

Neuropsychological Rehabilitation: An International Journal

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/pnrh20>

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Published online: 27 May 2015.

To cite this article: Asha Vas, Sandra Chapman, Sina Aslan, Jeffrey Spence, Molly Keebler, Gisella Rodriguez-Larrain, Barry Rodgers, Tiffani Jantz, David Martinez, Jelena Rakic & Daniel Krawczyk (2015): Reasoning training in veteran and civilian traumatic brain injury with persistent mild impairment, *Neuropsychological Rehabilitation: An International Journal*

To link to this article: <http://dx.doi.org/10.1080/09602011.2015.1044013>

Reasoning training in veteran and civilian traumatic brain injury with persistent mild impairment

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(Received 7 October 2014; accepted 17 April 2015)

Traumatic brain injury (TBI) is a chronic health condition. The prevalence of TBI, combined with limited advances in protocols to mitigate persistent TBI-related impairments in higher order cognition, present a significant challenge. In this randomised study ($n = 60$), we compared the benefits of Strategic Memory Advanced Reasoning Training (SMART, $n = 31$), a strategy-based programme shown to improve cognitive control, versus an active learning programme called Brain Health Workshop (BHW, $n = 29$) in individuals with TBI with persistent mild functional deficits. Outcomes were measured on cognitive, psychological health, functional, and imaging measures. Repeated measures analyses of immediate post-training and 3-month post-training demonstrated gains on the cognitive control domain of gist reasoning (ability to abstract big ideas/goals from complex information/tasks) in the SMART

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We would like to thank Lyda Hill, the Meadows Foundation, and Dee Wyly Endowed Chair fund for their support with various aspects of the study including advocacy and recruitments efforts.

No potential conflict of interest was reported by the authors.

This study received funding from the US Department of Defense (DOD) Congressionally Directed Medical Research Programs (CDMRP) [Award W81XWH-11-2-0194 to DCK] and [Award W81XWH-11-2-01945 to SBC]. The funding agency has not had a direct role in the design, data collection, analysis, or interpretation of the data for this study, nor have they had a direct role in the preparation of this manuscript or the decision to submit it.

group as compared to BHW. Gains following the SMART programme were also evident on improved executive function, memory, and daily function as well as reduced symptoms associated with depression and stress. The SMART group showed an increase in bilateral precuneus cerebral blood flow (CBF). Improvements in gist reasoning in the SMART group were also associated with an increase in CBF in the left inferior frontal region, the left insula and the bilateral anterior cingulate cortex. These results add to prior findings that the SMART programme provides an efficient set of strategies that have the potential to improve cognitive control performance and associated executive functions and daily function, to enhance psychological health, and facilitate positive neural plasticity in adults with persistent mild impairment after TBI.

Keywords: Brain plasticity and repair; CBF; Cognitive training; Gist reasoning; Mild-spectrum TBI in adults; Veterans

INTRODUCTION

Traumatic brain injury (TBI) is a chronic health condition and not an isolated event or incident in terms of treatment considerations (Masel & DeWitt, 2010; Rutherford & Corrigan, 2009). All too often, the effects of TBI endure and can even worsen over time when there is no further cognitive monitoring or interventions once individuals are dismissed from acute stage rehabilitation. In the last decade, researchers have documented that TBI-related impairments persist, particularly in cognitive functions of executive control, at all levels of injury severity (including mild TBI) and these impairments significantly impede progress in long-term functionality (Bales, Wagner, Kline, & Dixon, 2009; Marshall, Bayley, McCullagh, Velikonja, & Berrigan, 2012; Whitnall, McMillan, Murray, & Teasdale, 2006). As a result of this accumulating cognitive burden, the economic costs are immense given that TBI is one of the most prevalent causes of disability (Corrigan, Selassie, & Orman, 2010). To date, only a handful of methods exist that show strong efficacy in mitigating cognitive and functional sequelae of TBI at chronic stages, thereby presenting a major void (Buck, 2011; Helgeson, 2010). Regular monitoring and assessment of persistent symptoms, along with identification of TBI-associated risks and psychiatric comorbidities, e.g., depression, post-traumatic stress disorder, (PTSD), are recommended along with later-stage cognitive treatment protocols that address the capacity to reduce and overcome residual deficits (Corrigan et al., 2010; McAllister, 2008). Developing, testing, and identifying cognitive training protocols that benefit individuals with TBI is particularly critical given emerging evidence that retained neural and cognitive plasticity could

be harnessed to improve cognitive and behavioural goals (D'Esposito & Chen, 2006).

The current study examined cognitive training benefits in individuals with a history of TBI at chronic stages after injury (> 6 months post-injury). At the time of initial assessment, the participants reported mild impairments in basic functional skills (e.g., activities of daily living) and moderate-to-significant difficulties accomplishing complex tasks (e.g., involving flexible and innovative thinking, problem solving). Similar to Tiersky and colleagues, we refer to this group as “mild-spectrum TBI” (Tiersky et al., 2005).

Integrative neurocognitive therapies are standard practice to address mild-spectrum TBI impairments. Integrative therapies combine cognitive remediation techniques with psychotherapeutic education to help improve cognitive functioning and teach strategies to adapt to life post-injury (Cicerone et al., 2011; Ferguson & Mittenberg, 1996; Ho & Bennett, 1997; Rohling, Faust, Beverly, & Demakis, 2009; Tiersky et al., 2005). Evidence from integrative therapy studies, often conducted in an acute or sub-acute rehabilitation setting, report immediate gains in targeted cognitive processes (e.g., memory, attention) and post-injury social and vocational adaptation (Cicerone et al., 2011; Schretlen & Shapiro, 2003; Tiersky et al., 2005). Generalised and lasting benefits of these targeted therapies to higher-order cognition are limited and poorly understood. Thus, there is a critical need to examine the efficacy of higher-order cognitive training protocols in mild-spectrum TBI, irrespective of initial injury severity and stage post-injury. Researchers are recognising the limitations of relying on initial injury severity to guide recommendations about chronic-stage cognitive rehabilitation efforts. The diffuse nature of TBI, combined with myriad factors that contribute to initial and later stage recovery processes (e.g., premorbid intellectual attributes, rehabilitation efforts, and support system), make predicting TBI long-term functional outcomes based on initial injury severity unreliable (McAllister, 2011). Chen and colleagues proposed engagement of “integral/complex functions” to enhance overall daily function versus remediation of “specific cognitive processes” as a promising approach to advance TBI rehabilitation (Chen, Abrams, & D'Esposito, 2006). Recent rehabilitation studies have demonstrated that training paradigms targeting frontal lobe mediated cognitive control processes may have a beneficial impact on associated cognitive domains and improved daily function (D'Esposito & Gazzaley, 2006). Notable amongst these developments are top-down approaches to cognitive training that target control processes mediated by the prefrontal cortex (PFC) to guide goal-driven (versus stimulus-driven) and voluntary control (versus automatic) cognitive operations (Chapman & Mudar, 2014; D'Esposito & Chen, 2006; Levine et al., 2000; Vas, Chapman, Cook, Elliott, & Keebler, 2011). Neurally, top-down modulation involves bidirectional operations of both the enhancement of the brain regions relevant to

one's goals and subsequent suppression of neural activity in cortical regions involved in processing goal-irrelevant information (Gazzaley, Cooney, McEvoy, Knight, & D'Esposito, 2005). Examples of evidenced-based top-down cognitive training programmes for adults with TBI include, but are not limited to, Goal Management Training (GMT, Levine et al., 2000), Goal Oriented Attentional Self-regulation (GOALS, Novakovic-Agopian et al., 2011), and Problem-Solving Training (PST, Rath, Simon, Langenbahn, Sherr, & Diller 2004). Findings from these studies reported gains in cognitive processes (e.g., inhibition, working memory) and improvement in daily function in adults with TBI.

Similarly, the Strategic Memory Advanced Reasoning Training (SMART), developed at the Center for BrainHealth, The University of Texas at Dallas, has been shown to be effective as a training programme to improve higher-order cognitive control in several clinical and healthy populations (Chapman & Mudar, 2014). SMART is based on theoretical and empirical evidence that the brain's function is optimised when large chunks of information are managed by extracting transformed, big ideas rather than trying to encode and store all the pieces of information or tackle all aspects of a task at once (Chapman et al., 2012; Gabrieli, 2004; Lloyd & Reyna, 2009; Zwaan & Radvansky, 1998). In a series of studies, our team has shown that individuals benefit from SMART at multiple levels ranging from cognitive performance to neural function with gains in real-life function when provided with mental strategies to manage complex information/tasks (Chapman et al., 2015; Gamino, Chapman, Hull, & Lyon, 2010). With regard to TBI specifically, SMART yielded significant gains in cognition and daily life skills in individuals with moderate to severe TBI (initial severity of injury) who were experiencing moderate functional deficits at pre-training period (Cook, Chapman, Elliott, Evenson, & Vinton, 2014; Vas et al., 2011). However, it is not known whether top-down SMART training improves cognitive and neural functions in adults with mild-spectrum TBI at chronic stages post-injury, the majority of whom continue to show deficits in complex cognitive everyday life tasks. Therefore, the current study examined the benefits of SMART in a mild-spectrum, chronic stage adult TBI population.

Our primary aim in this study was to examine the benefits of SMART versus an education-based control protocol focusing on active learning, called the Brain Health Workshop (BHW, Bonnelle et al., 2011; Levine et al., 2011) in adults with mild-spectrum TBI. We predicted gains in the cognitive control function of gist reasoning and associated executive functions as well as memory immediately at post-training and at three-month post-training. Our second goal was to determine the effects of training on psychological health and daily function. We hypothesised significant gains in the SMART group as compared to the BHW group on self-report measures of psychological health (indicated by reduction in symptoms associated with depression

and stress-related behaviours) and daily function, both at post-training and at three-month follow-up. The third aim of the study was to investigate any training-induced neuroplasticity associated with SMART training via measuring resting cerebral blood flow (CBF) using pseudo-continuous arterial spin labelling (pCASL) MRI compared to the BHW group. Few studies have investigated the neural effects of strategy-based cognitive training protocols in TBI. MRI-derived CBF offers a promising physiological parameter that can serve as a biomarker to detect changes that typically occur prior to structural changes (Chapman et al., 2015). Empirical studies demonstrate that CBF is beginning to offer a reliable and sensitive method to measure brain changes resulting from various treatment regimens (Detre, Rao, Wan, Chen, & Wang, 2012). We propose that positive brain changes should be linked to cognitive training benefits based on experience-driven, neuroplasticity principles of a tight coupling of brain blood activity and neural activity. Moreover, empirical studies demonstrate that CBF is tied to neuronal health (Chen, Rosas, & Salat, 2013). In the present study, we were particularly interested in convergence of improved cognition with concomitant changes in brain function as measured by CBF.

METHOD

Participants

The current study is a subset of a larger ongoing Department of Defense (DoD) study (Krawczyk et al., 2013). Sixty community dwelling individuals (32 men and 28 women) between the ages of 19 and 65 years with a history of TBI in chronic stages of recovery (> 6 months post-injury) participated in the study. Out of the 60 participants, 47 were civilians and 13 were veterans. Impairment on gist reasoning and/or standardised executive function tests was not an inclusion criterion. However, all participants reported difficulty in returning to pre-TBI levels of work ability and/or obtaining gainful employment as a result of cognitive difficulties in their initial interview. We did not base inclusion on gist performance since prior training studies have shown improvement in gist reasoning, executive function capacities and frontal networks with similar training in healthy adults and teens (Chapman et al., 2015; Gamino et al., 2014).

Over two-thirds of the participants sustained their injuries nearly 10 years ago, so there was limited access to medical records that might provide reports of the severity of the TBI. Therefore, a valid and reliable self-reported functional measure, the Glasgow Outcome Scale – Extended (GOS-E), was used to characterise functional status at the time of initial testing (Wilson, Pettigrew, & Teasdale, 1998). The GOS-E tracks degree of functional recovery

with broad functional categories of cognition, mood, and behaviour on an 8-point scale. Possible scores range from 2 to 8, with 8 indicating good recovery and 2 indicating a vegetative state. Inclusion criteria included individuals with a GOS-E score of 6–7 (characterising mild levels of functional impairments supporting the classification of mild-spectrum TBI), native English speakers, and minimum of high school diploma or equivalent. Exclusion criteria included pre-TBI histories of stroke, learning disability, communication disorder, substance abuse, or major psychiatric disorder. Participants who were receiving concurrent cognitive treatment(s) at the time of the assessment were excluded from the study. Recruitment methods included flyers, website advertising, speaking at local brain injury support groups, and speaking to representatives from local veteran centres. Informed consent was obtained from all participants in accordance with the Institutional Review Board (IRB) of The University of Texas at Dallas and The University of Texas Southwestern Medical Center and the United States Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), and Human Research Protection Office (HRPO). The CONSORT diagram (Figure 1) shows the flow of participants from pre-training to three-month follow-up period after randomisation (Tables 1 and 2).

Procedure

The current study was a blinded randomised control trial where participants and examiners were blinded to the evaluation scoring and training groups. Participants were randomly assigned to one of two training protocols: (1) strategy-based Strategic Memory Advanced Reasoning Training (SMART) or (2) education-based Brain Health Workshop (BHW). Participants were informed that the goal of the study was to compare the benefits of two didactic and interactive programmes that could be beneficial to adults with TBI. The examiners involved in testing and scoring were blinded to the group and time (i.e., pre-, post-, and three-month post-training) status of the participants. Training was initiated within three weeks of initial testing. Post-testing took place within 2–3 weeks of completion of the training programme. Three-month follow-up testing took place 3–4 months after the training sessions were completed. Additional methodological details about the larger study are provided in Krawczyk et al. (2013).

Both SMART and BHW programmes offered 18 hours of training during 12 group sessions (1.5 hours each session) conducted over 8 weeks. The first 15 hours of training (i.e., 10 sessions) were conducted in the first 5 weeks (2 sessions per week). The final 3 hours of training (sessions 11 and 12) took place at spaced intervals over the next 3 weeks. Two trained clinicians who have experience in TBI rehabilitation led each group. Each group consisted of 4–5 participants. There was a comparable number of group members in

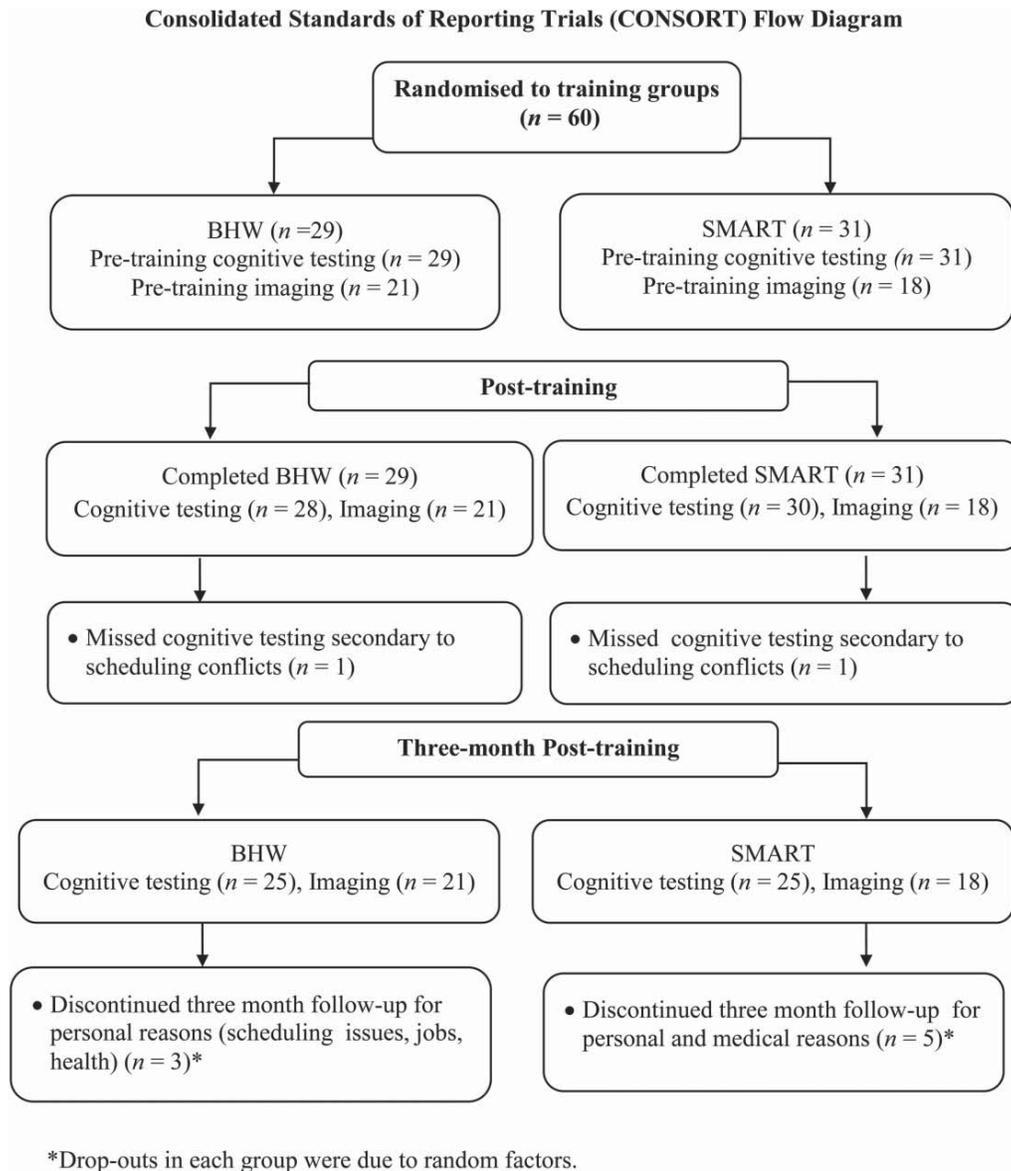


Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram. *Drop outs in each group were due to random factors.

both SMART and BHW groups to control for social bonding, which is considered therapeutic. To ensure adherence to the programme, the clinician facilitators stressed the importance of attending every session and diligence in completion of homework assignments. Makeup sessions were conducted for participants who missed their regular sessions. We originally planned to conduct an analysis eliminating those participants with less than 80% attendance. However, all participants in both groups had over 90% attendance and hence no participant from either group was excluded from the analyses.

TABLE 1
Demographic data across groups

<i>Characteristics</i>	<i>BHW (n = 29)</i> <i>Mean (SD)</i>	<i>SMART (n = 31)</i> <i>Mean (SD)</i>	<i>t (58)</i>
Age	42.76 (14.11)	41.00 (14.20)	0.63 n.s.
Gender: Number of men, women	15, 14	17, 14	0.80* n.s.
Status: Number of civilian, military	23, 6	24, 7	0.86* n.s.
Years of education**	17.54 (2.64)	17.11(3.09)	0.59 n.s.
Time post injury (years)	8.64 (5.80)	8.79 (9.03)	0.67 n.s.
GOS E	6.55 (0.50)	6.61 (0.49)	0.64 n.s.
SES	48.33 (9.86)	49.89 (7.38)	0.51 n.s.
Estimates of premorbid IQ	110 (8.33)	109.52 (8.87)	0.56 n.s.
Estimates of current IQ	112.96 (9.01)	108.68 (10.92)	0.11 n.s.
Processing speed			
D KEFS CW condition 1	8.41 (3.46)	9.16 (3.43)	0.40 n.s.
D KEFS CW Condition 2	9.37 (3.05)	9.25 (3.41)	0.88 n.s.
D KEFS, Trail Making 1	11.06 (2.85)	12.00 (1.84)	0.13 n.s.
Hayling Section A	5.41 (0.82)	5.74 (0.81)	0.14 n.s.

Note: In the full sample ($n = 60$), the cause of TBI in 10 participants was due to a motor vehicle accident, 13 were combat blast related, 7 were secondary to falls, 12 were sports related, and 18 participants sustained a combination of injuries (e.g., car accident and falls). *The group differences were examined on Chi square test. **The number of years of education did not always correspond with number of degrees of diplomas. n.s. Group differences were not significant. GOS E: Glasgow Coma Scale Extended, SES: Socio economic status, IQ: Intelligence quotient, D KEFS: Delis Kaplan Executive Function Systems, CW: Color Word.

Training protocols

The overall goal of the SMART programme is to teach metacognitive strategies to improve cognitive control functions of strategic attention, integrative reasoning, and innovation. The overall goal of BHW is to provide new learning about fascinating facts pertinent to brain health and brain injury (Table 3).

Strategic Memory Advanced Reasoning Training (SMART)

The SMART protocol trains a common set of three multidimensional and inter-related strategies to apply to a wide range of everyday tasks. The strategies draw upon top-down processes to improve cognitive control functions, including strategic attention, integrative reasoning and innovation (Table 3). Strategic attention strategies focus on intentional management of input by blocking distractions and irrelevant input, and factoring in regular mental breaks. The negative toll of multitasking on cognitive performance and productivity is integral to strategic attention. Integrative reasoning strategies build on strategic attention to engage in synthesis, abstraction, and

TABLE 2
Participant characterisation measures

<i>Characterisation domains</i>	<i>Measures</i>	<i>Description</i>
Estimate of premorbid verbal intellectual ability	Wechsler Test of Adult Reading (WTAR, Wechsler, 2001)	Participant reads a list of 50 words that have atypical grapheme to phoneme translations.
Estimate of current intellectual ability	WASI Vocabulary (Wechsler, 1999)	Participant describes the meanings of a set of 38 words. The Vocabulary subtest measures word knowledge and verbal concept formation.
	WASI Matrix Reasoning (Wechsler, 1999)	Participant performs four types of nonverbal reasoning tasks: pattern completion, classification, analogy, and serial reasoning. Participant chooses one of the five response options to complete a set of matrix designs.
Socio Economic Status (SES)	The Barratt Simplified Measure of Social Status (BSMSS, Barratt, 2005)	Estimation of SES based on combined scores of educational attainment, occupation, and employment status (retired individuals use their last occupation), marital status, and parental education and occupation.
Processing speed (time taken to complete each task accurately)	D KEFS Switching tasks 1 (Delis, 2001)	Participant connects numbers 1 to 23 in correct sequence.
	D KEFS Color Word task 1 and 2 (Delis, 2001)	Participant names the ink colour of colour patches (task 1) and read words (task 2).
	Hayling Sentence completion A (Burgess & Shallice, 1997)	Participant verbally produces a word to complete a set of 15 sentences in which the last word is missing.

implementation processes. Abstracting meanings (or ideas) from input/data to understand big ideas, take-home messages, and meaningful goals (that can be implemented) forms the core of this second part of the training. The engagement of top-down processes to improve cognitive control of information and goal management is further facilitated by innovation strategies of fluid and flexible thinking. Examining information/goals from divergent perspectives further strengthens abstraction capacity and more expansive problem solving skills to mitigate impairments of concrete thinking and status quo approaches to addressing problems that are often a common sequelae of TBI (Vas, Spence, & Chapman, 2015). Thus, the SMART programme provides an easily adoptable tool kit to tackle mental activities along with extensive practice to reinforce inculcation into regular habits.

TABLE 3.
Brief description of training groups

<i>SMART</i>	<i>BHW</i>
(1) Strategic attention: Input management <ul style="list-style-type: none"> • Block distractions • Inhibit irrelevant input • Focus on single task and avoid multitasking • Calibrate time and effort 	(1) Brain anatomy <ul style="list-style-type: none"> • Basic brain structures • Aetiology of brain diseases
(2) Integrated reasoning: Dynamic updating of input <ul style="list-style-type: none"> • Synthesise big ideas • Interpret meaning • Implement application 	(2) Brain functions <ul style="list-style-type: none"> • Memory • Attention • Executive functions • Movement, vision, language
(3) Innovation: Cognitive flexibility <ul style="list-style-type: none"> • Fluid perspectives • Diverse multiple solutions to problems • Finding novel directions 	(3) Neuroplasticity <ul style="list-style-type: none"> • Brain injury • Ageing
	(4) Effects of lifestyles on brain health <ul style="list-style-type: none"> • Sleep • Diet • Stress • Exercise • Social bonds

The SMART strategies are introduced in a sequential manner in a Power Point format. Mastery of individual strategies is not necessary to move on to the next level, as strategies are continually reinforced at each stage of the programme. Preselected materials of varying lengths, including newspaper articles, stories, pictures, and audio-video clips are used to illustrate the strategies. More importantly, the application of these strategies in daily function is emphasised. For example, strategic attention is illustrated by deleting less relevant information from news stories, less important tasks of the day, and eliminating distractions that hinder accomplishment of a goal. Following each session, participants are given homework assignments to ensure practice of strategy application. Participants are also encouraged to add material of their choice such as movies, TV shows, and books. Along with these informational sources, homework also includes participants' identification of specific life activities in which SMART strategies are to be incorporated.

Brain Health Workshop (BHW)

The BHW protocol has been previously used as a comparison-training programme in cognitive training trials (Binder, Turner, O'Connor, & Levine, 2008; Levine et al., 2000, 2011; Novakovic-Agopian et al., 2011). Similar to SMART, the BHW education topics are introduced in a sequential manner. Clinicians present the assigned topics in a Power Point format. The initial

four sessions include education on brain topics of relevance to the participants' health and brain injury. These topics include anatomy (using both written material and a 3D brain model), functioning of each lobe of the brain, neurotransmitters, effects of a TBI on cognitive functioning, and general principles of neuroplasticity. The rest of the sessions focus on understanding and learning the impact of diet, physical exercise, sleep (sleep cycles and sleep hygiene), and social bonds on brain health. In addition to providing education on these brain health-related topics, participants are encouraged to discuss relevance of this information to their daily lives. For example, participants discussed how their sleep patterns, food intake, and physical exercise impact job performance. At the end of each session, participants were given take-home reading assignments on related topics that were discussed in the sessions and could be shared with others outside of training. The take-home readings were discussed and quizzed at the beginning of the following session.

Neurocognitive measures

The primary outcome measure was the cognitive control function of gist reasoning, defined as the ability to abstract novel integrative interpretations from complex information. Secondary outcome measures included (1) executive function, (2) memory, (3) daily function, and (4) imaging measures of resting state CBF.

Gist reasoning was examined using the Test of Strategic Learning (TOSL, Chapman, Gamino, & Cook, under review). The TOSL measure examines the numbers of abstracted ideas (included in a summary format) that one can provide from a lengthy text (~ 600 words). The participant is provided with a copy of the text to read. The participant reads the text silently, and upon completion, the text is removed so that the participant does not have the option to refer to it further. Then the participant provides his/her abstracted ideas in the form of a written synopsis/summary. The TOSL measure has a manualised objective scoring system wherein each self-generated abstracted idea receives one point and verbatim or paraphrased ideas do not receive any credit. Two trained examiners blinded to the participants' group status independently scored the summaries for inclusion of gist-based meanings. Inter-rater reliability of scores assessed on intraclass correlation coefficients in both groups combined for gist reasoning performance was over 90% (Cronbach's $\alpha = .96$, CI .71 .99).

Secondary outcome measures of executive function (working memory, inhibition, switching, fluency), memory, psychological health (self-reports of symptoms associated with depression and stress-related behaviours), and daily function (e.g., home care, social participation, job performance, awareness) are described in Table 4. Imaging outcome measures included resting state MRI, pseudo-continuous arterial spin-labelled (ASL) cerebral

TABLE 4
Brief description of outcome variables

<i>Variable</i>	<i>Measure</i>	<i>Description</i>	<i>Scoring</i>
Gist reasoning	Test of Strategic Learning (TOSL, Chapman et al., under review)	Participant constructs as many abstracted ideas as possible from a lengthy text (~ 600 words)	Number of abstracted ideas
Working memory	Digit backward (Wechsler, 1999)	Participant orally recalls number strings in backward order.	0 14
	Listening span (Daneman & Carpenter, 1980)	Participant answers questions related to sentences followed by recalling last word of each sentence.	1 7
Inhibition	D KEFS Color word inhibition task 3 (Delis, 2001)	Participant names the colour of ink a word is printed in versus reading the word (word colour spellings are incongruent with ink colour)	Total time to complete the task
	Hayling sentence completion (Burgess & Shallice, 1997)	Participant orally completes a sentence set with semantically unrelated word.	Total time to complete the sentences + number of errors
Switching	D KEFS Trail Making 4 (Delis, 2001)	Participant alternately connects a set of numbers and letters in ascending alphabetical order.	Total time + number of errors
	Category switching (Delis, 2001)	Participant verbally produces as many names of fruits and furniture while alternating categories.	Number of successful switches between categories in 60 seconds
Memory	Logical memory (WMS; Wechsler, 2002)	Participant orally recalls (immediate and delayed) details of a short story read aloud.	0 25
	Memory for text details (TOSL, Chapman et al., under review)	Participant recalls (on cued questions) specific details of the text used to assess gist reasoning.	0 24
Daily function	FSE (FSE; Dikmen, Machamer, Miller, Doctor, & Temkin 2001)	Self report of performance on 10 functional categories: personal care, mobility, travel, work and/or school, leisure and recreation, home management, social integration, cognitive and behavioural competency, standard of living, and financial independence.	10 41, lower is better

(Continued)

TABLE 4
Continued

<i>Variable</i>	<i>Measure</i>	<i>Description</i>	<i>Scoring</i>
	CIQ (CIQ; Willer, Ottenbacher, & Coad, 1994)	Self report of a general overview of an individual's functioning based on responses to 15 questions related to participation in activities at home, social, and education or vocation settings.	0 29, higher is better
	Awareness Questionnaire (Sherer, 2004)	A 17 item self report questionnaire to examine one's awareness of cognitive and social performance after the injury versus before the injury.	Total score range 17 85
Psychological health	Beck Depression Inventory Second Edition (BDI II, Beck et al., 1996)	A 21 item self report instrument to examine presence of depressive symptoms in the last 2 weeks.	Total score range 0 63, lower is better.
	PTSD Check List (PCL, Weathers, Litz, Herman, Huska, & Keane 2013)	A 17 item self report instrument to examine presence of stress related symptoms in the last month.	Total score range 17 85, lower is better

Notes: FSE, functional status examination; CIQ; community integration questionnaire.

blood flow. The MRI acquisition and MRI data processing is described in [Appendix 1](#).

Data analysis

We utilised standard general statistical linear models (GLM) on each of the outcomes measured in this study. These included behavioural measures of gist reasoning, executive functions, memory, psychological health, and daily function assessments; as well as voxel-wise neuroimaging measures of brain blood flow. Voxel-wise analyses were performed on relative CBF (rCBF) maps, which were obtained from dividing the absolute CBF (aCBF) maps by a measure of whole brain blood flow, calculated as the average of all voxels in the aCBF map. Analyses on rCBF maps have been shown to improve the sensitivity of detecting regional differences by reducing physiological variations (Aslan & Lu, 2010).

Each GLM included terms to assess the effect of type of training (i.e., SMART or BHW), time of assessment (pre-training, post-training and

3-months post-training) and the interaction between training type and time on the mean outcome measure. In addition, variance components to accommodate both within- and between-subject variability were included in the models. Interest was primarily in the interaction contrasts to assess how the training groups differed over time. Two orthogonal contrasts were tested based on the hypothesis that the training effects would be evident either immediately or by 3 months post-training. These are described as “linear” training differences between pre-training and 3-months post or as “quadratic” training differences, which peak immediately post-training (i.e., post-training minus the average of pre-training and 3-month post-training).

For imaging analyses, we also assessed the relationship between gist reasoning and rCBF, and whether the relationship differed between groups. This was accomplished including gist reasoning as a covariate in the linear model, as well as its interaction with groups. Multiple testing was accommodated by (1) constraining the false discovery rate at 10% (in the case of behavioural measure outcomes), and (2) using cluster extent inference based on distributions of multiple clusters from null images (in the case of neuroimaging analyses).

RESULTS

Descriptive analyses of baseline characteristics at initial testing did not yield significant differences between groups (Table 1). Similarly, performance on outcome measures of gist reasoning, executive function, memory, psychological health and daily function did not differ significantly ($p > .05$) between SMART and BHW groups at pre-training.

We found significant time by group linear interaction effects ($p < .05$) in SMART versus BHW on measures of gist reasoning. Significant group \times time interaction effects of improved SMART group performance as compared to BHW were also found on the executive function of switching (reduced time taken to complete the task and reduced number of errors) and memory (cued recall of text details and delayed recall on factual information) (Table 5).

We also found significant gains in the SMART group as compared to BHW on self-reported measures of psychological health. These gains were manifested by significant reduction in symptoms associated with depression and stress-related behaviours. We also identified self-reported improvement in daily functions (Table 5).

MRI measurements

Absolute CBF was measured by pCASL MRI in both SMART and BHW groups at rest. The global CBF at T1 for both SMART and BHW groups were similar (38.5 ml/100g/min and 39.3 ml/100g/min, respectively,

TABLE 5
Linear group x time interactions

Variables	Group	Pre training Mean (SE)	Post training Mean (SE)	3 month post Mean (SE)	<i>p</i>
Gist reasoning	BHW	3.72 (0.37)	4.25 (0.38)	3.32(0.41)	.02
	SMART	4.19 (0.36)	5.16 (0.36)	5.14 (0.40)	
D KEFS, Trail making 4 (time)	BHW	81.58 (6.65)	77.65 (6.76)	79.32 (6.87)	.03
	SMART	77.61 (6.44)	62.30 (6.48)	62.00 (6.72)	
D KEFS, Trail making 4 (errors)	BHW	0.51 (0.24)	1.08 (0.25)	1.34 (0.26)	<.001
	SMART	1.41 (0.23)	0.65 (0.24)	0.68 (0.26)	
D KEFS Contrast*	BHW	8.89 (0.41)	8.79 (0.43)	8.49 (0.44)	.01
	SMART	8.25 (0.40)	9.52 (0.40)	9.29 (0.43)	
Memory for details	BHW	12.34 (0.91)	11.98 (0.93)	12.42 (0.97)	.003
	SMART	10.41 (0.88)	12.48 (0.88)	14.48 (0.93)	
WMS Delayed recall	BHW	10.75 (0.83)	11.38 (0.84)	10.53 (0.88)	.002
	SMART	10.48 (0.80)	10.71 (0.80)	13.73 (0.86)	
Awareness	BHW	35.65 (2.16)	40.66 (2.19)	38.90 (2.30)	.02
	SMART	36.93 (2.09)	42.96 (2.09)	46.29 (2.24)	
BDI	BHW	16.58 (1.99)	11.62 (1.99)	12.51 (1.99)	.003
	SMART	18.83 (1.93)	13.61 (1.93)	7.90 (1.93)	
PCL	BHW	41.20 (3.81)	30.79 (3.81)	31.00 (3.81)	.004**
	SMART	38.93 (3.68)	37.29 (3.68)	22.64 (3.68)	

At pre training BHW $n = 29$, SMART $n = 31$; Post training: BHW $n = 28$, SMART $n = 30$; 3 month post training BHW $n = 25$ SMART $n = 25$. *Scaled score contrast of Condition 4 minus Condition 2 motor speed. SE: Standard Error D KEFS: Delis Kaplan Executive Function System, WMS: Wechsler Memory Scale, BDI: Beck Depression Inventory, PCL: Post traumatic stress disorder Check List. **Significance was from post training to 3 month post training.

$p = .74$) and did not change significantly across time points (Linear: $p = .85$, Quad: $p = .94$). To evaluate local resting CBF changes, we conducted voxel-wise analyses on rCBF. The whole-brain results from the voxel-based analysis (VBA) are shown in Figure 2. The SMART group showed an increase in

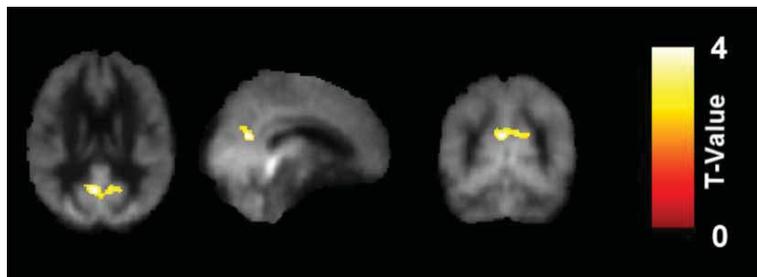


Figure 2. Results of voxel based analysis of CBF, group x time interaction, superimposed on an average CBF map of all participants. The bilateral precuneus' CBF increased linearly in the SMART group (shown in yellow) compared to the BHW group, $p < .05$ (Family wise correction [FWE] corrected) and $k \geq 2456 \text{ mm}^3$.

TABLE 6
CBF regions with significant blood flow change at rest in SMART compared to BHW

Brain Regions	BA	Cluster Size (mm ³)	MNI			T Value
			X	Y	Z	
<i>Linear: SMART > BHW</i>						
L/R Precuneus	31	2528	6	60	20	4.18

resting-state blood flow from pre-training to three month post-training in bilateral precuneus compared to the BHW group (FWE corrected $p < .05$) (Table 6).

Additionally, covariate analysis between rCBF and gist reasoning (i.e., TOSL performance) showed increased CBF in the left inferior frontal region, left insula, and bilateral anterior cingulate cortex (Figure 3, Table 7). The reverse contrast (SMART < BHW) did not yield significant findings.

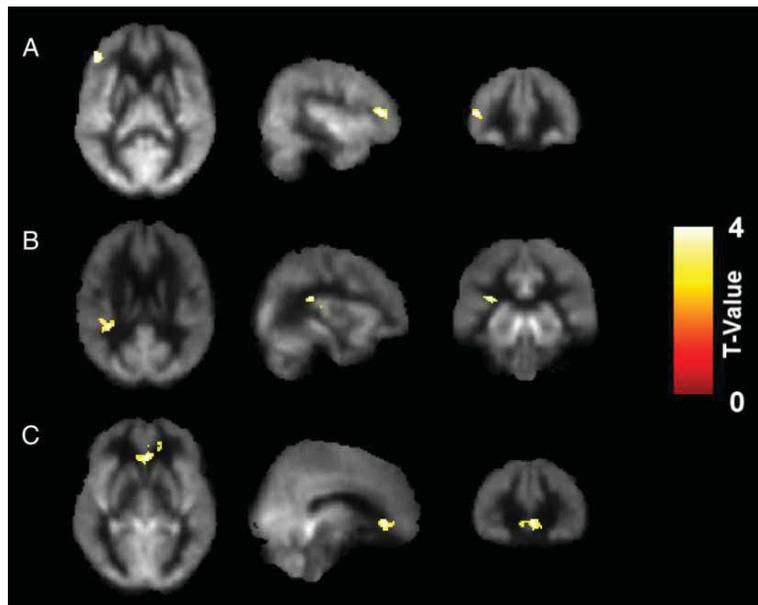


Figure 3. Results of voxel wise covariate analysis are superimposed on an average CBF map of all participants (A) The left inferior triangular frontal gyrus' linear CBF increase correlated with the linear increase of Gist reasoning score in the SMART group compared to the BHW group, $p < .005$ (uncorrected) and $k \geq 800$ mm³. (B) The left insula's quadratic CBF increase correlated with the quadratic increase of Gist reasoning score in the SMART group compared to the BHW group, $p < .005$ (uncorrected) and $k \geq 800$ mm³. (C) The bilateral anterior cingulate cortex's quadratic CBF increase correlated with the quadratic increase score of Memory for details score in the SMART group compared to the BHW group. The reverse contrast (BHW > SMART) did not show any significant results, $p < .005$ (uncorrected) and $k \geq 800$ mm³.

TABLE 7.
CBF regions with significant blood flow change at rest in SMART compared to BHW

<i>Brain Regions</i>	<i>BA</i>	<i>Cluster Size (mm³)</i>	<i>MNI</i>			<i>T Value</i>
			<i>X</i>	<i>Y</i>	<i>Z</i>	
<i>Linear CBF vs. Linear Gist reasoning:</i>						
<i>SMART > BHW</i>						
L. Inferior Triangular Frontal G.	46	944	46	40	10	4.73
<i>Quad CBF vs. Quad Gist reasoning:</i>						
<i>SMART > BHW</i>						
L. Insula	13	1128	36	36	20	3.96
<i>Quad CBF vs. Quad Memory for details:</i>						
<i>SMART > BHW</i>						
L/R Anterior Cingulate Cortex	32	1208	4	34	2	3.98

DISCUSSION

The current study presents empirical evidence demonstrating efficacy for a strategy-based approach to improve higher-order cognitive abilities in adults with mild-spectrum TBI in chronic stages after sustaining the injury. To our knowledge, this is the first double-blinded randomised control trial that has examined the benefits of higher-order cognitive training in mild-spectrum TBI on a broad range of outcomes. We emphasise three levels of improvement observed in our participants: (1) cognitive, (2) psychological health and daily function, and (3) neural gains in the SMART group as compared to BHW. Convergence of changes in neural and cognitive measures is also discussed.

Gist reasoning

Improved performance on gist reasoning (ability to abstract meanings from complex text) in the SMART group extends prior evidence of similar gains following the SMART programme in both clinical and healthy populations (e.g., adults with TBI with moderate functional deficits, adults with mild cognitive impairment, adolescents with TBI, healthy senior adults, middle school youth) (Chapman & Mudar, 2014). In the current study, at pre-training levels, both SMART and BHW group participants demonstrated comparable levels of gist reasoning ability while processing a complex text (TOSL measure). The summaries at baseline for both groups reflected a concrete ‘copy and paste’ cognitive style of condensing lengthy information into a

short summary as contrasted with a more sophisticated cognitive strategy of condensing information by abstracting ideas that is typical of adults with no history of TBI (Vas & Chapman, 2012). The pre-training summaries predominantly contained verbatim (concrete) information such as key characters and important details of the text. This pattern of reduced gist reasoning capacity in mild-spectrum TBI (although not the aim of the study) brings to light the prevalence of abstraction deficits (from complex information) in chronic stages of recovery.

At post-training periods, the majority (22 out of 31) of the SMART group participants' summaries reflected a higher-level synthesis of the complex text as compared to the pre-training level. Both participants with lower and higher gist scores at pre-training improved at post-training and/or at three-month post-training. Post-training summaries included an increased number of abstracted ideas and novel interpretations of the text as compared to pre-training levels. The finding of improved synthesising ability is encouraging, since it has not been previously documented that impaired abstraction of complex information skills can be improved years after sustaining a brain injury in those with persistent mild deficits. These findings extend prior work showing that SMART's utilisation of multi-dimensional thinking strategies serves to improve the ability to synthesise information in healthy adults, teens with chronic-stage TBI, and teens living in poverty (Anand et al., 2011; Cook et al., 2014; Gamino et al., 2014; Vas et al., 2011). The present evidence suggests that the SMART programme has the potential to enhance higher-order abstract thinking capacity in adults with mild-spectrum TBI (who constitute the majority of the TBI population). The data showing sustained higher performance at three-months post-training supports the claim that the gains were maintained or even improved over time. Previously, interventions drawing upon metacognitive strategies have shown gains in sustained attention and visuospatial problem-solving (Levine et al., 2011), as well as attention and executive control (Novakovic-Agopian et al., 2011). This is the first randomised clinical treatment trial that we are aware of to show gains in abstraction of meanings from complex information. The significant improvements in gist reasoning responses are not likely attributable to test practice effects since the active control group did not show similar gains across the three time intervals.

Executive function and memory

Another promising finding of this study is the improved performance on measures of switching and memory in the SMART group as compared to BHW. Similar generalised gains following SMART were reported in prior studies, including adults with TBI with moderate functional impairments (Vas et al., 2011), adolescents with TBI (Cook et al., 2014), and healthy

senior adults (Anand et al., 2011). These findings of generalised effects observed in the current study suggest that a strategy-oriented approach has the potential not only to strengthen cognitive control but also to improve associated executive functions such as switching, immediate and delayed memory. Improved switching ability in the current study could be secondary to habitual use/mastery of SMART strategies that focus on flexible manipulation of information with a bigger goal in mind. Similarly, higher memory performance could be a result of the gist reasoning skills of connecting the details with a bigger idea/meaning/goal. Extant evidence has suggested that memory for details is improved when individuals engage in abstracting meanings from complex input rather than working to encode, store, or recall specific details only (Gabrieli, 2004; Zwaan & Radvansky, 1998).

The present evidence supports the growing view that strategy-driven training of cognitive control may provide more far-reaching and lasting gains than those achieved when training specific cognitive processes (Levine et al., 2011). Whereas top-down cognitive control training spills over to benefit specific cognitive processes (Cook et al., 2014; Levine et al., 2011; Novakovic-Agopian et al., 2011; Vas et al., 2011), previous studies have shown that strengthening specific processes fails to show generalised effects to improve higher-order, integrative functions. For example, Gamino and colleagues found that typically developing middle schoolers trained to improve memorisation skills did not improve on gist reasoning performance, despite showing improved memory for factual information. On the other hand, middle school students who improved gist reasoning (following SMART) also showed comparable gains in memory as the students who received memorisation training (Gamino et al., 2010). That is, SMART strategies facilitate cognitive efficiency in managing complex data, a skill that applies broadly across academic courses and everyday tasks. In addition, SMART studies have shown engagement of broad-based brain networks to improve top-down processing, with a spillover benefit to specific processes (Chapman et al., 2015). Moreover, evidence has shown that performance on specific executive functions (e.g., switching, working memory, and inhibition) only partially predict gist reasoning performance (Vas et al., 2015). Additional well-designed cognitive training trials are needed to inform whether training paradigms achieve unidirectional versus bidirectional gains, with the latter being a more efficient goal. The question remains open as to whether or not trainings designed to improve specific bottom-up processes such as working memory, immediate memory, delayed memory, or switching bring about generalised gain in improved top-down cognitive control. Some evidence from working memory training in healthy adults suggests it may be possible (Buschkuhl, Hernandez-Garcia, Jaeggi, Bernard, & Jonides 2014). We propose that the present pattern of findings offers support for training cognitive control functions to achieve bi-directional gains with generalisation to specific component cognitive processes.

The current findings of generalised effects to executive functions and memory are consistent with other TBI studies showing benefits of top-down, strategy-based training programmes such as GMT (Levine et al., 2000, 2011), GOALS, (Novakovic-Agopian et al., 2011), and PST (Rath et al., 2003). For example, GMT, which introduces goal lists and divides tasks into small subtasks, has shown generalised benefits to executive function in people with frontal lobe damage. Our work extends the findings of cognitive gains to include generalisable gains at neural level and in daily function. We propose that top-down cognitive training programmes may share common foundational principles, yet introduce unique and novel strategies. It would be informative to conduct future randomised trials that compare or combine SMART with other top-down training programmes such as GMT.

Generalised effects of SMART found in multiple studies across clinical and healthy populations reflect its practical and adaptable approach to cognitive training (Chapman & Mudar, 2014). We postulated that a top-down approach to training, that provides strategies to improve cognitive control of massive information input such as offered by SMART, teaches participants to be strategic and deeper-level thinkers by actively constructing “the essence” of information or tasks encountered rather than keeping information at a literal, non-transformed level of processing. The latter process can quickly overload a limited memory capacity. For example, abstracting high-level ideas (themes or take away messages) of a movie engages effortful synthesis of the key information of the movie versus a rote restatement of the sequential recall of key events in the movie. Furthermore, the training teaches participants to combine all strategies as “efficiency tools” in various real-life activities. For example, the strategic attention application of “blocking less relevant details” is practised in (1) conversations during the SMART session activities, (2) prioritising two big items on a “to-do” list to focus brain “prime time”, (3) strategic control of actively eliminating distractors and interruptions at an office desk or while working on an important project, or (4) having a meaningful conversation, to mention a few. That is, similar to GMT that focuses on improving executive dysfunction difficulties, SMART targets executive control of information. As an individual encounters unique situations or novel information, he/she is equipped with the metacognitive SMART strategies to reduce cognitive overload and enhance understanding and interpretation of complex information encountered in real-life applications.

In addition to using the strategies during sessions and in homework assignments, adoption of the strategies to daily life tasks by the majority of SMART participants could be due to motivation inherent in a therapeutic milieu provided in a group setting. Participants had an opportunity to discuss and brainstorm different ways to apply strategies to process information, accomplish a

task or problem-solve a difficult life situation. However, the therapeutic milieu in itself is not likely the key factor in achieving cognitive gains. The BHW participants were also in a comparable group setting with active discussions of the topics presented and application of the knowledge to their lives, yet the results did not demonstrate significant gains on executive functions.

We propose that the top-down metacognitive strategies of the SMART programme provided new and adoptable learning and task management tools to enhance cognition in adults with mild-spectrum TBI in chronic stages of recovery. The strategies emphasise inhibition of less relevant information (e.g., distractions), abstraction of deeper meanings from information, and engagement in innovatively seeking multiple solutions to problems. The importance of these promising benefits from short-term training are that individuals with residual cognitive sequelae after TBI may be able to show increased capacity to become productive members of their community at time intervals far removed from the initial injury. That is, the habitual engagement in the use of the strategies has the potential not only to strengthen and rewire brain networks, but also to enrich life activities. The paradox is that these individuals are seldom identified as potential candidates for intensive cognitive training as they present with only mild levels of functional impairments on basic everyday activities.

Psychological health and daily function gains

The current finding of generalised effects of improved cognitive control to reduction in symptoms associated with depression and stress-related behaviours extends emerging evidence of mutual benefits of cognitive and psychological therapies in adults with mild-spectrum TBI (Ho & Bennett, 1997; Miller & Mittenberg, 1998; Tiersky et al., 2005). A negative impact of impaired cognition on psychological functioning is widely reported in the TBI literature (Dikmen, Bombardier, Machamer, Fann, & Temkin 2004; Fann, Hart, & Schomer, 2009; Seel et al., 2003). Specially, recent studies highlight the comorbidity of depression and PTSD in chronic TBI (Corrigan et al., 2010). Therefore, the current study included measures to assess symptoms associated with depression and stress-related symptoms signalling PTSD as key functional outcome measures.

We speculate that improved frontal lobe functions, including gist reasoning and executive function, may have led to improved ability to down-regulate emotional responses, bringing about improvement in mood and reduction in self-reported stress symptoms. Furthermore, improved cognitive control abilities may have led to increased neural health manifested in higher resting CBF (i.e., the inferior frontal cortex, bilateral anterior cingulate and precuneus) with a concomitant reduction in stress-related symptoms. Prior evidence has shown an association between TBI severity and lower

metabolism in the precuneus (Soman et al., 2014). Furthermore, lower neuronal activity in the precuneus is reported in TBI participants with PTSD (Yan et al., 2013). Based on the neurovascular coupling principle, our results of an increase in blood flow in bilateral precuneus after cognitive training indicates higher neuronal activity suggestive of improved neural health in this key brain region. This finding suggests SMART has the potential to mitigate or reverse some degree of psychological health symptoms, although attainment of such benefits needs to be replicated. Large-scale studies are needed to further validate the complex relations between the precuneus and PTSD symptomatology, especially the impact of higher-order cognitive training and PTSD symptoms.

Additionally, improved cognition and psychological health could have a positive impact on one's confidence, cognitive control, sense of well-being and self-worth, as reflected by the current gains on daily function of improved awareness and adaptations reported by participants in the SMART group. Current findings extend prior evidence of a strong correlation between awareness and favourable employment and daily function outcomes (Sherer et al., 2003). Again, these generalised gains are not likely due solely to the social interactions with other group participants, since the BHW control group had similar social interactions and yet failed to show similar positive changes on daily function measures.

CBF correlates of cognitive changes

In addition to the cognitive, psychological health, and daily function gains, evidence from the current study provides promise of neural plasticity following higher-order cognitive training. In recent years, measures of cerebral blood flow are increasingly recommended to serve as indirect indicators of neuronal integrity and function, especially in chronic stage TBI (Kim et al., 2009; 2012). In the current study, pCASL MRI quantified cerebral blood flow allowing us to incorporate a resting baseline as an outcome measure. The results of an increase in regional blood flow in bilateral precuneus from pre-training to post-training support the possibility of achieving a new homeostasis level in adults with mild-spectrum TBI. The precuneus is a key region of default-mode network and is known to be highly sensitive to dementia, ageing and severity of TBI (Bonnelle et al., 2011; Soman et al., 2014). In addition, prior imaging evidence demonstrated correspondence between higher-order cognitive functioning and the precuneus in healthy adults (Cavanna & Trimble, 2006). Thus, CBF increase in this region can be viewed as an enhancement since hypometabolism of the precuneus has been associated with increased severity of TBI (Soman et al., 2014).

Additionally, the positive correlations between improved gist reasoning, memory and increased blood flow at regions that mediate cognitive control

are promising. The role of the left inferior frontal gyrus, left insula, and bilateral anterior cingulate cortex in cognitive control operations is well established. Evidence suggests that the inferior frontal gyrus/anterior insula network is involved in elaborate attentional and working memory processing as well as adapting to changes in processing demands to the complexity of the task (Tops & Boksem, 2011). With regard to cognitive training in TBI, Kim et al. (2009) reported increased activation of the anterior cingulate cortices and the precuneus following cognitive training in adults with TBI. The capacity to increase regional brain blood flow as an outcome of higher-order cognitive training may have clinical implications in light of evidence that resting blood flow is an indicator of neural integrity (Chen, Rosas, & Salat, 2013). MRI-based CBF is beginning to show promise as a way to monitor treatment effects in neurological and neuropsychiatric syndromes (Detre et al., 2012).

Clinical implications

Rehabilitation clinicians are cognisant of the strengths and limitations of existing cognitive interventions. Supported by advances in technology, there is a growing desire to identify and/or develop intervention protocols that (1) train higher-order cognitive control functions, (2) are adoptable to daily life function, (3) are time efficient, and (4) enhance underlying brain function. We believe that the top-down strategy-based SMART may address these four issues, especially by providing tools applicable to a broad range of complex skills required for home, social, and vocational integration, especially at chronic stages of recovery. That is, the wide-ranging applicability of SMART strategies to real-life functions makes it suitable across levels of TBI severities and could certainly add to the sparse but promising clinical evidence emerging from other training programmes targeting executive or integrative functions (e.g., GMT, Levine et al., 2011, and GOALS, Novakovic-Agopian et al., 2011). Moreover, clinicians and researchers may soon be able to implement relatively brief MRI scans to measure changes in CBF as an objective and adjunct measure of improved neural plasticity. The potential exists, especially in cognitive trainings, given the widely accepted principles of a tight coupling between CBF and coordinated neural activity, but may well extend to pharmacological treatments (Detre et al., 2012).

LIMITATIONS AND FUTURE DIRECTIONS

The current findings, while promising, must be interpreted cautiously, as they require further validation to address four major limitations. First, we

recognise that the participants in the present study were recruited primarily from the community with self-reported TBI and in chronic stages of recovery. Thus, there was limited access to reliable documentation of acute severity of TBI and relevant medical history that could prove informative in characterising the sample. Despite the shortcoming of limited access to history, we find the current results consistent with prior evidence of training benefits where initial injury documentation was available (Levine et al., 2000). The promising outcomes motivate researchers and clinicians to monitor and manage TBI from the time of injury at regular intervals, just as is commonly done in most conditions that are likely to have recurrent problems such as cancer, with the goal to provide timely treatments to mitigate worsening prognosis. Second, participants' medication use was not monitored in the current study. Future studies should consider this factor since pharmacological agents could affect cognitive functioning and influence results of cognitive training. Third, the current study included a heterogeneous sample with regard to chronicity of TBI (1 to over 20 years post-injury). It is possible that certain age groups may benefit from SMART more than others. The young adults (in their 20s) whose frontal networks are still undergoing active myelination may respond to training differently versus relatively older adults in the sample (aged 55 and over) who may present with decline in cognitive processes including speed of processing or short-term memory. We are currently in the process of investigating integrative metrics to determine individual responsiveness since we recognise that one size does not fit all in terms of dose, type or timing of treatment. Future studies could examine the age variable either as an outcome measure or treatment factor. The fourth limitation is the self-report nature of functional measures, which represent one's perception of gains made post-training. Objective assessment of real-life task performance, via either virtual assessment platforms, or onsite visits, or corroborations with family members could complement participants' subjective assessments of daily function. In addition to addressing these limitations, future endeavours should monitor benefits of SMART at longer intervals (e.g., yearly). The scalability to monitor and deliver trainings as soon as deficits emerge or worsen are likely to require technology-delivered protocols, when possible.

CONCLUSION

Advancing the field of cognitive training in TBI has never been more vital, particularly considering the prevalence of persistent cognitive functional sequelae of TBI. Findings from the current randomised trial provide evidence that the top-down SMART cognitive training can enhance higher-order cognition (e.g., gist reasoning) in adults with mild-spectrum TBI in chronic stages

of recovery. The SMART strategies engaging strategic attention, integration, and innovation, also have the potential to improve the cognitive domains of executive function and memory. Perhaps even more significant is the potential for a cognitive control, strategy-based training to have a positive impact on reducing the widespread sequelae of depression and stress, and improving daily function, both immediately and in the short-term, at least up to three months post-training. Furthermore, positive neural gains linked to cognitive and psychological gains following SMART hold promise for extending efforts to harness the residual neural and cognitive plasticity in the growing number of adults with mild-spectrum TBI at stages far-removed from the time of injury. SMART is one protocol that could be added to the growing armamentarium of strategy-based cognitive training protocols that are showing promise.

The growing evidence of improved higher-order cognitive ability following short-term strategy-based training, at chronic stages of recovery, can inform public health policy. Foremost, attention should be given to improving long-term management of TBI as a chronic health condition, especially as evidenced-based protocols are identified. Hopefully, the evidence and availability of interventions that substantially mitigate the persistent or worsening deficits in TBI will increase, with the ultimate goal for these to be implemented for the betterment of those who experience TBI to help them rejoin the ranks of productive citizens.

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APPENDIX 1

MRI acquisition

MRI investigations were performed on a 3 Tesla MR system (Philips Medical System, Best, The Netherlands). A body coil was used for radiofrequency (RF) transmission and a 32-channel head coil with parallel imaging capability was used for signal reception. We used an MRI technique called pseudocontinuous (pCASL) MRI to measure CBF (Aslan & Lu, 2010). Additionally, a high-resolution T1-weighted image was acquired as an anatomical reference. Imaging parameters for pCASL experiments were: single-shot gradient-echo EPI, field-of-view (FOV) = 220×220 , matrix = 64×64 , voxel size = $3.44 \times 3.44 \text{ mm}^2$, 29 slices acquired in ascending order, slice thickness = 5 mm, no gap between slices, labelling duration = 1650 ms, time interval between consecutive slice acquisitions = 35.5 ms, TR/TE = 4020/14 ms, SENSE factor 2.5, number of controls/labels = 35 pairs, RF duration = 0.5 ms, pause between RF pulses = 0.5 ms, labelling pulse flip angle = 18° , bandwidth = 2.7 kHz, echo train length = 35, and scan duration 4.5 minutes. The high resolution T1-weighted image parameters were: Magnetisation Prepared Rapid Acquisition of Gradient Echo (MPRAGE) sequence, TR/TE = 8.3/3.8 ms, shot interval = 2100 ms, inversion time = 1100 ms, flip angle = 12° , 160 sagittal slices, voxel size = $1 \times 1 \times 1 \text{ mm}^3$, FOV = $256 \times 256 \times 160 \text{ mm}^3$, and duration 4 minutes.

MRI data processing

pCASL image series were realigned to the first volume for motion correction (SPM5's realign function, University College London, UK). Participants with head motion of $> 3\text{mm}$ and $> 3^\circ$ were excluded from further analysis. An in-house MATLAB (Mathworks, Natick, MA) programme was used to calculate the difference between averaged control and label images. Then, the difference image was corrected for imaging slice delay time to yield a CBF-weight image, which was normalised to the Brain template from Montreal Neurological Institute (MNI). Last, the absolute CBF (aCBF) was estimated by using Alsop and Detre's equation in the units of mL blood/min/100g of brain tissue (Alsop & Detre, 1996). This method is represented by the following equation:

$$f_{pCASL}(x, y, z) = \frac{\lambda \cdot e^{(\delta/T_{1a})}}{2\alpha \cdot M_b^0 \cdot T_1 \cdot \left[e^{((\min(\delta - w_z), 0)/(T_1))} e^{(w_z/T_1)(1 - (T_{1RF}/T_1))} \right]} \times \Delta M(x, y, z)$$

where f_{pCASL} is the blood flow value at voxel (x, y, z) obtained from pCASL in ml blood/min/100g brain, α is the labelling efficiency (0.86), λ is the blood-brain partition coefficient (0.98 ml/gram), δ is the arterial transit time of blood from the tagging plane to the imaging slice (2 seconds), w is the delay between the end of labelling and the start of acquisition (1.525 seconds), T_1 is the brain tissue T_1 (1.165 seconds), T_{1a} is the T_1 of arterial blood (1.624 seconds), T_{1RF} is the T_1 in the presence of off-resonance irradiation (0.75 seconds) and M_b^0 is the value of equilibrium magnetisation of brain tissue, which was obtained from a manual ROI drawing of a mid-axial slice of the control image.