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Training attention in children with acquired brain injury: a study protocol of a randomised controlled trial of the TALI attention training programme

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ABSTRACT

Introduction Childhood inattention has been linked with poor academic outcomes, and increased lifetime social, occupational and psychiatric morbidity. Children with an acquired brain injury (ABI) are particularly susceptible to attention deficits and may benefit from interventions aimed at enhancing attention. The primary objective of this study is to evaluate the short-term efficacy of the TALI Train programme, compared with a placebo, on the outcome of attention in children with ABI.

Methods and analysis The study is a parallel, double-blind, randomised controlled trial. Participants will consist of 80 children with a diagnosis of ABI aged 4–9 years 11 months. Participants will be randomly allocated to either (1) TALI Train (intervention group), an adaptive game-based attention training programme, or (2) a non-adaptive placebo programme (control group). Both programmes are delivered on a touchscreen tablet, and children complete five 20 min sessions per week for a 5-week period at home. Assessment of selective, sustained and executive attention (primary outcomes), and behavioural attention, working memory, social skills and mathematics ability (secondary outcomes) will occur at baseline, post-training, and at 3-month and 6-month follow-up to assess immediate and long-term efficacy of TALI Train compared with placebo. Assessments will be completed at the Royal Children's Hospital in Melbourne, Australia. All assessments and analyses will be undertaken by researchers blinded to group membership. Latent growth curve modelling will be employed to examine primary and secondary outcomes.

Ethics and dissemination Ethics approval has been obtained from the Royal Children's Hospital Human Research Ethics Committee (HREC) (38132) and the Monash University HREC (17446). Results will be disseminated through peer-reviewed journals, conference presentations, media outlets, the internet and various community/stakeholder activities.

Trial registration number ACTRN12619000511134.

Strengths and limitations of this study

- This is a double-blind, randomised, controlled, superiority trial comparing the TALI attention training programme with an active placebo control group.
- The study will examine psychosocial and social factors as potential moderators of attention training outcomes in children with acquired brain injury.
- The study has a long-term follow-up of 3 months and 6 months.
- A small sample size is a potential limitation and multiple recruitment strategies will be implemented to increase the likelihood of obtaining an adequate number of participants.

INTRODUCTION

Childhood inattention has been linked with poor academic outcomes, an increased lifetime of social, occupational and psychiatric morbidity, and overall poorer quality of life.[1–4] Inattention is typically characterised by a lack of focus and concentration, distractibility, poor task completion, and forgetfulness, which in turn can have an insidious impact on health and education.[5] Children with an acquired brain injury (ABI: stroke, infection and traumatic brain injury (TBI)) are particularly susceptible to attention deficits as a result of their injuries.[6–9] Difficulties with attention are a frequently reported impairment following ABI,[9–11] with an estimated 20% of children with ABI developing a clinically significant attention disorder, often labelled secondary attention deficit hyperactivity disorder.[12 13] Given the prevalence and impact of inattention for children with ABI, there is a need to provide interventions that target attention in this population.

Children with an ABI undergo a period of acute recovery and improvement in functioning following their injury,[9 14] but for some children injury-related deficits often persist, with evidence of ongoing deficits in attention to 24 months[14 15] and as long as 4 years postinjury.[9] The risk factors for developing an attention deficit subsequent to an ABI include severe injury and repeated injury

events.[12 16 17] As domains of everyday functioning, such as academic achievement and social skills, rely heavily on the ability to direct and sustain attention, attention deficits can have significant consequences for children with an ABI, including difficulties forming and maintaining peer relationships and behavioural issues.[7 9 11 16–18] The functional impact of attention deficits for children with an ABI can extend beyond school to negatively influence emotional well-being and quality of life.[7 9 11 12 16–18] As a result, there is a need for paediatric interventions to maximise recovery and function.

Although the burden of attention deficits has been recognised for paediatric ABI, few evidence-based interventions have been specifically developed to improve attention in these children. More commonly, interventions for children with ABI target working memory using programmes such as Cogmed,[19 20] or a combination of working memory and attention such as the Attention Improvement and Management (AIM) and the Amsterdam Memory and Attention Training for Children (Amat-c).[21 22] These cognitive interventions commonly target a particular cognitive function, and improvements are mostly seen on the trained task or on cognitive tasks similar to the trained tasks.[23] While the AIM[21] and the Amat-c[22 24] demonstrate some improvements in cognitive measures of attention, a common shortfall has been the lack of transfer to other domains, with little to no improvements seen in academic achievement, behaviour or parent ratings of attention.[21] Many of these interventions require extensive time commitments, resulting in poor compliance and high attrition,[25 26] and fail to consider the influence of broader psychosocial factors, such as family functioning, when assessing the efficacy of cognitive training.[23 27]

The premise of cognitive training is that repeated practice of a cognitive skill will result in gains for that skill. When gains are also observed for tasks that share many elements with the practised task they are said to illustrate near transfer, whereas tasks that share fewer elements are said to illustrate far transfer.[28] An optimal result will be that training benefits generalise and improvements will be observed both across similar tasks (near transfer) and in domains associated with the trained skill (far transfer). Neuroplasticity, the brain's capacity to alter structure and function in response to environmental factors, is one possible explanation for cognitive gains observed following adaptive training.[29] Neuroplasticity, however, has been criticised as it does not explain the lack of support for far transfer, that is, why cognitive training typically only improves the trained skill and not untrained but associated skills.[30] An alternative explanation is that far transfer should only be observed when training and transfer tasks both place demands on exactly the same cognitive process.[30] Despite these assertions, a comprehensive theory of transfer is yet to be developed and confirmed.[28]

Despite the lack of far transfer observed in cognitive training studies, one programme that has promoted training-related improvements in untrained domains (eg, numeracy) is an adaptive cognitive training programme, TALI Train. TALI Train was developed to address the lack of effective, non-pharmacological treatments for children and young people with attention deficits, and is based on evidence that targeted training can produce lasting improvements in cognitive functioning. The TALI Train programme comprises a series of tablet-based exercises presented to children via game modules. A key benefit of the TALI Train programme is that it can be used at home, in schools or in clinical settings, without the need for coaching or attendance at regular appointments. TALI Train was originally developed for children experiencing heightened attention difficulties due to an underlying developmental disorder and intellectual disability, and has been shown to improve attention capacity and learning outcomes in children (4–10 years) with intellectual delay due to conditions such as autism spectrum disorder and Down syndrome,[31] conditions which affect an estimated 650 000 Australian children.[32]

Objectives

TALI Train is yet to be trialled in children with ABI, and as such its feasibility and efficacy in this group are unknown. The primary objective of this study is therefore to evaluate whether the TALI Train programme is able to reduce attention difficulties in children with ABI. It is hypothesised that the training intervention will promote greater gains in cognitive attention (selective, sustained and attentional control) than the active placebo control programme. Secondary objectives include assessing comparative effects of the intervention and placebo programme on untrained domains including academic achievement, working memory and social functioning. Further this study will examine potential predictors of training outcomes in children with ABI, including baseline attention abilities, the family environment, socioeconomic status and parental mental health.

Trial design

This study is designed as a double-blind, randomised, controlled, superiority trial with two parallel groups (equal allocation ratio).[28] The efficacy of the TALI Train programme compared with the placebo control programme will be assessed at baseline, post-training, and at 3-month and 6-month follow-up. The trial will be conducted and reported in accordance with the Consolidated Standards of Reporting Trials statement. Roles and responsibilities for the trial (site signature and delegation of duties log) are provided in online supplementary file 1.

METHODS AND ANALYSIS

Study setting

The study will be conducted in a predominantly urban setting. All assessments will occur face-to-face at the Royal Children's Hospital (RCH), Parkville, Australia. The

intervention and the control programme will both be completed by participants at home for the duration of the 5-week training period.

Eligibility criteria

To be eligible to participate in the trial, children must be (1) aged 4.0 and 9.11 years at time of randomisation; (2) have a primary diagnosis of ABI; (3) a minimum of 6 months postinsult (TBI, infection, stroke) or post-treatment (tumours); and (4) have elevated attention difficulties reported by primary caregivers. Eligibility will be assessed through screening of electronic medical records (EMR) and the Victorian Paediatric Rehabilitation Service (VPRS) registry. Attention difficulties will be screened via a 108-item parent-report online questionnaire (Conners 3 (6–10 years) or Conners Early Childhood (EC) (4–6 years) parent rating scale; table 1). Participants scoring above the clinical cut-off of 60 (elevated range) on either of the two subscales relating to inattentive behaviour (inattention or Inattentive Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, Text Revision, DSM-IV-TR) on the Conners 3 or on the inattention/hyperactivity subscale of the Conners EC will be deemed eligible for the current study. Children will be excluded from the study if they (1) are unable to comprehend and follow study instruction, including where sensory or physical impairments are present; (2) have had a prior ABI or diagnosis of developmental delay; (3) are diagnosed with or have borderline intellectual delay (IQ <80 on the Wechsler Abbreviated Scale of Intelligence - Second Edition, WASI-II or Wechsler Preschool and Primary Scale of Intelligence - Fourth Edition, WPPSI-IV; table 1); and (4) are more than 6 years after injury/treatment.

Intervention and control programmes

The intervention and placebo control programmes are administered on touchscreen tablet devices provided to participants for the duration of the intervention. The programmes each consists of four game-based tasks that are completed during a 20 min training session. At the end of each training session, children are rewarded with a virtual toy. TALI Train exercises target selective attention, sustained attention, interference (attentional) control and response inhibition. Tasks are designed to be adaptive, such that the difficulty level increases or decreases depending on the participant's performance. Both intervention and control conditions consist of 25 training sessions completed over a 5-week period. Training compliance will be monitored by an independent unblinded researcher via weekly support calls. Compliance is determined by the number of sessions completed, with non-compliance to be recorded if a participant completes less than 20 full training sessions or takes longer than 6 weeks to complete the programme.[33] The suggested schedule is five sessions a week over a 5-week period. However, if participants miss sessions for a period of time, they will be encouraged to try and make up for these missed sessions. For example, if only two sessions are completed in week 1 of training, then participants should strive to complete the missed three sessions in the subsequent 4–5 weeks. All participants regardless of compliance will be invited to attend the post-training and follow-up assessments. The active control programme focuses on basic motor skills such as touching, dragging, moving and rotating shapes on a screen and is not adaptive with children completing the same exercises at each training session. The features of the control programme have been designed to match the intervention programme in all other respects.

Discontinuation criteria

Participants may be withdrawn if they (1) experience a subsequent ABI; (2) undergo any neurosurgical intervention; (3) commence medication for the purpose of treating inattention, or any therapy or other intervention for the purpose of treating inattention; (4) violate the study protocol; (5) experience a serious or intolerable adverse event (AE); or (6) experience a decline in well-being.

All participants will be withdrawn if the study is terminated. Termination of the study can only be made by the chief investigator (KC). Participants are free to withdraw from the study at any time on their request. Withdrawing from the study will not impact their ability to access interventions in future, nor will this affect their relationship with the hospital.

Adherence

Adherence to the training schedule for the intervention group will be monitored via the secure TALI online platform and through weekly contact (eg, phone calls or emails) with participants' families. Compliance for the control group will be monitored through weekly contact (eg, phone calls or emails) with participants' families. Dates and times of all contacts (including attempted contacts) with participating families will be recorded. Both programmes provide information on the number of sessions completed, including date and time completed. All parents are additionally asked to complete a training log to record each completed session, to be provided to researchers at the post-training assessment. At each point of contact, where possible, researchers will ask participants and their caregiver 'How have you felt since your last visit/phone-call' to elicit any changes in well-being. If researchers notice a decline in the child's or parent's/caregiver's well-being during weekly check-ins or during follow-up assessment, they are able to provide a referral to an appropriate service for support. Alternatively where the child is currently receiving care from another department, permission may be sought to notify the child's treating clinician to ensure that support is being provided.

Outcomes

All outcome and predictor measures have been developed for children between the ages of 4 and 9 years, with the exception of the Test of Everyday Attention for Children (TEA-Ch). TEA-Ch2 has two versions: the TEA-Ch2 J (5–7 years) and the TEA-Ch2 A (8–15 years). As the sample for this study extends down to children aged 4 years,

Table 1 Schedule of measures

Outcome	Measure	Administration	Screening	Time 1	Time 2	Time 3	Time 4
Screening							
Inattention and DSM-5 inattention/ inattention-hyperactivity	Conners 3/Conners EC	Parent report	x	–	–	–	–
FSIQ/FSIQ 4*	WASI-II/WPPSI-IV	Child	x	–	–	–	–
Demographics	Demographic and Medical Questionnaire	Parent report	x	–	–	–	–
Primary outcomes							
Selective attention	TEA-Ch2 J, Balloon Hunt/TEA-Ch2 A, Hector Cancellation† TEA-Ch2 J Balloons 5/TEA-Ch2 A, Hector B‡	Child Child	–	x x	x x	x x	x x
Sustained attention	TEA-Ch2 J /TEA-Ch2 A Sustained Attention to Response Task† TEA-Ch2 J/TEA-Ch2 A Simple Reaction Time‡	Child Child	–	x x	x x	x x	x x
Interference control	Child Attention Network Task	Child	–	x	x	x	x
Response inhibition	Anticipated Response Task	Child	–	x	x	x	x
Secondary outcomes							
Inattentive and impulsive/ hyperactive behaviour	Strengths and weaknesses of ADHD symptoms and normal behaviour	Parent report	–	x	x	x	x
Visuospatial working memory	Corsi Block Tapping Test	Child	–	x	x	x	x
Social cognition and social communication	Paediatric Evaluation of Emotions, Relationships and Sociability (PEERS): emotion perception, emotion recognition, non-verbal gestures and social perception subtests	Child	–	x	x	x	x
Verbal working memory	Digit Span Task	Child	–	x	x	x	x
Numeracy	WIAT-II: numerical operations and mathematical reasoning subtests	Child	–	x	x	x	x
Predictors							
Intrinsic motivation	Intrinsic Motivation Scale	Child	–	x	x	x	x
Sleepiness	Stanford Sleepiness Scale	Child, preassessment and postassessment	–	x	x	x	x
Child sleep habits	Children's Sleep Habits Questionnaire	Parent report	–	x	x	x	x
Parental adjustment to child's chronic illness	The Parent's Experience of Child Illness	Parent report	–	x	x	x	x
Parental mental health	General Health Questionnaire	Parent self-report	–	x	x	x	x

Continued

Table 1 Continued

Outcome	Measure	Administration	Screening	Time 1	Time 2	Time 3	Time 4
Depressive symptoms child	Children's Depression Scale	Parent report	–	x	x	x	x
Anxiety symptoms—child	Spence Children's Anxiety Scale	Parent report	–	x	x	x	x
Social skills in daily life—child	PEERS-Q	Parent report	–	x	x	x	x

*Children who have not undergone IQ testing postinjury and within the last 2 years will be asked to complete either the WASI-II or the WPPSI-IV (dependent on age).
†Outcome, number of responses.
‡Outcome, response time.
ADHD, attention deficit hyperactivity disorder; Conners EC, Conners Early Childhood; DSM-5, Diagnostic and Statistical Manual of Mental Disorder, Fifth Edition; FSIQ, Full Scale Intelligence Quotient; TEA-Ch2 A, Test of Everyday Attention in Children (adolescent version, 8–15 years); TEA-Ch2 J, Test of Everyday Attention in Children (junior version, 5–7 years); WASI-II, Wechsler Abbreviated Scale of Intelligence - Second Edition; WIAT-II, Wechsler Individual Achievement Test - Second Edition; WPPSI-IV, Wechsler Preschool and Primary Scale of Intelligence - Fourth Edition .

advice was sought from TEA-Ch2 developer Professor Vicki Anderson, who advised the test could be used with this age group. All measures were selected based on their frequency of use within paediatric ABI samples and their psychometric properties (refer to table 2).

Primary outcomes

The primary outcomes will be change in cognitive attention, and selective, sustained and attentional control, between the intervention and control group post-training. Selective and sustained attention will be measured by the TEA-Ch2. Children aged 4–7 will complete the subtests of the junior version (TEA-Ch2 J) and children aged 8–9 years 11 months will complete the equivalent subtests from the adolescent version, TEA-Ch2 A. Selective attention is defined as the mean number of targets located across four trials of 15 s duration from the Balloon Hunt (junior) or Hector Cancellation (adolescent) subtest. Sustained attention is defined as the total number of responses to no-go trials from the sustained attention to response subtest (junior and adolescent). This subtest involves the sequential presentation of a set of shapes where participants were instructed to withhold a response if the shape was a triangle.

Attentional control will comprise measures of interference control and response inhibition. Interference control will be measured by the Child Attention Network Task, which is a child-friendly version of the flanker task.[34] The task will include three blocks: a practice block with 16 trials of targets and flankers (4 congruent left, 4 congruent right, 4 incongruent right, 4 incongruent left); and two experimental blocks with 32 trials of targets and flankers (64 trials in total, equal proportions of the 4 conditions, randomly sampled). Interference control will be defined as the mean accuracy of the experimental trials. Response inhibition will be measured by the Anticipated Response Task, a stop-signal task which measures the ability to rapidly prevent already initiated actions.[35] The task will include a practice block and four experimental blocks with 148 trials in total (33% stop trials[35]). Response inhibition will be defined as the stop-signal reaction time estimated by the integration method.[35]

Secondary outcomes and predictors

The secondary outcome and predictor measures and their psychometric properties are listed in tables 1 and 2, respectively. The secondary outcome measures cover the following domains—behavioural attention (inattention and hyperactivity), working memory, social cognition and numeracy—and have been included to assess whether far transfer occurs as a result of the intervention.[27 36 37] The predictor measures cover the domains of sleep, intrinsic motivation, family relationships, mental health and social cognition (parent report).[15 17 38–43] Predictor measures were selected because they have been linked to cognitive development in children and may influence the efficacy of the intervention.[38–43]

Participant timeline

The time schedule of enrolment, interventions and assessments is presented in figure 1. The trial will involve a 5-week intervention period with assessments at postintervention, and at 3-month and 6-month follow-up.

Sample size calculation

To determine the sample size required to detect significant changes in the primary outcome measures from baseline to post-training (between-subjects), we conducted a priori power analysis using G*Power V.3.1. For a power of 80%, a sample size of 40 is required to detect a large effect (f=0.40) and a sample size of 98 for a medium effect (f=0.25). Three previous cognitive training randomised controlled trials have reported medium to large effect sizes (eta-squared range 0.15–0.27[44]). Therefore, assuming an allocation ratio of 1:1, a sample between 40 and 98 participants should be sufficient to achieve adequate statistical power. This study will aim to recruit 80 participants, 40 per group.

Table 2 Psychometric properties of study measures

Measure	Domain	Administration	Psychometrics
Conners 3/Conners EC	Behavioural inattention	Parent report	Conners, population 6–18 years; US norms; reliability, internal consistency parent report >0.90; test–retest reliability parent coefficients, 0.72–0.98; established discriminant validity.[51] Conners EC, population 2–6; US norms; reliability, internal consistency parent coefficients 0.64–0.94 (behaviour scales); retest reliability parent, 0.73–0.98; convergent and divergent validity established.[52]
WASI-II/WPPSI-IV	Intelligence	Child	WASI-II, population 6–90 years; US norms; reliability, internal consistency coefficients moderate to high >0.83; test–retest reliability children, 0.87–0.95; established content validity, internal structure data and construct validity.[53] WPPSI-IV, population 2 years and 6 months – 7 years and7 months; internal consistency (0.95–0.96 for FSIQ), test–retest stability and interscorer agreement established; established content validity, internal structure data and convergent validity.[54]
Demographic and Medical Questionnaire	Demographics	Parent report	Not applicable.
TEA-Ch2 J/A	Selective and sustained attention	Child	Population, ages 5–16 years; Australian norms; test–retest reliability, 0.57–0.87; strong to moderate correlations for construct validity.[55]
Child Attention Network Task*	Interference control	Child	Population, 6–10 years; test–retest reliability, 0.94 overall RT, 0.93 overall error rate.[34]
Anticipated Response Task*	Response inhibition	Child	More reliable estimate of stop-signal response time than choice response and simple response time versions of the stop-signal paradigm.[35]
Stanford Sleepiness Scale	Sleep	Child	One-item questionnaire; 7-point Likert scale ranging from 'Feeling active, vital, alert, or awake' to 'No longer fighting sleep…'; one item, therefore internal consistency and inter-rater reliability not applicable; adequate content validity in adults.[56 57]
Corsi Block Tapping Test*	Working memory	Child	Developmental norms available; inconsistencies in task administration have generated inconsistent psychometrics.[58]
Paediatric Evaluation of Emotions, Relationships and Sociability (PEERS): emotion perception, emotion recognition, non-verbal gestures and social perception subtests*	Social cognition	Child	Psychometrics assessed as suitable for paediatric TBI population.†[59]
Digit Span Task*	Working memory	Child	Computerised tests of digit span, increased test–retest reliability and precision.[60]
WIAT-II: numerical operations and mathematical reasoning subtests	Numeracy	Child	WIAT-II, population 4–85 years; US norms; reliability, internal consistency coefficients generally high >0.85; test–retest reliability college/adult sample >0.75; validity, correlations with Wide Range Achievement Test-Third Edition (0.68–0.77) and the Differential Ability Scales (0.32–0.64).[61]
Intrinsic Motivation Scale	Intrinsic motivation	Child	17 items, 5-point Likert scale ranging from 'not at all true from me' to 'very true for me'. Population, school age, internal consistency coefficient >0.9; test–retest reliability correlation 0.74; internal structure data; discriminant and convergent validity evidence.[62]

Continued

Table 2 Continued

Measure	Domain	Administration	Psychometrics
Strengths and weaknesses of ADHD symptoms and normal behaviour	Behavioural attention and hyperactivity	Parent report	18 items, 7-point Likert scale ranging from 'far below' to 'far above'; adequate reliability and validity reported in recent review.[63 64]
Children's Sleep Habits Questionnaire	Sleep	Parent report	33 items, 3-point Likert scale from 'usually' to 'rarely'; low to moderate construct validity compared with actigraphy and polysomnography.[65–67]
The Parent's Experience of Child Illness	Support and relationships	Parent self-report	25 items, 5-point Likert scale ranging from 'Never' to 'Always'; psychometrics assessed as suitable for paediatric TBI population.‡
General Health Questionnaire	Psychological status	Parent self-report	12 items; 4-point Likert scaling, ranging from 'xx' to 'xx'; reliability, internal consistency (for GHQ) 0.84–0.93 and split-half 0.95; internal structure data.[45 68 69]
Children's Depression Scale	Psychological status	Parent report	50 items; 5-point Likert scale ranging from 'Very Wrong' to 'Very Right'; assessed as suitable for paediatric TBI population.‡[70]
Spence Children's Anxiety Scale	Psychological status	Parent report	39 items; 4-point Likert scale ranging from 'Never' to 'Always'; psychometrics assessed as suitable for paediatric TBI population‡[71 72]
PEERS-Q	Social cognition	Parent report	55 items; 5-point Likert scale ranging from 'Strongly Disagree' to 'Strongly Agree'; psychometrics assessed as suitable for paediatric TBI population.†[59]

*Computerised administration.
†Recommended as an emerging outcome instrument following paediatric TBI for intervention studies, according to WHO's International Classification of Functioning, Disability and Health taxonomy.[37]
‡Recommended as a supplemental outcome instrument following paediatric TBI for intervention studies, according to WHO's International Classification of Functioning, Disability and Health taxonomy.[37]
ADHD, attention deficit hyperactivity disorder; Conners EC, Conners Early Childhood; FSIQ, Full Scale Intelligence Quotient; GHQ, General Health Questionnaire; PEERS-Q, Paediatric Evaluation of Emotions, Relationships and Sociability - Questionnaire; RT, Reaction Time; TBI, traumatic brain injury; TEA-Ch2 A, Test of Everyday Attention in Children (adolescent version, 8–15 years); TEA-Ch2 J, Test of Everyday Attention in Children (junior version, 5–7 years); WASI-II, Wechsler Abbreviated Scale of Intelligence - Second Edition; WIAT-II, Wechsler Individual Achievement Test Second Edition; WPPSI-IV, Wechsler Preschool and Primary Scale of Intelligence - Fourth Edition .

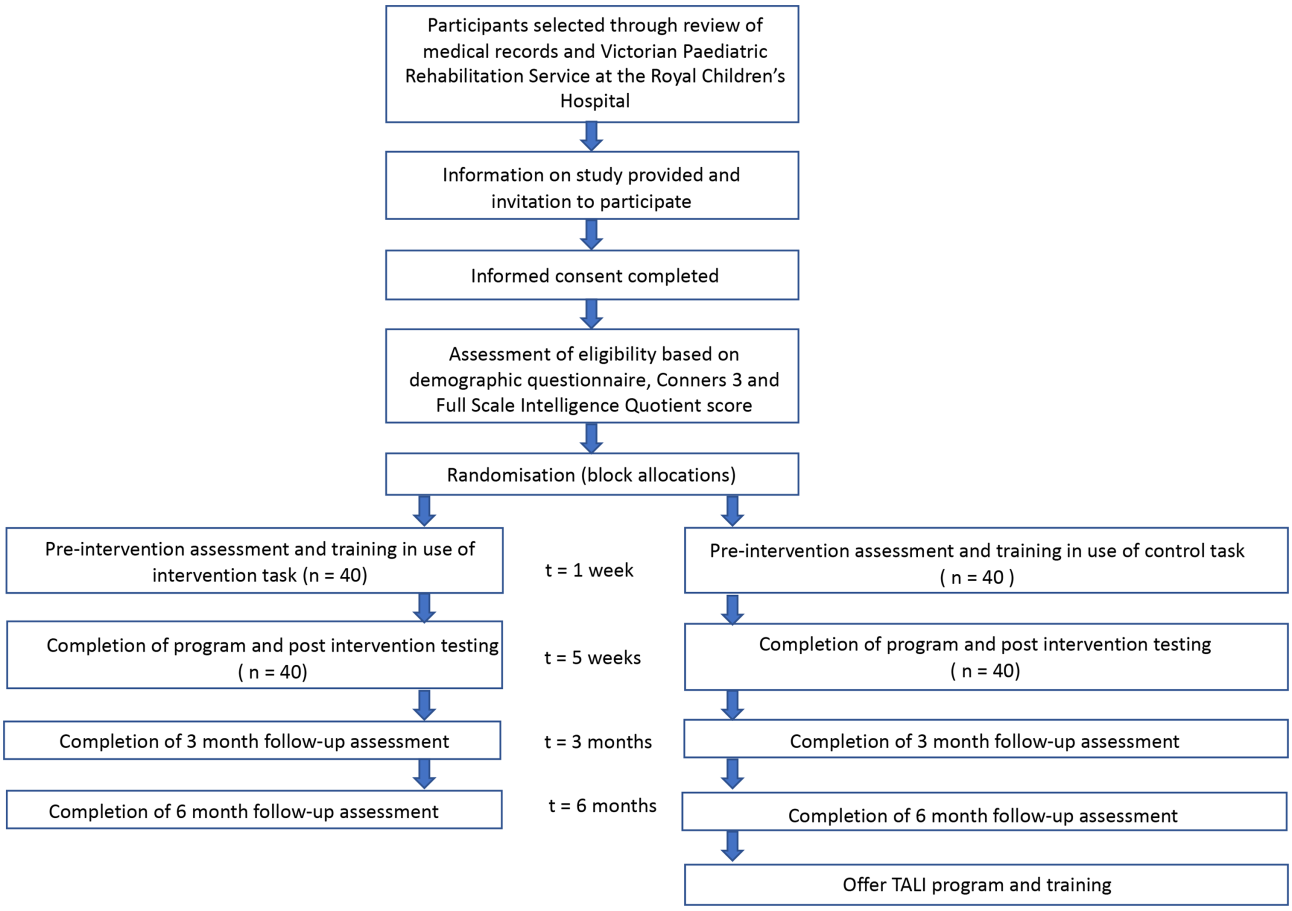

Figure 1 Protocol flow chart.

Recruitment

Potential participants will be recruited through a number of avenues. (1) The primary recruitment method will be via the VPRS database, VPRS clinicians and review of RCH EMRs. (2) Information about the trial will be disseminated via both the Murdoch Children's Research Institute (MCRI) and Monash University social media channels, website and intranet. (3) Information on the study (fliers, links to MCRI social media) will be provided to community-based ABI support services. Recruitment commenced in April 2019 and is anticipated to finish in April 2020, with data collection to be completed in October 2020.

Members of the research team will contact the parents/guardians of children who meet the inclusion criteria. Participants identified through the VPRS database or EMR will be contacted by a senior member of the research team, and if requested further project information will be sent. For participants engaged with a VPRS clinician, an information pack relating to the study will be provided to them by their clinician. Parents/guardians will be given at least 2 weeks to consider participation and will also be provided with an opportunity to ask any questions, and to ensure that participants understand the purpose, extent and possible risks associated with their involvement in the study. If informed consent is received, families will be invited to participate in the second stage of screening. Due to the location and scope of the recruitment avenues, it is anticipated that participants will reside in the state of Victoria.

The second stage of screening will be conducted online. Parents/guardians of participants will be emailed an invitation to complete the Demographic and Medical Questionnaire, and the Conners 3 or Conners EC (table 1). The Demographic and Medical Questionnaire will include questions pertaining to injury type (traumatic vs non-traumatic injury) and injury severity to aid with stratification, and this will be confirmed with Glasgow Coma Scale (GCS) score, where available (GCS <8 severe, GCS 9–12 moderate, GCS 13–15 mild[45]). Following completion of the second stage of screening, researchers will assess eligibility for the study based on the inclusion/exclusion criteria. For children who have completed an IQ assessment in the previous 2 years (and since their injury), consent will be sought to obtain the results of this assessment. Children who have not undergone IQ testing postinjury and within the last 2 years will be asked to complete either the WASI or the WPPSI (dependent on age). The WASI/WPPSI will be administered by a trained member of the research team at RCH. Should the child be unable to attend RCH, an offer will be made to conduct this assessment at the child's school or within the family home.

Allocation

An independent statistician will be responsible for the implementation of the allocation. Block randomisation (ratio 1:1, blocks of 4) will be used to maintain balance between intervention arms. Randomisation will be stratified by parent-reported injury severity with three strata: mild, moderate to severe, and other (where injury severity cannot be classified).[46] Computer-generated random numbers will be used to allocate participants.

Concealment mechanism

The documentation pertaining to the randomisation will be securely stored and inaccessible to researchers undertaking recruitment and testing. Researchers conducting screening and assessments will be unaware of group allocation for the duration of the trial (including data analysis). Prior to the commencement of each assessment session, participants will be explicitly instructed not to discuss the contents of their assigned programme with the researcher. Group allocation details and randomisation codes will only be available once all data collected have been entered into the study database for every participant and the database has been finalised, except in the case of an emergency. For any participant for whom the study blind is broken, the date, time, participant identification (ID) and reason for unblinding must be documented.

Data collection

Researchers blinded to participants' group allocation will conduct preintervention, postintervention and follow-up assessments at RCH (refer to table 1 for schedule for assessments). Two researchers will be present at each visit. Participants may find the assessment sessions to be tiring and small breaks will therefore be provided when needed. The assessments are estimated to take 2–2.5 hours to complete. If children are unable to complete the full assessment, remaining measures will not be administered. While children are completing the assessment, parents will be asked to complete a number of tablet-based parent-report measures. If the parent who completed the measures at the first time point does not attend any subsequent assessment session with the child, for that time point a link will be provided via email to allow them to complete the measures from home. All study measures are described in table 1, with reliability and validity information, if available, in table 2.

Researchers will be trained in the study requirements, including the assessment measures. For each participant, especially designed checklists will be used to monitor data collection, and all data will be recorded in a case report form (CRF). Where possible two researchers will be present at each assessment to ensure that at least one researcher from the initial assessment will be present at subsequent assessments.

Data management

Study data will be stored as a combination of paper and electronic files and then entered into and managed within a Research Electronic Data Capture (REDCap) database, which acts as an electronic CRF. Data will be held, administered, checked and analysed according to study standard operating procedures. The coordinating site will maintain a register of data checks for monitoring purposes. Collected data, including AE reports and file notes, will be securely stored and identified by ID number only. All confidential participant contact information and identifiable data (eg, signed consent forms) will be stored separately within the database. All study documents will be stored in accordance with relevant government regulations regarding retention and disposal of participant records.

For the purposes of this study the investigators are responsible for recording all AEs, regardless of their relationship to study intervention, with the exception of conditions that are present at screening and do not deteriorate. The description of each AE on the participant's file will include a description of the AE, onset date, duration, date of resolution, severity (mild, moderate or severe), any action taken, outcome (recovery, continuing, worsening) and the likelihood of the relationship of the AE to the study intervention (unrelated, possible, probable, definite).

The clinical monitoring plan has been provided in online supplementary file 2 and includes requirements for data monitoring.

Statistical methods

Screening data will be analysed to assess the attention profiles of participants. No further interim analyses will be conducted. At the conclusion of the trial, investigators approved by the RCH Human Research Ethics Committee (HREC) will have access to the trial data. An intention-to-treat approach will be taken, where data from all children enrolled in the trial will be analysed regardless of compliance. Initial comparisons will assess whether the intervention and active control groups differ on characteristics such as age and IQ. Latent growth curve modelling (LGCM) is regression-based and can quantify systematic individual differences. LGCM will be applied to examine changes in attention over time using the nlme package in R.[47 48] Models will be estimated using robust maximum likelihood. A multigroup approach will be used so that the trajectories of the intervention group with the active control group can be compared. Individual differences measured at baseline, including age and IQ, will be added to the growth model as fixed effects. Individual differences related to the longitudinal design of the trial will be estimated as random effects. An LGCM will be created for each primary and secondary outcome.

Given the trial has multiple outcomes and that these outcomes may be correlated with each other, the family-wise error rate will be controlled for statistically. Assuming the assumptions of the method are met, the Hommel adjustment for multiple comparisons will be

applied.[49] A sensitivity analysis will be conducted to assess whether training outcomes differed for those who did (compliers) and did not (non-compliers) adhere to the required training schedule. Analysis of whether training compliers differed from non-compliers on any baseline characteristics (eg, age, intrinsic motivation) will also be conducted. Management of missing data will be determined based on the amount and pattern of missing data. Less than 20% data missing at random across all time points will indicate good retention and low concern for study validity.[50]

ETHICS AND DISSEMINATION

Reporting of the protocol adheres to the Standard Protocol Items: Recommendations for Interventional Trials checklist. For all participants between the age of 4 years and 9 years and 11 months assent and written parental consent will be obtained. The parent/guardian information and consent form has been provided in online supplementary file 3.

Families of participants in the study will receive a 6 monthly email newsletter that will update them on the research outcomes to date and future research direction. At the conclusion of the study, a summary of their child's results will be provided to parents if requested. In addition, the overall collated results of the trial and its outcomes will be provided to parents electronically, and the researchers will also organise an information evening to present the findings to participants and answer any questions. The research findings will be published in journal articles and conference proceedings, and will form part of a PhD thesis. All data used for this purpose will be de-identified and analysed as a group to protect the privacy of participants and ensure confidentiality is maintained. Relevant anonymised participant-level data will be made available on reasonable request to the research team.

PATIENT AND PUBLIC INVOLVEMENT

The research questions and outcomes measures developed in the study were informed by the extensive experience of the principal investigators in their work on attention and with children with ABI. We are aware that participants with ABI are susceptible to cognitive fatigue, and consequently participants and their families will be asked to comment on the time required for each assessment visit and for the intervention. We will monitor this feedback and make adjustments to the project where possible and with approval from RCH HREC and Monash University HREC (MUHREC).

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Contributors KC is the chief investigator of the current study. HK provides expertise in digital interventions and trial design. VA and CC provide clinical expertise in acquired brain injury and access to the proposed participant sample. KC, HK, VA, CC, EM and SR were all involved in the study design. EM and SR are involved in data collection. All authors will contribute to the development of interim and final drafts, and read and approve the final manuscript. EM and SR wrote the first and subsequent drafts of this manuscript. HK and CC provided feedback on subsequent drafts. The final manuscript was approved by all authors.

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Competing interests HK and KC are coinventors of the TALI Train programme. All intellectual property (IP) associated with TALI Train is currently owned by Monash University, which has granted licence to commercialise their IP to TALI Health. As a result, Monash University, including coinventors HK and KC, receive a small portion of predefined royalties from the licensee (TALI Health). HK holds a small number of personal shares in TALI Health's public-listed holding company Novita Healthcare (ASX: NHL). VA, CC, SR, EM and other team members are independent researchers and as such do not have any personal or financial interests in TALI Health.

Patient consent for publication Not required.

Ethics approval The study was approved by the RCH Human Research Ethics Committee (HREC) on 19 November 2018 (reference number 38132) and confirmed by the Monash University HREC on 10 December 2018 (reference number 17446).

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