were a member of a research database (custodian is DH); and (3) were able to follow simple verbal instructions in English indicating they would understand what was required during cognitive function testing. The intervention group comprised participants who completed an exercise programme as part of the clinical trial or the *FitSkills* programme during 2018. The control group comprised all other participants who expressed interest.

Exclusion criteria were: (1) having participated in a structured exercise program within 3 months prior to enrolment; (2) having an acute or concurrent medical condition rendering them unfit to exercise (e.g. a severe cardiac condition); (3) having a substantial behavioural problem that would impact community exercise participation or interfere with performance on cognitive tests; or (4) showing any six of the items identified in the National Task Group Early Detection Screen for Dementia.

Intellectual ability measures at baseline

At baseline, participants completed the Kaufman Brief Intelligence Test (2nd Edition, KBIT-2), a measure of verbal and nonverbal intelligence (Kaufman & Kaufman 2004). The KBIT-2 comprises three subsets, two which assess verbal IQ (Verbal Knowledge and Riddles) and one which assess non-verbal IQ (Matrices). Each subset was started at item 1 and stopped after four consecutive incorrect answers. The KBIT-2 provides raw scores for each subset which are converted into age-based standard scores (M = 100, SD = 15). As floor effects for IQ scores were expected, raw scores were used as the main measure of general cognitive ability. The subset standard scores combine to give a composite standard score (IQ Composite), with higher IQ Composite scores indicative of greater IQ, and scores below 70 on the lower extreme end of IQ levels. The KBIT-2 has demonstrated strong reliability with split-half reliability coefficients ranging from .80 to .95, and high correlations with the Weschler Intelligence Scales for Children (Canivez 1995).

Adaptive functioning at baseline

The Vineland Adaptive Behaviour Scales, Second Edition – Vineland-II (parent survey) (Sparrow *et al.* 2005) was completed at baseline to measure adaptive functioning. This measure contains 11 subdomains, grouped into four domain composites (Communication, Daily Living Skills, Socialisation, Motor Skills). Domains combine to form the

Adaptive Behaviour Composite. Subdomain raw scores were converted into standard scores (M = 100, SD = 15) based on chronological age. Lower domain scores are reflective of greater maladaptive behaviour, with scores two standard deviations below normative mean (score of 69) indicative of overall lower-level adaptive functioning. These scales demonstrate excellent internal consistency (0.97 to 0.99), test–retest reliability (0.95 to 0.99) and inter-rater reliability (0.93 to 0.99) (Sparrow & Cicchetti 1989).

Intervention

Participants in the experimental group completed a 12-week exercise programme. Each participant was matched with a student mentor from their community, who provided social support, and the pair exercised together, one-to-one at their local gym. Both the participant with Down syndrome and their mentor exercised. Each exercise session ran for an hour, twice a week for 12 weeks. The programme was individually tailored and included aerobic training (e.g. running, cycling); resistance training (e.g. pin-loaded weight machines); and other exercises focused on core strengthening and balance. Programmes were prescribed by a physiotherapist or exercise physiologist according to international best practice guidelines. The mentors supported the participants to document their programmes in an exercise diary including details of any injuries or problems (adverse events) and any missed sessions. The feasibility of this type of programme for young people with disability has been documented elsewhere (Shields *et al.* 2019, Shields *et al.* 2022).

Mentors were volunteers enrolled in a health-related degree (any discipline or year level) from two universities in Melbourne, Australia. They completed police and government mandated child safety checks and were not expected to have pre-existing knowledge of exercise or Down syndrome. Students were invited to become mentors through advertising flyers and information sessions at the beginning of lectures and tutorials. They were matched with a participant with Down syndrome based on location and in some instances gender. As it was not a prerequisite for mentors to have experience of disability, all students completed a 3-hour training programme comprising knowledge (e.g. motivational strategies) and practical elements (e.g. orientation to gym equipment). Mentors maintained contact every 2 to 3 weeks with a member of the research team to check the exercise programme was proceeding as planned, and to help address any issues.

Participants in the control group continued with their usual activities for 12 weeks and were then invited to complete a 12-week exercise programme after a follow-up assessment.

Outcomes measures

Outcomes measures designed for people with intellectual disability were selected. The outcomes were assessed before (Week 0) and immediately after (Week 13) the 12-week exercise programme by an assessor who was not blind to group allocation but who had no involvement in the intervention. Assessment order was counterbalanced across participants to reduce the likelihood of learning or habituation effects. Demographic data were also collected (Table 1).

Executive functioning

Everyday cognitive function was assessed using the Cognitive Scale for Down syndrome (Startin *et al.* 2016). This informant-rated questionnaire assesses everyday abilities relating to executive function, memory and language, regardless of cognitive ability. The scale comprises 61 questions pertaining to executive function (36 questions), memory (16 questions), and language (9 questions). Each question is answered on a 3-point Likert scale (never/rarely true, sometimes true, and often/always true) which are scored from 0 to 2 resulting in a possible score range from 0 to 122, with higher scores indicating better cognitive function. For this study, only the executive function scores were analysed and reported. This questionnaire is a valid measure of everyday cognitive function with change in scores correlating with other informant measures of adaptive abilities and symptoms associated with dementia in adults with Down syndrome (Startin *et al.* 2019).

Everyday executive functioning behaviour was also assessed using the Behaviour Rating Inventory of Executive Function (informant report form). The adult version (BRIEF-A; 75 items) was used for participants aged 18–35 years and the child version (BRIEF-C; 85 items) for participants aged 13–17 years (Gioia *et al.* 2000). The BRIEF-A comprises nine

Table 1 Participant characteristics (n = 20)

Characteristic	Exp (n = 9)	Con (n = 11)	Comparison
Age (year) mean (SD)	21.4 (7.1)	25.3 (5.9)	$t_{(18)} = 1.323$, $P = 0.203$
Age range (year)	13 to 32	14 to 35	
Gender, female	3	6	
Type of DS, *n*			
Trisomy 21, *n*	7	10	
Translocation, *n*	1	1	
Mosaic, *n*	1	0	
Intellectual ability (K-BIT2)			
IQ standard score (SD)	52.7 (15.7)	49.0 (7.1)	$t_{(18)} = -0.693$, $P = 0.497$
IQ standard score (min, max)	40 to 91	40 to 61	
Mild, *n*	6	9	
Moderate, *n*	3	2	
Verbal mental age, mean (SD)	8.0 (3.3)	7.4 (2.2)	
Verbal mental age, (min to max)	5 to 16	4 to 11	
Non-verbal mental age, mean (SD)	5.8 (3.2)	5.2 (1.2)	
Non-verbal mental age, (min to max)	4 to 14	4 to 8	
Adaptive Functioning (Vineland Adaptive Behaviour Scales-II)			
Adaptive Behaviour Composite, mean (SD)	71.0 (14.5)	55.7 (16.6)	$t_{(16)} = -1.951$, $P = 0.069$
Communication Domain, mean (SD)	62.2 (24.3)	52.7 (24.8)	$t_{(17)} = -.825$, $P = 0.421$
Daily Living Skills Domain, mean (SD)	75.7 (13.4)	61.4 (16.24)	$t_{(17)} = .917$, $P = 0.059$
Socialisation Domain, mean (SD)	80.6 (14.0)	61.7 (19.0)	$t_{(17)} = -2.403$, $P = 0.029$
Motor Skills Domain, mean (SD)	88.3 (16.4)	74.7 (18.1)	$t_{(17)} = -1.677$, $P = 0.113$
Vocational status			
Attending school/education, *n*	4	5	
Working at least some of the time, *n*	2	4	
Day programme, *n*	3	2	
Living arrangements			
Lives with parents, *n*	8	10	
Lives in group accommodation, *n*	1	0	
Lives alone, *n*	0	1	
Health conditions			
None documented, *n*	0	4	
Heart defect, *n*	4	1	
Musculoskeletal problems, *n*	3	4	
Hypothyroid, *n*	3	0	
Sleep apnoea, *n*	2	1	
Gastrointestinal conditions, *n*	2	1	
Vision or hearing impairment, *n*	3	1	

Exp, experimental group; Con, control group; SD, standard deviation; *n*, number.

scales combined to form two indexes (Behaviour Regulation Index, Metacognition Index), that produce a T score (with M = 50, SD = 10) based on chronological age, and an overall score representing the global executive composite. The BRIEF-C comprises eight subscales, that produce equivalent indices, T score and overall score. Higher scores indicate greater degrees of executive dysfunction, with scores above 65 being clinically relevant. Psychometric properties for both questionnaires show high internal consistency (.80 to .98), and high test–retest reliability ranging (.91 to .94) (Gioia *et al.* 2002; Roth & Gioia 2005).

Higher order planning was assessed using the Tower of London DX, Second Edition (Culbertson & Zillmer 1998) and validated for use in child and

adult populations with developmental and acquired disorders, including intellectual disability. The test comprises two wooden peg boards (one each for participant and assessor) with three vertical pegs of differing length and three beads (one red, green, and blue). Participants were asked to recreate the demonstrated configuration of beads on the peg board. Ten problems are completed in a minimum of two to four moves. A move involves taking a bead off a peg and placing it on another. The number of problems solved with the minimum number of moves specified is scored. Higher scores are indicative of the number of configurations the participant completed within the minimum move and maximum time allocation. We measured total correct score (how many problems completed in minimum number of moves) where a higher score is better, total move score (sum of all moves across all 10 problems) where a lower score is better, total initiation time (time between examiner saying 'go' and participant making first move in milliseconds) where a higher score is indicative of greater planning, total execution time (time between first move and last move in milliseconds, where a lower score is better) and total time (total initiation time plus total execution time in milliseconds, where a lower score is better). This version is a valid measure with strong correlations with related neuropsychological measures, and good internal consistency ($\alpha = .75$) (García-Alba *et al.* 2017).

Response inhibition was assessed using the Sustained Attention to Response Task (Robertson *et al.* 1997). Participants were asked to respond to non-target digits (e.g. numbers 0–2 and 4–9) and withhold their response to a target digit (e.g. number 3). The continual response required on the non-target digits formed an automatic response that was then inhibited for the target digit. The outcome measure was total taps on wrong number, with lower scores indicative of better inhibitory control. This task is a valid measure with significant correlations with self-reported attention-related errors in everyday life (Smilek *et al.* 2010).

Attention shifting was assessed using the CANTAB Intra-Extra Dimensional Set Shift test (Edgin *et al.* 2010). This non-verbal test is administered using an iPad providing immediate feedback and less reliance on verbal comprehension. Instructions were given via an automated voice and were designed specifically for people with intellectual disability. Participants were required to learn rules about which was the 'correct' of two presented patterns by listening to audio feedback, which indicated whether their previous choice was 'correct' or 'incorrect'. Participants were required to use this feedback to determine their next choice. Once a rule was established (6 consecutive 'correct' answers) the rule changed and participants had to discover the new rule. If a particular stage was not complete (the rule was not learnt) in a maximum of 50 trials, the task was terminated. The two scores were (i) number of stages completed (measure of set-shifting where a higher score is better) and (ii) total time adjusted for the number of stage 1 errors (rule learning measured as the number of trials completed on all attempted stages with an adjustment for any stages not reached, where a lower score is better). The completion of stages 8–9 required an intra-dimensional shift (stage 1 only required rule learning). This task has acceptable test–retest reliability of .70 for total errors to extra-dimensional shift (Lowe & Rabbitt 1998).

Working memory

Working memory was assessed using the CANTAB Paired Associates Learning task (Edgin *et al.* 2010) which measures visuospatial memory. After an instructional script was read by the researcher, participants were asked to remember the location of an increasing number of patterns in progressive stages, hidden behind boxes displayed on an iPad tablet. After the contents of each box was revealed, patterns were presented one at a time and participants were required to indicate in which box they saw each pattern by tapping on the corresponding box. If a stage was not completed in a maximum of 10 attempts, the test was concluded. The main scores were (1) first trial memory score, which is the number of pattern locations correctly remembered on the first attempt for each stage and (2) number of patterns reached which measured the number of patterns presented on the last stage completed. Higher scores are indicative of greater visual working memory and new learning. This measure has good test–retest reliability quotient of .86 for average number of trials to success (Lowe & Rabbitt 1998).

Processing speed

Information processing speed (reaction time) was assessed using the CANTAB Motor Screening Task (Edgin, Mason *et al.* 2010). An instructional script was read aloud, and crosses were presented in different locations on an iPad screen one at a time. Participants were required to tap the cross on the screen as quickly and accurately as possible. The score was the mean time between the display of the cross on the screen until the participant was able to tap on the cross, where a lower score indicated better reaction time.

Data analysis

As this was a pilot study, using a convenience sample, we did not complete a sample size calculation *a priori*. We included as many participants as were willing to take part.

Statistical analyses were performed using R version 3.6.1 (R Core Team 2013) and significance was assessed using an alpha level of .05. To ensure groups were equivalent on potential confounders, *t*-tests and the Wilcoxon signed rank tests compared groups for chronological age and mental age (derived from the KBIT-2). Analysis of covariance (ANCOVA) was used to examine differences in post-intervention (week 13) scores on the outcome measures of executive function between groups controlling for baseline (week 0) scores (Vickers & Altman 2001; Vickers 2005). As ANCOVA is a linear regression analysis with two independent variables (baseline
and group), the sample size for this study meets what is often regarded as minimum recommended size of 10 observations per independent variable (Harrell 2001). Data were checked to ensure there was no violation of the assumptions of linearity and homogeneity of regression slopes (Pallant 2020). Quantile-Quantile (Q-Q) plots of the residuals were also checked for violations of normality. While no obvious model violations were present in any plots, one or two outliers were observed for a small number of outcomes. As an extra precaution against outliers, robust regression analyses using M-estimators (Huber 2011) from the MASS package (Venables & Ripley 2013) were conducted, with no notable changes that affected the conclusions. Where more than 5% of data were missing, a multiple imputation process was also used as a sensitivity analysis for the difference between groups (Table 3). Multiple imputation was carried out using multivariate imputation by chained equations via the mice package (Buuren & Groothuis-Oudshoorn 2010) and 100 imputations.

The mean difference within each group and between groups and the associated 95% confidence intervals were calculated. Effect size as omega squared (ω^2), which are bias corrected eta squared values, were also calculated for each dependent variable. These values can be interpreted as follows: values of 0.01 represent small effects; values of 0.06 represent medium-sized effects; values of 0.14 represent large effects. Negative values of ω^2 may result due to bias correction. While truncation to zero is possible when reporting bias-corrected effect size estimates, this is not recommended due to bias and lack of transparency (Okada 2017).

Results

Participants

Twenty participants (mean age 23.6 years, SD 6.6 years) were recruited (Figure 1 and Table 1). At baseline, there were no differences between groups for chronological age or intelligence quotient as measured by the KBIT-2 (Table 1). Analysis of baseline adaptive functioning scores showed no differences between the groups for adaptive behaviour composite scores or for three of the four domain composite scores. There was a difference between groups at baseline for the socialisation domain score indicating the experimental group had slightly lower adaptive functioning than the control group, for this domain.

Compliance with the trial method

Participants in the experimental group attended 177 of 192 scheduled exercise sessions (attendance rate 92%, SD 12%). Reasons for missed sessions were holidays (n = 4), death in family (n = 4), student exams or placement (n = 6), or illness (n = 1). No major adverse events were reported. Reasons for missing outcome data are outlined in Table 2.

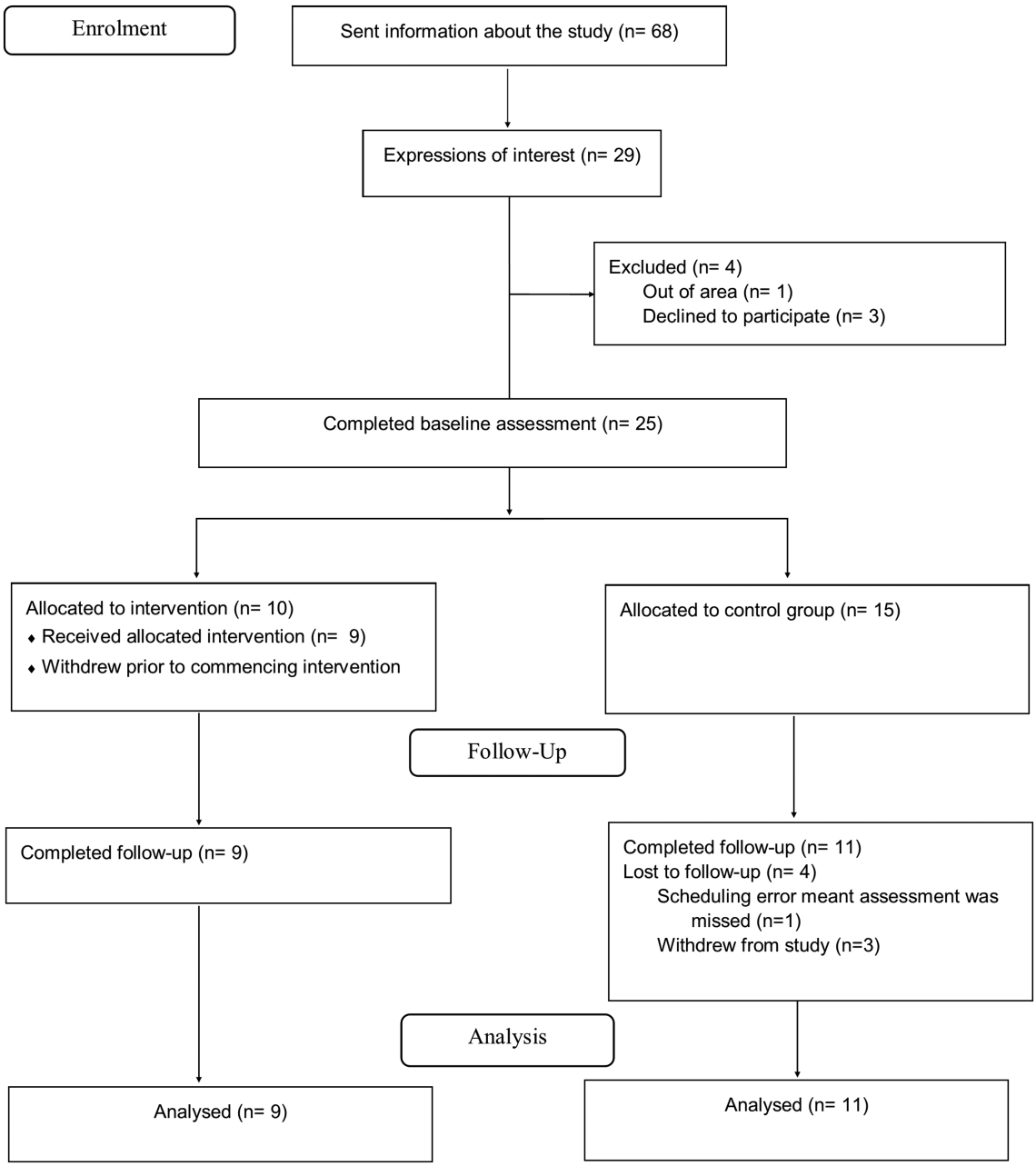

Figure 1. Flow of participants through the trial

Executive functioning

There was a significant between-group difference in favour of the experimental group for the Global Executive Composite score (mean difference −4.77 units, 95% CI −9.30 to −0.25) of the BRIEF. There were no differences between the groups for either of the two indexes (Behaviour Regulation Index, Metacognition Index).

There were no differences between the groups for everyday executive function as measured by the Cognitive Scale for Down syndrome or for any of the

Table 2 Number of participants (out of 20) with missing data at baseline and follow-up

Measure	Baseline	Follow-up	Reasons
Cognitive Scale for Down syndrome	1	2	Questionnaire not returned (3)
Behaviour Rating Inventory of Executive Function	1	2	Questionnaire not returned (3)
Tower of London	3	1	Fatigue (3); test not available (1)
Sustained Attention to Response Task	0	1	Fatigue (1)
Intra-extra dimensional set shift test (from CANTAB)	1	2	iPad malfunction (2); refused (1)
Paired Associates Learning (from CANTAB)	1	3	iPad malfunction (2)

CANTAB, Cambridge Neuropsychological Test Automated Battery.

planning, inhibitory control, or attention shifting assessments (Table 3).

Working memory

There were no between group differences at follow-up for working memory (Table 3).

Processing speed

There were no between group differences at follow-up for reaction time (Table 3).

Discussion

Our findings showed a community-based exercise programme was effective in improving everyday executive functioning behaviours (informant reported) of young people with Down syndrome. We found those who exercised, twice a week for 12 weeks, improved their daily executive functioning. This novel finding is important because the exercise programme was completed in a mainstream community venue with non-specialist social support. However, no corresponding improvement was found on any other informant or performance-based measures of executive function across the two timepoints. Also, our findings were not in line with previous studies that reported positive effects of exercise on performance-based measures of executive function in young adults with Down syndrome (Holzapfel *et al.* 2015; Holzapfel *et al.* 2016; Ringenbach *et al.* 2016; Ptomey *et al.* 2018) using similar outcome measures. Together these results provide preliminary evidence that regular community-based exercise can have a positive effect on real-world executive functioning in Down syndrome.

Our results suggest commonly used informant rating scales of everyday executive functioning behaviour (BRIEF-C and BRIEF-A) were sensitive to improvements in cognitive abilities following exercise. These scales assess specific executive function behaviours presenting as a problem over the previous 4 weeks. In contrast, there were no improvements on a newly developed informant scale of everyday abilities related to executive function, memory and language, specific to adults with Down syndrome (Cognitive Scale for Down Syndrome). However, the latter scale was developed to capture cognitive decline over a longer time period (18 to 24 months) (Startin *et al.* 2019). Thus, it is possible this scale lacks sensitivity to short-term changes in executive functioning in response to an intervention among younger people with Down syndrome who would be less likely to experience cognitive decline. However, it is also possible our study was underpowered to detect a change in informant reported scores on the Cognitive Scale for Down Syndrome given our data suggested a large effect size ($\omega^2 = 0.6$, 95% CI 0.22 to 0.79) for this outcome.

In contrast to previous studies using similar performance-based measures of executive functioning in response to moderate physical activity (Holzapfel *et al.* 2016; Ringenbach *et al.* 2016; Ptomey *et al.* 2018), we did not observe positive changes on neuropsychological measures of executive function in young people with Down syndrome. The reasons for this are unclear. Ptomey *et al.* (2018) reported a between-group difference for visuospatial memory (CANTAB paired associates test) that approached significance for an exercise programme of similar

Table 3 Mean (SD) score, mean (SD) difference within groups, and mean (95% CI) difference between groups for all outcomes for the experimental group ($n = 9$) and the control group ($n = 11$)

Outcome	Score				Difference between groups				
	Baseline (week 0)		Post-intervention (week 13)		Difference within groups		Week 13–Week 0 (95% CI)[†]	Multiple imputation	ω^2 (95% CI)[‡]
	Exp	Con	Exp	Con	Exp	Con	Exp-Con		
Everyday executive cognitive function (Cognitive Scale for Down syndrome)									
Executive function domain	55.00	47.64	57.38	47.20	2.86	0.3	4.17	3.7	0.6
	(6.76)	(10.45)	(7.93)	(10.06)	(4.1)	(5.25)	(−1.49 to 9.83)	(−1.68, 9.07)	(0.22, 0.79)
Everyday executive function behaviour (BRIEF)									
Behaviour regulation index	50.75	54.91	46.00	52.40	−3.71	−2.9	−3.37	−3.35	0.42
	(10.15)	(9.91)	(6.19)	(7.40)	(5.06)	(6.01)	(−7.69, 0.96)	(−7.32, 0.63)	(0.03, 0.68)
Metacognition index	55.50	53.82	58.12	57.30	2.29	3.7	−0.25	0.62	−0.06
	(9.12)	(20.05)	(17.03)	(12.45)	(17.79)	(16.18)	(−14.82, 14.32)	(−11.86, 13.11)	(−0.07, 0.05)
Global executive composite score	55.75	56.91	50.62	55.70	−5.71	−1.5	−4.77	−4.63	0.29
	(12.87)	(11.83)	(9.44)	(9.83)	(7.54)	(4.3)	(−9.30 to −0.25)	(−8.75, −0.51)	(−0.04, 0.6)
Planning (Tower of London)									
Total correct score	2.89	4.00	5.57	5.30	2.29	1.25	0.77	0.77	−0.06
	(2.47)	(2.14)	(2.51)	(2.06)	(1.11)	(2.25)	(−1.11 to 2.66)	(−1, 2.55)	(−0.08, 0.23)
Total move score	35.11	30.62	29.86	19.30	−3.86	−12.75	11.35	10.85	0
	(20.38)	(39.67)	(29.94)	(14.51)	(19.91)	(41.82)	(−14.00 to 36.70)	(−10.38, 32.08)	(−0.08, 0.37)
Total initiation time (ms)	32.38	37.99	54.26	35.35	18.8	−5.05	20.68	17.17	0.08
	(20.15)	(11.12)	(35.86)	(16.11)	(46.53)	(16.47)	(−10.18 to 51.54)	(−9.81, 44.15)	(−0.08, 0.45)
Total execution time (ms)	139.38	127.26	246.03	150.85	90.55	−7.53	131.84	105.05	0.07
	(69.72)	(104.15)	(234.47)	(92.78)			(−60.1, 323.78)	(−66.15, 276.26)	(−0.08, 0.44)
Total time (ms)	174.33	172.13	226.76	182.28	33.22	−24.4	76.6	46.58	0.13
	(83.54)	(101.81)	(112.5)	(102.38)			(−19.52, 172.72)	(−60.87, 154.03)	(−0.08, 0.5)
Inhibitory control									
Sustained Attention to Response Task	1.55	3.09	3.71	3.36	2.0	0.27	1.17	1.08	−0.05
	(1.67)	(3.39)	(3.20)	(3.11)	(3.27)	(2.61)	(−1.71 to 4.05)	(−1.67, 3.83)	(−0.06, 0.16)
Attention shifting (IED set shift test)									
Total time adjusted	184.78	246.36	212.56	230.00	27.78	−30.88	58.16	55.94	−0.05
	(94.32)	(126.68)	(120.77)	(154.66)	(82.57)	(56.83)	(−23.61, 139.92)	(−22.52, 134.39)	(−0.07, 0.23)
Stages completed	6.56	5.27	6.00	5.38	−0.56	0.50	−0.88	−0.88	−0.04
	(2.46)	(3.23)	(2.96)	(3.70)	(2.13)	(1.77)	(−3.06 to 1.31)	(−2.92, 1.16)	(−0.07, 0.26)

Table 3. *(Continued)*

Outcome	Score				Difference between groups			
	Baseline (week 0)		Post-intervention (week 13)		Difference within groups		Week 13–Week 0 (95% CI)[†]	Multiple imputation	ω^2 (95% CI)[‡]
Working memory (PAL task)									
First trial memory score	4.44	5.82	6.11	6.88	1.67	1.38	0.17	0.19	−0.04
	(2.60)	(2.89)	(3.10)	(4.32)	(2.74)	(2.62)	(−2.75 to 3.09)	(−2.53, 2.92)	(−0.07, 0.25)
Number of patterns research	5.56	8.36	7.33	8.25	1.78	0.25	0.77	0.72	−0.04
	(1.94)	(3.20)	(3.32)	(4.06)	(2.91)	(3.62)	(−2.96 to 4.49)	(−2.8, 4.25)	(−0.07, 0.24)
Processing speed									
Motor screening task (ms)	960.60	952.79	1025.82	939.64	65.18	−51.86	97.4	98.06	0 −0.07, 0.32)
	(317.29)	(193.08)	(197.46)	(203.87)	(243.61)	(241.57)	(−93.3, 288.11)	(−75.64, 271.77)	

Interpretation of cognitive function scores: Cognitive Scale for Down syndrome: higher scores indicate better cognitive function. BRIEF: Higher scores indicate greater degrees of executive dysfunction. Tower of London: Total correct score = higher score is better; Total move score = lower score is better; Total initiation time = higher score is indicative of greater planning; Total execution time = lower score is better; Total time = lower score is better. Sustained attention to response task: lower scores indicate better inhibitory control. IED set shift test: number of stages completed = a higher score is better; total time adjusted = a lower score is better. PAL: Higher scores for each domain are indicative of greater visual working memory and new learning. Motor screening task: a lower score indicated better reaction time. BRIEF, Behaviour Rating Inventory of Executive Function; IED, Intra-extra dimensional; PAL, Paired Associates Learning; Exp, experimental; Con, control; ω^2, omega squared.

[†]Derived from ANCOVA with dependent variable at baseline as covariate.

[‡]Omega squared required biased corrected eta squared values. Bias correction can lead to negative numbers which is not an error. Interpretation: values of 0.01 represent small effects; values of 0.06 represent medium-sized effects; values of 0.14 represent large effects.

duration to the current study (12 weeks) but led by a specialist educator to groups of five to eight participants randomised to receive either one or two 30-min exercise sessions per week. Similarly, a non-randomised trial, also in young adults with Down syndrome, with a similar training volume (24 cycling sessions over 8 weeks) found between-group differences in favour of assisted cycling, for working memory and reaction time, and between-group differences, in favour of voluntary cycling, in set-shifting and fluency, compared with a control group (Ringenbach, Holzapfel *et al.* 2016). It is possible differences in exercise type, exercise intensity and exercise progression may provide an explanation for these discrepancies. This is supported by studies that indicate a possible dose–response in facilitating improvements in executive functioning in adults with Down syndrome in response to exercise (Chen *et al.* 2015, Ptomey *et al.* 2018).

An important difference between this study and previous studies is the inclusion of informant reports of everyday executive function. The discrepancy between informant report and direct assessments of executive function might reflect a lack of overlap in cognitive processes required in structured laboratory environments versus everyday life. Given performance-based assessments tap into individual components of executive function over a short time period, these single component tests may not be sensitive to more complex, integrated processes often demanded in real-world situations (Gioia & Isquith 2004). Thus, we suggest the current findings of an improvement in only informant reports of executive function after exercise is suggestive of changes in behaviour across multiple settings in everyday life.

Another difference in the current study is the use of a student mentor to provide the social support necessary to facilitate exercise participation for young people with Down syndrome. It assists with motivation, ensures participants exercise at the correct intensity and provides an opportunity for social interaction. In this study, therefore, the intervention had two components – exercise and social support. The improvement in everyday executive functioning could potentially be driven by either component. This might particularly be the case among young adults with Down syndrome who may be at higher risk of social isolation (van Asselt-Goverts *et al.* 2015), and often have smaller social networks compared with their peers without disability. Hence, the social support component might have increased psychological wellbeing (Shields *et al.* 2019) and facilitated additional social interactions that lead to improvements in everyday executive functioning. Therefore, future studies need to be designed so they control for the social aspect of exercise interventions to determine the extent to which cognitive changes are the result of a socially motivating community environment versus positive effects attributed to exercise only.

There are some study limitations that merit consideration. First, participants were not randomised and neither participants nor assessors were blind to group allocation and therefore potential bias in informant reports of executive function cannot be ruled out. Second, the small sample size may have reduced power to detect changes in performance-based measures of executive function. Third, there was no follow-up as to whether the effects were maintained after the intervention ceased and whether there were any longer-term outcomes from engaging in exercise. Fourth, the study design was unable to determine the optimal dosage of exercise to attain improvement in executive function. A future randomised controlled trial should examine the potential for a dose–response relationship.

In summary, this study provides preliminary evidence a student-mentored, community-based exercise programme is effective in improving everyday executive functions of young people with Down syndrome. However, a positive effect of exercise on performance-based measures of executive function was not found. Given cognitive improvements were seen in ecologically valid informant ratings, these findings highlight the importance of community-based programmes in improving real world functioning and accessibility to exercise programmes without the need to attend specialist clinics. This research paves the way for future trials with larger sample sizes to determine the effectiveness of exercise programmes in improving cognitive function.

Acknowledgments

The authors graciously acknowledge the contributions of the participants, their families, and

the student mentors who volunteered their time for this study and to Down Syndrome Victoria for assistance in the recruitment of participants.

Open access publishing facilitated by La Trobe University, as part of the Wiley - La Trobe University agreement via the Council of Australian University Librarians.

Source of funding

This study was funded by a Research Focus Area (Sport, Exercise & Rehabilitation) internal grant awarded by La Trobe University. DH was supported by a Discovery Early Career Researcher Award (DE160100042). Some of the participants in this study were recruited as part of a larger trial supported by Australian National Health and Medical Research Council (NHMRC) partnership project number 1132579. That trial received financial (cash contributions) and substantial in-kind support from each of seven partners: Victorian Department of Health and Human Services, City of Boroondara, Cerebral Palsy Support Network, Down Syndrome Victoria, Disability Sport and Recreation, YMCA Victoria, and Joanne Tubb Foundation. The NHMRC has no role in the design, conduct, analysis or interpretation of the findings of this study, report writing or decision to this protocol for publication.

Conflict of interest

No author has any conflicts of interest to declare.

Ethics approval statement

Ethics approval was obtained from the La Trobe University Human Ethics committee (HEC 18052).

Data availability statement

The data that support the findings of this study are available from the corresponding author, [NS], upon reasonable request.

References

Ballard C., Mobley W., Hardy J., Williams G. & Corbett A. (2016) Dementia in Down's syndrome. *The Lancet Neurology* **15**, 622–36.

Barr M. & Shields N. (2011) Identifying the barriers and facilitators to participation in physical activity for children with Down syndrome. *Journal of Intellectual Disability Research* **55**, 1020–33.

Basten I. A., Boada R., Taylor H. G., Koenig K., Barrionuevo V. L., Brandão A. C. *et al.* (2018) On the design of broad-based neuropsychological test batteries to assess the cognitive abilities of individuals with down syndrome in the context of clinical trials. *Brain Sciences* **8**, 205.

Buuren S. V. & Groothuis-Oudshoorn K. (2010) Multivariate imputation by chained equations in R. *Journal of Statistical Software* **45**, 1–68.

Canivez G. L. (1995) Validity of the Kaufman Brief Intelligence Test: Comparisons with the Wechsler Intelligence Scale for Children—Third edition. *Assessment* **2**, 101–11.

Chen C. C., Ringenbach S., Crews D., Kulinna P. & Amazeen E. L. (2015) The association between a single bout of moderate physical activity and executive function in young adults with Down syndrome: a preliminary study. *Journal of Intellectual Disability Research* **59**, 589–98.

Culbertson W. C. & Zillmer E. A. (1998) The construct validity of the Tower of London DX as a measure of the executive functioning of ADHD children. *Assessment* **5**, 215–26.

Diamond A. (2013) Executive functions. *Annual Review of Psychology* **64**, 135–68.

Edgin J. O., Mason G. M., Allman M. J., Capone G. T., DeLeon I., Maslen C. *et al.* (2010) Development and validation of the Arizona Cognitive Test Battery for Down syndrome. *Journal of Neurodevelopmental Disorders* **2**, 149–64.

Fleming V., Piro-Gambetti B., Patrick A., Zammit M., Alexander A., Christian B. T. *et al.* (2021) Physical activity and cognitive and imaging biomarkers of Alzheimer's disease in Down syndrome. *Neurobiology of Aging* **107**, 118–27.

García-Alba J., Esteba-Castillo S., López M. Á. C., Hidalgo E. R., Vidal N. R., Díaz F. M. *et al.* (2017) Validation and normalization of the Tower of London-Drexel University Test 2nd Edition in an adult population with intellectual disability. *The Spanish Journal of Psychology* **20**, E32.

Gioia G. A. & Isquith P. K. (2004) Ecological assessment of executive function in traumatic brain injury. *Developmental Neuropsychology* **25**, 135–58.

Gioia G. A., Isquith P. K., Guy S. C. & Kenworthy L. (2000) Test review behavior rating inventory of executive function. *Child Neuropsychology* **6**, 235–8.

Gioia G. A., Isquith P. K., Kenworthy L. & Barton R. M. (2002) Profiles of everyday executive function in acquired and developmental disorders. *Child Neuropsychology* **8**, 121–37.

Harrell F. E. (2001) *Regression modeling strategies: with applications to linear models, logistic regression, and survival analysis*. Springer, New York.

Holzapfel S. D., Ringenbach S. D., Mulvey G. M., Sandoval-Menendez A. M., Birchfield N. & Tahiliani S. R. (2016) Differential effects of assisted cycling therapy on short-term and working memory of adolescents with Down syndrome. *Journal of Cognitive Psychology* **28**, 990–1003.

Holzapfel S. D., Ringenbach S. D., Mulvey G. M., Sandoval-Menendez A. M., Cook M. R., Ganger R. O. *et al.* (2015) Improvements in manual dexterity relate to improvements in cognitive planning after assisted cycling therapy (ACT) in adolescents with down syndrome. *Research in Developmental Disabilities* **45**, 261–70.

Huber P. J. (2011) Robust Statistics. In: *International Encyclopedia of Statistical Science* (ed. M. Lovric). Springer, Berlin 1248–51.

Kaufman A. S. & Kaufman N. L. (2004) *Kaufmann Brief Intelligence Test*, 2nd edn. Pearson Assessments, Bloomington, MN.

Lee N. R., Anand P., Will E., Adeyemi E. I., Clasen L. S., Blumenthal J. D. *et al.* (2015) (XXX and XXY). *Frontiers in Behavioral Neuroscience* **9**, 1-15, 264.

Livingston G., Huntley J., Sommerlad A., Ames D., Ballard C., Banerjee S. *et al.* (2020) Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet* **396**, 413–6.

Livingstone N., Hanratty J., McShane R. & Macdonald G. (2015) Pharmacological interventions for cognitive decline in people with Down syndrome. *Cochrane Database of Systematic Reviews* **10**.

Lourida I., Hannon E., Littlejohns T. J., Langa K. M., Hyppönen E., Kuźma E. *et al.* (2019) Association of lifestyle and genetic risk with incidence of dementia. *Journal of the American Medical Association* **322**, 430–7.

Lowe C. & Rabbitt P. (1998) Test\re-test reliability of the CANTAB and ISPOCD neuropsychological batteries: theoretical and practical issues. *Neuropsychologia* **36**, 915–23.

Mahy J., Shields N., Taylor N. & Dodd K. (2010) Identifying facilitators and barriers to physical activity for adults with Down syndrome. *Journal of Intellectual Disability Research* **54**, 795–805.

Okada K. (2017) Negative estimate of variance-accounted-for effect size: How often it is obtained, and what happens if it is treated as zero. *Behavior Research Methods* **49**, 979–87.

Pallant J. (2020) *SPSS survival manual: A step by step guide to data analysis using IBM SPSS*, 7th edn. Routledge.

Pape S. E., Baksh R. A., Startin C., Hamburg S., Hithersay R. & Strydom A. (2021) Association between physical activity and CAMDEX-DS changes prior to onset of Alzheimer's disease in Down syndrome. *Journal of Clinical Medicine* **10**, 1882.

Perrot A., Maillot P., Le Foulon A. & Rebillat A.-S. (2021) Effect of exergaming on physical fitness, functional mobility, and cognitive functioning in adults with Down syndrome. *American Journal on Intellectual Developmental Disabilities* **126**, 34–44.

Phillips A. C. & Holland A. J. (2011) Assessment of objectively measured physical activity levels in individuals with intellectual disabilities with and without Down syndrome. *PLoS ONE* **6**, e28618.

Ptomey L. T., Szabo A. N., Willis E. A., Gorczyca A. M., Greene J. L., Danon J. C. *et al.* (2018) Changes in cognitive function after a 12-week exercise intervention in adults with Down syndrome. *Disability and Health Journal* **11**, 486–90.

R Core Team (2013) *R: A language and environment for statistical computing*. Austria, Vienna. https://www.R-project.org/

Ringenbach S., Holzapfel S., Mulvey G., Jimenez A., Benson A. & Richter M. (2016) The effects of assisted cycling therapy (ACT) and voluntary cycling on reaction time and measures of executive function in adolescents with Down syndrome. *Journal of Intellectual Disability Research* **60**, 1073–85.

Robertson I. H., Manly T., Andrade J., Baddeley B. T. & Yiend J. (1997) Oops!': performance correlates of everyday attentional failures in traumatic brain injured and normal subjects. *Neuropsychologia* **35**, 747–58.

Roth R. M. & Gioia G. A. (2005) *Behavior rating inventory of executive function-adult version*. Psychological Assessment Resources Lutz, Lutz, FL.

Shields N., Dodd K. J. & Abblitt C. (2009) Do children with Down syndrome perform sufficient physical activity to maintain good health? A pilot study. *Adapted Physical Activity Quarterly* **26**, 307–20.

Shields N. & Taylor N. (2015) The feasibility of a physical activity programme for young adults with Down syndrome: a phase II randomised controlled trial. *Journal of Intellectual and Developmental Disabilities* **40**, 115–25.

Shields N. & Taylor N. F. (2010) A student-led progressive resistance training program increases lower limb muscle strength in adolescents with Down syndrome: a randomised controlled trial. *Journal of Physiotherapy* **56**, 187–93.

Shields N., Taylor N. F., Wee E., Wollersheim D., O'Shea S. D. & Fernhall B. (2013) A community-based strength training programme increases muscle strength and physical activity in young people with Down syndrome: A randomised controlled trial. *Research in Developmental Disabilities* **34**, 4385–94.

Shields N., van den Bos R., Buhlert-Smith K., Prendergast L. & Taylor N. (2019) A community-based exercise program to increase participation in physical activities among youth with disability: a feasibility study. *Disability and Rehabilitation* **41**, 1152–9.

Shields N., Willis C., Imms C., McKenzie G., van Dorsselaer B., Bruder A. M. *et al.* (2022) Feasibility of scaling-up a community-based exercise program for young people with disability. *Disability and Rehabilitation* **44**, 1669–81.

Smilek D., Carriere J. S. & Cheyne J. A. (2010) Failures of sustained attention in life, lab, and brain: ecological validity of the SART. *Neuropsychologia* **48**, 2564–70.

Sparrow S. S., Balla D. A. & Cicchetti D. V. (2005) *Vineland II: Vineland Adaptive Behavior Scales*. American Guidance Service, Circle Pines, MN.

Sparrow S. S. & Cicchetti D. V. (1989) *The Vineland adaptive behavior scales*. Allyn & Bacon.

Startin C. M., Lowe B., Hamburg S., Hithersay R., Strydom A., Fisher E. *et al.* (2019) Validating the cognitive scale for Down syndrome (CS-DS) to detect longitudinal cognitive decline in adults with Down syndrome. *Frontiers in Psychiatry* **10**, 158.

Startin C. M., Rodger E., Fodor-Wynne L., Hamburg S. & Strydom A. (2016) Developing an informant questionnaire for cognitive abilities in Down syndrome: The Cognitive Scale for Down Syndrome (CS-DS). *PLoS ONE* **11**, e0154596.

Tungate A. S. & Conners F. A. (2021) Executive function in Down syndrome: A meta-analysis. *Research in Developmental Disabilities* **108**, 103802.

van Asselt-Goverts A., Embregts P., Hendriks A., Wegman K. & Teunisse J. P. (2015) Do social networks differ? Comparison of the social networks of people with intellectual disabilities, people with autism spectrum disorders and other people living in the community. *Journal of Autism and Developmental Disorders* **45**, 1191–203.

Venables W. N. & Ripley B. D. (2013) *Modern applied statistics with S-PLUS*. Springer Science & Business Media.

Vickers A. J. (2005) Parametric versus non-parametric statistics in the analysis of randomized trials with non-normally distributed data. *BMC Medical Research Methodology* **5**, 35.

Vickers A. J. & Altman D. G. (2001) Analysing controlled trials with baseline and follow up measurements. *British Medical Journal* **323**, 1123–4.

Accepted 17 August 2022