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## Review Article

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# Cognitive remediation of attention deficits following acquired brain injury: A systematic review and meta-analysis

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### Abstract.

**BACKGROUND:** Attention deficits are common after acquired brain injury (ABI) and adversely impact academic, vocational and social outcomes. The role of cognitive interventions in post-ABI attention rehabilitation remains unclear.

**OBJECTIVE:** To evaluate effectiveness of cognitive interventions in treating attention deficits following ABI and to explore differences in treatment effect between ABI etiologies.

**METHODS:** MEDLINE, EMBASE, PsycINFO and CENTRAL databases were searched for randomized controlled trials (RCTs). Studies were selected by three reviewers. Study quality was assessed using Cochrane Collaboration tool for RCTs. Effect sizes (Hedge's *g*) for each attentional domain were meta-analyzed with subgroup analysis by ABI etiology.

**RESULTS:** Twelve RCTs with 584 participants were included, representing individuals with stroke, traumatic brain injury (TBI) and CNS-impacting malignancy. Cognitive rehabilitation improved divided attention in stroke survivors (*g* 0.67; 95% confidence interval, 0.35–0.98; *p* < 0.0001) but not other ABI populations. Sustained, selective and alternating attention, and inhibition were not significantly improved in any ABI population. Follow-up data showed no evidence of long-term benefit.

**CONCLUSION:** Cognitive rehabilitation resulted in short-term improvements in divided attention following stroke, but not after TBI or CNS-impacting malignancy. Cognitive interventions did not significantly improve other attentional domains in participants with stroke, TBI or CNS-impacting malignancy.

Keywords: Acquired brain injury, cognitive rehabilitation, attention, meta-analysis, systematic review

## 1. Introduction

Cognitive rehabilitation is the systematic provision of neuropsychological interventions aimed at treating, or teaching to manage, cognitive deficits (Cicerone, 2000). Cognitive rehabilitation has come

to be a standard component of medical care following acquired brain injury (ABI) (McCrea, 2008; Rohling, 2009). The cognitive sequelae of ABI include deficits in attention, speed of processing, memory and executive functioning (Dams-O'Connor, 2010). Attentional impairments are particularly frequent, affecting 40–60% of patients suffering mild brain injury (Sivan, 2010). In the case of severe ABI, longitudinal studies have demonstrated persisting deficits in more than 60% of patients ten years post-injury (Ponsford 2014). Post-ABI attentional impairments

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are associated with difficulties in academic and vocational tasks (Ponsford, 2014), sleep-wake disturbances (Bloomfield, 2010), increased fatigue (Ziino, 2006) and poorer overall quality of life (Dijkers, 2004).

The cognitive approaches used to treat attentional deficits either involve direct training through repetition on attention-specific exercises, or the teaching of compensatory strategies to promote functional adaptation (Park, 2001). Although stimulant medications such as Methylphenidate have shown some promise in treating attention deficits (Rees, 2007), there remains uncertainty regarding the frequency and nature of their adverse effects in the long-term (Sivan, 2010). In response to these concerns, cognitive rehabilitation has been increasingly highlighted as a potential adjuvant or alternative treatment.

However, the effectiveness of post-ABI attention rehabilitation remains unclear with previous meta-analyses producing conflicting results (Park, 2001; Rohling, 2009). Of note, the findings of these previous meta-analyses were largely based on uncontrolled or non-randomized studies, the majority of which were conducted over fifteen years ago. This represents a significant gap in the literature given the exponential growth in cognitive rehabilitation in recent years (McMillan, 2013). Prior meta-analyses also reported on attention as a composite endpoint, thus not accounting for the distinct components comprising it. These distinctions may be critical in the evaluation of cognitive interventions as specific domains of attention may require targeted training with minimal generalizability of benefit from one domain to another (Sturm, 1997).

The objective of this study is thus to systematically review, update and synthesize the evidence for the effectiveness of cognitive interventions for post-ABI attention rehabilitation. The present meta-analysis will also be the first to compare the efficacy of cognitive interventions across different ABI etiologies and attentional domains to elicit any domain- or etiology-specific effects.

## 2. Methods

### 2.1. Search strategy

We searched MEDLINE, EMBASE, PsycINFO and the Cochrane Central Register of Controlled Trials (CENTRAL) from their dates of inception to August 2014. The search terms “attention”, “neuropsychological or cognitive” and “remediation or therapy or rehabilitation or intervention or treatment” were combined as either keyword or MeSH terms, together with study design filters for randomized controlled trials. The reference lists of all relevant studies and key reviews were hand searched to identify additional studies.

### 2.2. Eligibility criteria and study selection

The criteria for study inclusion were: (1) randomized controlled trial; (2) participants had sustained an ABI and demonstrated attention deficits at baseline, either self-reported or elicited by neuropsychological testing; (2) a cognitive intervention of any type was administered to remediate attention; (3) attention-specific effects of the intervention could be determined if the intervention was part of a broader cognitive rehabilitation program; (4) at least one quantitative outcome measure for attention was reported with sufficient detail to compute an effect size; (5) etiology-specific outcomes were presented if study participants had different ABI etiologies; and (6) published in a peer-reviewed journal. There was no restriction relating to the age of participants, meaning studies involving pediatric subjects were also eligible for inclusion.

Non-randomized trials, case series, theoretical papers, reviews and editorials were excluded. Studies examining mixed populations (with and without ABI) or combination therapy (e.g. pharmacological and cognitive) were excluded if data required to determine the effect of the cognitive intervention in the ABI population could not be obtained after contacting the corresponding authors. Studies exclusively examining spatial neglect were also excluded as its clinical features, pathology and management differ markedly from other forms of inattention (Park, 2001).

Three reviewers (S.V, T.W and R.B) independently screened all titles and abstracts to identify relevant studies. The full-text of all relevant articles were assessed for study eligibility in accordance with the selection criteria. Disagreements about final study inclusion were resolved by consensus and consultation with a fourth reviewer (A.M).

### 2.3. Data extraction and critical appraisal

For each study, data were extracted independently by two reviewers (S.V. and T.W.). This included information on: participants (age, gender, etiology and duration of injury), intervention (description, intensity

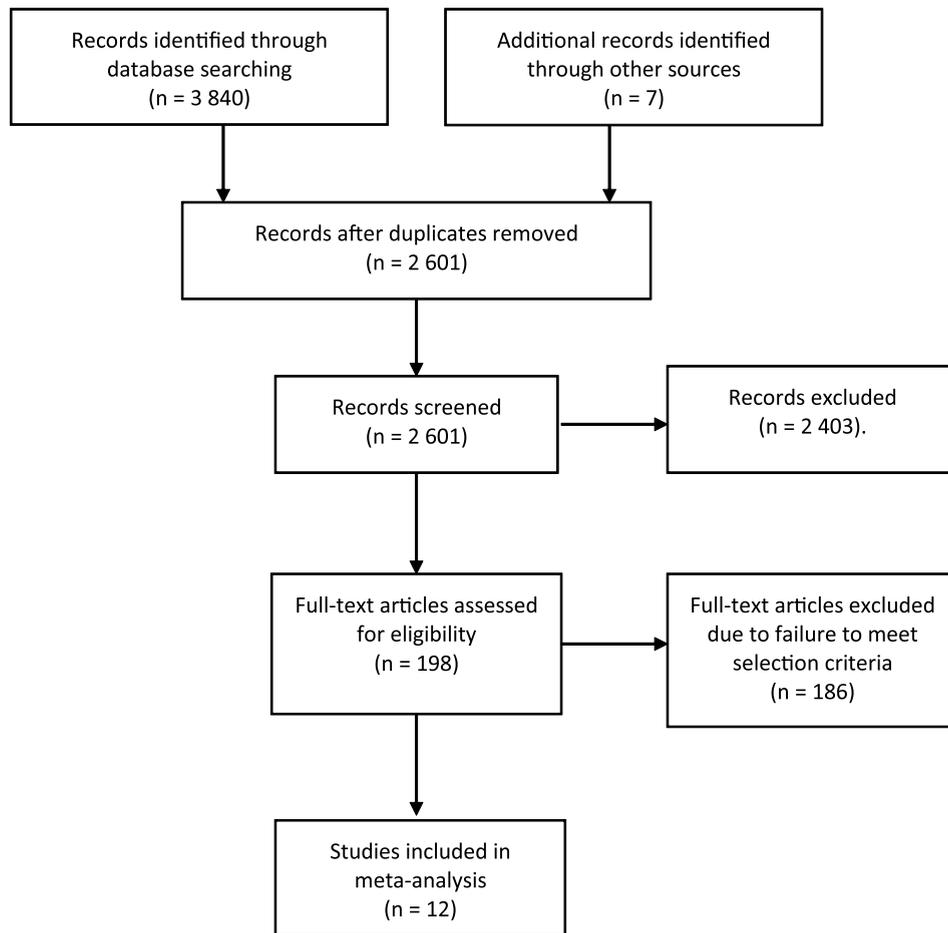


Fig. 1. PRISMA flow chart for literature search.

and length), nature of control group, and results for each outcome measure of attention. Any discrepancies were resolved by consultation with a third reviewer (R.B). If this data could not be obtained from the article, the corresponding authors were contacted.

All included studies were critically appraised for risk of bias using the current Cochrane Collaboration tool for RCTs (Higgins, 2011). We assessed method of randomization, concealment of group allocation, adequacy of blinding, completeness of outcome data and possibility of selective reporting. Each of these domains was judged to be either at low, unclear or high risk of bias.

#### 2.4. Outcome measures

There is no consensus on the classification of subtypes of attention, but several key domains are widely

recognized. For the purpose of this review, we categorized attention into the following components: selective (ability to focus exclusively on particular stimuli while suppressing awareness of competing distractions), sustained (ability to maintain attentional activity over a prolonged period of time), divided (ability to allocate attentional resources to two or more tasks simultaneously) and alternating (ability to shift focus from one task to another). Inhibition was also included as a measure of an individual's ability to exercise attentional resources in order to override execution of automated tasks (Lezak, 2004).

Two clinical neuropsychologists (T.W. & R.B.) independently assigned each attentional test in the included studies to an attentional domain. For each trial, only one test was included for a specific domain. In studies where multiple tests were used to assess a single attentional domain, each clinical neuropsychologist chose the test they judged to be of greater

reliability, relevance and validity for that domain, and that provided the most consistency across studies. Discrepancies between assignments were resolved by reference to Strauss, Sherman & Spreen's *Compendium of Neuropsychological Tests* (Strauss, 2006). A summary of the tests used for specific attentional domains in each study is displayed in Supplementary Table 1.

### 2.5. Statistical analysis

For each outcome measure of attention, an effect size was computed with 95% confidence intervals (CI). As our review was expected to yield both large and small sample sizes, the effect size of Hedge's  $g$  was used. It is calculated as the difference between treatment and control means divided by the weighted average of the standard deviations of both groups. The magnitude of Hedge's  $g$  can be interpreted using Cohen's convention of small (0.2), medium (0.5) and large (0.8) (Durlak, 2009). For attention tests whereby higher values equate to increasing attentional impairment (e.g. reaction time), mean values were multiplied by  $-1$ . This enabled direct comparison and consistent interpretation across attentional tests as lower values always reflected poorer performance (Higgins, 2011).

The present meta-analysis was conducted using a fixed-effects model if there was acceptably low heterogeneity between trials. Otherwise, a random-effects model was used for the analysis. The  $I^2$  statistic was used to estimate the percentage of total variation across studies due to heterogeneity rather than chance, with values exceeding 50% indicative of considerable heterogeneity. In such cases, the possible clinical and methodological reasons for heterogeneity were explored qualitatively.

Publication bias was assessed using funnel plots comparing the pooled effect size for each attentional domain with its standard error. The Egger regression test was used to detect funnel plot asymmetry (Egger, 1997), and the Trim-and-Fill method was used to explore the impact of studies potentially missing due to publication bias (Duval, 2000).

Statistical analyses were conducted with Review Manager Version 5.2.1 (Cochrane Collaboration, Software Update, Oxford, UK) and publication bias assessed using Comprehensive Meta-analysis v2.2 (Biostat Inc., Englewood, NJ, USA). All  $p$ -values were two-sided, and values  $<0.05$  were considered statistically significant.

### 2.6. Subgroup and sensitivity analyses

It was recognized that the effect of rehabilitation may differ significantly between patients of different ABI etiologies. In order to identify potential etiology-specific impact of cognitive interventions, a subgroup analysis was performed whereby studies of different etiologies were meta-analyzed separately.

It was also anticipated the retrieved studies would vary in regards to injury duration. It is believed restoration of cognitive function becomes increasingly more difficult the further a patient is removed from injury (Wilson, 2000). To account for the potential influence this may have on our results, a sensitivity analysis was performed in which studies representing outliers of injury duration were excluded.

## 3. Results

### 3.1. Study characteristics

A total of 3 840 references were identified through the database searches. Manual search of reference lists identified seven additional studies. After exclusion of duplicate or irrelevant references, 198 potentially relevant articles were retrieved for more detailed evaluation. After applying the selection criteria, 12 studies were eligible for inclusion in the present meta-analysis. The selection process is summarized in Fig. 1 according to the PRISMA statement (Moher, 2009).

A summary of included trials is presented in Table 1. Across all studies, a total of 584 patients were enrolled to either receive an intervention targeting attention ( $n = 319$ ) or as control subjects ( $n = 265$ ).

The included studies covered three different ABI etiologies. Six studies assessed stroke (Barker-Collo, 2009; Rohring, 2004; Schottke, 1997; Sturm, 1991; Westerberg, 2007; Winkens, 2009), four examined traumatic brain injury (Couillet, 2010; Fasotti, 2000; McMillan, 2002; Tiersky, 2005) and two studied CNS-impacting malignancy (Butler, 2008; Ferguson, 2012). There were no RCTs found assessing attention rehabilitation in patients with hypoxic injury, CNS-impacting infections or other ABI etiologies.

The median duration of intervention was 6.8 weeks (range, 3 to 18). Interventions varied considerably in intensity, ranging from 20 minutes to 7.5 hours a week. In the four studies reporting on long-term outcomes, duration of follow-up ranged from 2 to 12 months.

Table 1  
Summary of trials evaluating the effectiveness of cognitive interventions in remediation of attention deficits

First Author	Study Year	Sample Size		Participants			Description	Intervention		Length	Results Follow-Up Duration
		I	C	Male (%)	Mean Age	Mean ABI		Control Group			
<i>Stroke</i>											
Barker-Collo	2009	38	40	60	68.9	18.6 days	Up to 30 hours of hierarchically graded attention-specific exercises for one hour on weekdays	Standard care	4 weeks	6 months	
Rohring	2004	24	24	63	53.3	26 months	30–45 minutes of computer-based training on attention-specific exercises for five days a week	No treatment	11 weeks	NA	
Schottke	1997	16	13	52	64.7	45.3 days	Thirteen sessions of repetition on attention-specific exercises, cognitive-behavioral therapy and relaxation therapy	Standard care	3 weeks	NA	
Sturm	1991	13	14	70	50.5	15.7 weeks	Fourteen 30-minute sessions of computer-based training on attention-specific exercises	No treatment	3 weeks	NA	
Westerberg	2007	9	9	72	54.3	20.1 months	40-minutes of hierarchically graded, computer-based working memory and attention exercises five days a week	No treatment	5 weeks	NA	
Winkens	2009	20	17	57	51.5	13.6 months	Up to 10 hours of compensatory strategy teaching for time pressure management administered in 1–2 hour/week blocks, involving education for self-awareness and self-regulation.	Standard hospital care	5–10 weeks	3 months	
<i>TBI</i>											
Couillet	2010	5	7	NR	25.5	12.0 months	Four one-hour sessions a week of hierarchically graded specific dual-task training	Placebo therapy not targeting attention	6 weeks	NA	
Fasotti	2000	12	10	68	27.9	9.1 months	Four biweekly visits of 30–50 minute duration, involving education for self-awareness/self-regulation and compensatory strategy teaching for slowed mental processing.	Placebo therapy not targeting attention	8 weeks	NA	
McMillan	2002	44	48	77	35.4	3–12 months	Five 45-minute sessions of breathing-based practice of sustained attentional control training using audiotapes	No treatment	4 weeks	12 months	
Tiersky	2005	11	9	45	46.8	5.2 years	Three 50 minute sessions a week consisting of hierarchically graded attention-specific exercises, teaching of compensatory problem-solving strategies and cognitive-behavioral psychotherapy	Wait-list	11 weeks	NA	
<i>CNS-Impacting Malignancy</i>											
Butler	2008	108	53	65	10.9	5.7 years	Up to 20 two-hour sessions consisting of hierarchically graded exercises, teaching of learning strategies and cognitive-behavioral psychotherapy	Wait-list	4–5 months	NA	
Ferguson	2012	19	21	0	50.3	>18 months	Four biweekly visits of 30–50 minute duration, involving education and self-awareness, self-regulation and compensatory strategy training	Wait-list	8 weeks	2 months	

ABI, acquired brain injury; C, control participants; CNS, central nervous system; I, intervention; NA, not available.

Table 2  
Summary of risk of bias in included studies

	Method of randomization	Allocation concealment	Blinding of assessors	Incomplete outcome data	Selective reporting
Barker-Collo	Low	Low	Low	Low	Low
Westerberg	Low	Low	High	Low	Low
Rohring	Low	Unclear	Low	Low	Low
Schottke	Low	Unclear	High	Low	Low
Sturm	Low	Unclear	Unclear	Low	Low
Winkens	Unclear	Low	Low	Low	Low
Couillet	Unclear	Unclear	High	Low	Low
Fasotti	Unclear	Unclear	Low	Low	Low
McMillan	Unclear	Unclear	Low	Low	Low
Tiersky	Low	Low	Low	Low	Low
Butler	Unclear	Unclear	Low	Low	Low
Ferguson	Low	Unclear	Low	Low	Low

In five studies, rehabilitation involved direct retraining of attention through repetitive practice on hierarchically graded exercises (Barker-Collo, 2009; Couillet, 2010; Rohring, 2004; Sturm, 1991; Westerberg, 2007). Three studies employed compensatory strategies to overcome deficits (Fasotti, 2000; Ferguson, 2012; Winkens, 2009). A combination of both direct retraining and compensatory strategy were employed in the remaining four studies (Butler, 2008; McMillan, 2002; Schottke, 1997; Tiersky, 2005).

The presence of attentional deficits at baseline was determined by objective neuropsychological testing in six studies (Barker-Collo, 2009; Couillet, 2010; Fasotti, 2000; Schottke, 1997; Winkens, 2009), subjective self-reporting in three studies (Ferguson, 2012; Tiersky, 2005; Westerberg, 2007) and either objective testing or self-report in one study (McMillan, 2002). In two studies, all participants had established baseline deficits of attention but the criteria for determining these were not specified (Rohring, 2004; Sturm, 1991).

The population of this meta-analysis is comprised of 237 stroke survivors, 146 TBI sufferers and 201 patients with CNS-impacting malignancy. The control group had a significantly shorter duration of injury in one study (Schottke, 1997) and significantly greater baseline impairment in another study (Sturm, 1991). In the remaining studies, there were no significant differences in demographic or neurological variables between intervention and control groups. There were, however, significant differences between ABI groups (Table 1). Stroke patients had a significantly higher weighted mean age (59.3 years) than TBI participants (35.0 years). Of the two studies examining patients with CNS-impacting

malignancy, one involved a pediatric population (Butler, 2008) and the other an adult, female-only cohort (Ferguson, 2012).

The mean duration of injury was greater than five years in two studies (Butler 2008; Tiersky 2005) and less than 2 months in two studies (Barker-Collo, 2009; Schottke, 1997) Cohorts in the remaining studies had median injury duration of 12.8 months at baseline (range, 4 to 26).

### 3.2. Assessment of risk of bias

The risk of bias in included studies is summarized in Table 2. In several studies, the methods of randomization and allocation concealment were not specified, making it difficult to assess the risk of selection bias. Due to the nature of the interventions, blinding of participants and personnel was not possible in any of the studies. Three studies (Couillet, 2010; Rohring, 2004; Sturm, 1991) were identified as being at high risk of detection bias as the outcome assessors were not blinded to group allocation. There was no evidence of attrition bias or selective reporting in any of the included studies.

### 3.3. Effects of intervention

#### 3.3.1. Divided attention

Eight studies comprising 305 participants assessed divided attention. For the ABI population as a whole, a beneficial treatment effect was observed for divided attention following intervention ( $g$  0.41; 95% CI,  $-0.02$ – $0.83$ ;  $I^2 = 65\%$ ) but this did not reach statistical significance ( $p = 0.06$ ).

A subgroup analysis by etiology elicited a significant, medium-to-large effect size for cognitive rehabilitation in the stroke population (Fig. 2;  $g$  0.67; 95% CI, 0.35–0.98;  $p < 0.0001$ ;  $I^2 = 0\%$ ). Conversely, in participants with TBI, intervention did not improve divided attention relative to control subjects ( $g$  0.13; 95% CI,  $-0.59$ – $0.85$ ;  $p = 0.72$ ;  $I^2 = 67\%$ ).

### 3.3.2. Alternating attention

Six studies comprising 371 participants assessed alternating attention. There was no benefit of intervention observed following stroke ( $g$  0.18; 95% CI,  $-0.23$ – $0.59$ ;  $p = 0.38$ ;  $I^2 = 33\%$ ), TBI ( $g$   $-0.12$ , 95% CI,  $-0.46$ – $0.22$ ;  $p = 0.50$ ;  $I^2 = 0\%$ ) or CNS-impacting malignancy ( $g$   $-0.18$ ; 95% CI,  $-0.52$ – $0.16$ ;  $p = 0.30$ ).

### 3.3.3. Sustained attention

Sustained attention was examined in nine studies with a total of 457 participants. A wide variety of tests were used to measure this outcome and heterogeneity exceeded 50% in both the subgroup and overall analyses. Cognitive rehabilitation was not significantly effective in either stroke survivors ( $g$  0.28; 95% CI,  $-0.19$ – $0.75$ ;  $p = 0.24$ ;  $I^2 = 61\%$ ), TBI sufferers ( $g$  0.58; 95% CI,  $-0.48$ – $1.65$ ;  $p = 0.28$ ;  $I^2 = 76\%$ ) or those with CNS-impacting malignancy ( $g$  0.02; 95% CI,  $-0.32$ – $0.36$ ;  $p = 0.90$ ).

### 3.3.4. Selective attention

In seven studies and 309 participants, outcome measures for selective attention were reported. Cognitive rehabilitation did not display a significant treatment effect in either the stroke ( $g$   $-0.08$ ; 95% CI,  $-0.35$ – $0.18$ ;  $p = 0.53$ ;  $I^2 = 0\%$ ) or TBI ( $g$   $-0.05$ ; 95% CI,  $-0.48$ – $0.38$ ;  $p = 0.82$ ) population.

### 3.3.5. Inhibition

Five studies comprising 241 participants assessed inhibition. It was not significantly improved relative to control conditions in stroke survivors ( $g$   $-0.15$ ; 95% CI,  $-0.71$ – $0.41$ ;  $p = 0.60$ ;  $I^2 = 37\%$ ), participants with TBI ( $g$   $-0.73$ ; 95% CI,  $-1.93$ – $0.47$ ;  $p = 0.24$ ) or those with CNS-impacting malignancy ( $g$  0.23; 95% CI,  $-0.07$ – $0.53$ ;  $p = 0.14$ ;  $I^2 = 0\%$ ).

### 3.3.6. Impact of injury duration

Four studies were identified as representing outliers of injury duration; two with participants less than two months post-stroke (Barker-Collo, 2009; Schottke, 1997) and two with greater than five years injury duration (Butler, 2008; Tiersky, 2005). A sensitivity analysis

was conducted by removing these outliers but this did not result in any meaningful change to the results. Rehabilitation was still effective for divided attention in stroke survivors ( $g$  0.59; 95% CI, 0.18–1.00;  $p = 0.004$ ;  $I^2 = 0\%$ ) but not in those with TBI ( $g$  0.98; 95% CI,  $-0.81$ – $2.77$ ;  $p = 0.28$ ;  $I^2 = 77\%$ ). For all other attentional domains, a significant treatment effect did not emerge for patients of any etiology.

### 3.3.7. Long-term outcomes

Four studies followed up both intervention and control groups after the initial post-intervention assessment (Barker-Collo, 2009; Ferguson, 2012; McMillan, 2002; Winkens, 2009). At follow-up, the treatment effect for intervention was found to be non-significant for all domains and in all etiologies: selective attention ( $p = 0.76$ ), sustained attention ( $p = 0.95$ ), alternating attention ( $p = 0.70$ ) and inhibition ( $p = 0.72$ ). The benefit seen for divided attention in the stroke population was no longer evident at follow-up ( $p = 0.18$ ).

### 3.3.8. Assessment of publication bias

Using Egger's regression method, there was no evidence of publication bias for divided attention ( $p = 0.31$ ), selective attention ( $p = 0.95$ ), sustained attention ( $p = 0.13$ ) or alternating attention ( $p = 0.45$ ). Funnel plot asymmetry was detected for the endpoint of inhibition ( $p = 0.043$ ) and the addition of imputed studies using trim-and-fill analysis shifted the effect size from 0.10 (95% CI,  $-0.16$  –  $0.36$ ) to 0.23 (95% CI, 0.01 – 0.45).

## 4. Discussion

This is the first quantitative comparison of attention remediation between different ABI etiologies and across attentional domains. In this meta-analysis of 12 RCTs and 584 participants, cognitive remediation was found to have both an etiology- and domain-specific effect. Divided attention showed significant improvement in stroke survivors, but other attentional domains did not. For patients with TBI, cognitive rehabilitation did not reduce deficits in any attentional domain. Only two studies were identified for patients with CNS-impacting malignancy and these also did not demonstrate any benefit of attention rehabilitation.

The fact that only divided attention displayed significant improvement in any population group suggests cognitive remediation may have a domain-specific

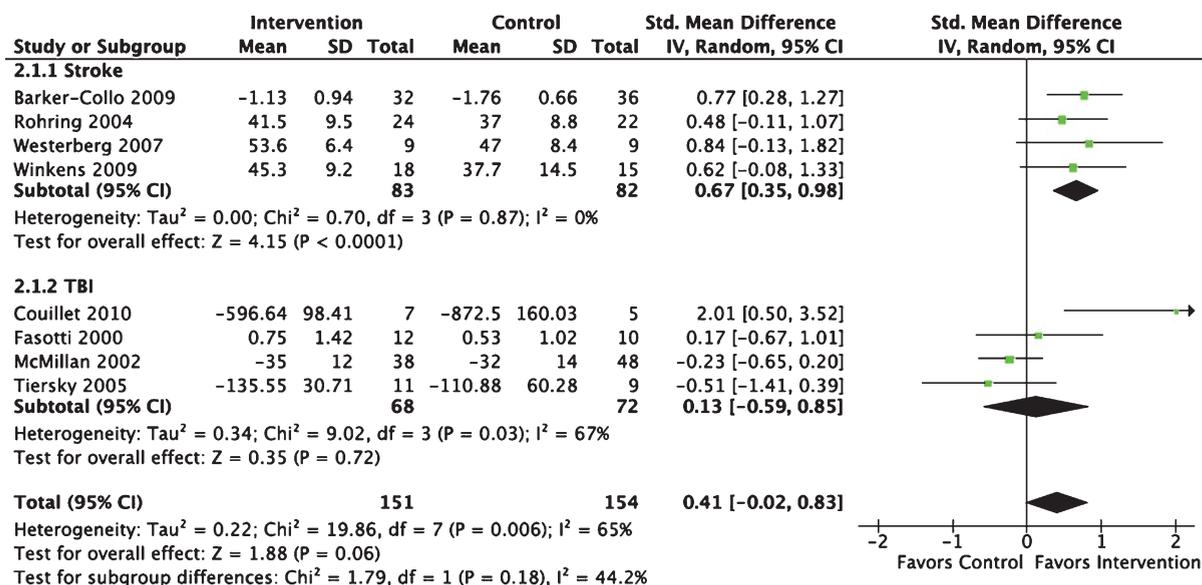


Fig. 2. Forest plots displaying effectiveness of cognitive interventions for remediation of divided attention following stroke and traumatic brain injury (TBI). The estimated effect size corresponds to the middle of the squares and the horizontal line shows the 95% confidence interval (CI). The sum of the statistics, along with the summary effect size, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials is given below the summary statistics. IV, inverse-variance.

effect on attention. Divided attention, the ability to conduct two tasks at once, has a closer link with executive functioning than other aspects of attention (Couillet, 2010). Cognitive rehabilitation has been shown to be somewhat effective in treating impairments of executive functioning post-ABI (Cicerone, 2011) and our findings suggest this amenability to improvement also extends to the more executive processes of attention.

The impact of etiology of ABI on effectiveness of attention rehabilitation had previously only been qualitatively explored. Previous meta-analyses were not able to perform subgroup analyses by etiology as most included studies reported on patients with a mixture of etiologies (Rohling, 2009). Recognition of etiology of ABI as a potential moderator of attention rehabilitation has led to more studies examining specific ABI populations (Halligan, 2005). Our subgroup analysis found only stroke patients experienced a significant improvement in any attentional domain with rehabilitation having no significant impact on TBI. The differential responsiveness in these populations is unlikely to be due to chance alone as the summary point estimate for the TBI group was considerably lower (0.13) than that observed for stroke survivors (0.67). Two stroke and one TBI study were identified as being at high risk of detection bias due to unmasked outcome assessment (Couillet, 2010; Schottke, 1997; Westerberg, 2007).

However, excluding these from analysis actually produced an even greater disparity in treatment effect size for stroke (0.72) and TBI (-0.20) participants. Possible confounding variables between these populations include differences in age, type and intensity of intervention, and severity of brain injury.

In the present meta-analysis, four studies followed up participants after the post-intervention assessment. The intervention group did not display improvement in any attentional domain at follow-up. This finding contributes to the existing concerns over the sustainability of attentional improvements following rehabilitation. Participants were only followed up for three months or fewer in two studies, both of which employed compensatory strategy teaching (Ferguson, 2012; Winkens, 2009). Compensatory interventions may require a longer duration of follow-up to display a “delayed” intervention effect as patients need time to integrate the learned strategies into their daily routine (Gehring, 2012). However, this remains conjecture given the scarcity of long-term outcomes reported in the attention rehabilitation literature.

Our findings have several implications for clinical practice. Our meta-analysis demonstrated a significant improvement in divided attention following cognitive rehabilitation of stroke survivors. Although this benefit did not remain evident in longer follow-up,

even temporary improvements in attention may provide benefit by allowing stroke patients to better engage in rehabilitation of other impairments, thereby maximizing overall functional recovery (Hyndman, 2008). However, these potential benefits need to be weighed against the costs and resources required to incorporate cognitive interventions into routine clinical care.

#### 4.1. Limitations

In our meta-analysis, exclusion of non-RCTs resulted in fewer studies but those included were at low risk of bias (Table 2) with well-balanced intervention and control groups. The limited number of studies (and paucity of raw data available) prevented further subgroup or sensitivity analyses from being performed. We were thus unable to investigate the impact of factors such as intensity, duration and type of rehabilitation intervention. The poor ecological validity of neuropsychological tests employed in most included studies (Chaytor, 2003) poses another barrier to clinical applicability. It is difficult to gauge how much improvement on psychometric tests of attention is required to positively impact clinical outcomes and everyday functionality. Our meta-analysis also included studies that identified attentional deficits by either neuropsychological testing or self-reporting. This was decided because subjective complaints may actually be more indicative of difficulties in everyday functioning. However, this remains a potential confounder given the poor correlation between subjective and objective measures of attentional impairment (Gehring, 2012). Lastly, funnel plot asymmetry was detected in the analysis of the domain of inhibition, but this is unlikely to be due to publication bias as the asymmetry favored a null result.

#### 4.2. Directions for future research

Further studies are required to increase the power of analysis and enable comparisons between different rehabilitation approaches. There is currently insufficient evidence to support either direct attention training or compensatory strategy teaching alone. It is also not known how the duration or intensity of cognitive interventions impacts on attentional outcomes. This makes it difficult to apply our findings to clinical practice in a cost-effective manner. Given the poor ecological validity of neuropsychological tests, future trials should also include measures of real-world outcomes and functionality. Current studies on TBI participants have largely

been restricted to patients with severe injury, which limits the generalizability of their findings. Studies in patients with milder traumatic injury are warranted to determine if these individuals are responsive to cognitive interventions. Lastly, as preliminary evidence suggests a combination of pharmacological and cognitive rehabilitation is more effective than either alone (Jabalera, 2012), further studies examining potentially synergistic effects are warranted.

In conclusion, post-ABI cognitive remediation appears to have both a domain and etiology-specific effect on attention. Pooled evidence from the current literature found cognitive rehabilitation resulted in short-term improvements in divided attention following stroke. However, no benefit of remediation was found for patients with TBI or CNS-impacting malignancy. Given the current scarcity of RTCs, more trials are required to further comparisons between different patient populations, attention domains and rehabilitation approaches.

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#### Conflict of interest

The authors declare no conflicts of interest.

#### Author contributions

S.V: screening of search records, quality assessment of included studies, data extraction, analysis of data and writing of manuscript.

T.W: screening of search records, study selection, data extraction, selection of outcome measures, interpretation of analysis and manuscript revision.

R.B: screening of search records, study selection, clarifying discrepancies in data extraction, selection of outcome measures and manuscript revision.

F.S: design of search strategy, execution of database searches, input into conception and design of study.

A.M: conception and design of study, resolution of discrepancies in study selection and critical revision of the manuscript.

## Supplementary Material

Supplementary Table 1  
Summary of neuropsychological tests used to assess domains of attention in included studies

Study	Divided Attention	Alternating Attention	Sustained Attention	Selective Attention	Inhibition
Barker-Collo	PASAT	Trail Making Test B	IVA-CPT Full-Scale Attention Quotient	Trail Making Test A	–
Westerberg	PASAT	–	–	Ruff 2&7	Stroop Test
Rohring	TAP divided attention	–	d2 (Hits-Errors)	TAP selective attention	–
Schottke	–	–	Konzentrations-Verlaufs-Test	Zahlen-Verbindungstest	–
Sturm	–	–	Wiener Hits	Wiener Choice RT	–
Winkens	PASAT	Trail Making Test B	Simple Reaction Time	Trail Making Test A	Stroop Test
Couillet	TAP divided attention	Trail Making Test B-A	–	–	Go-no-go Single Task
Fasotti	PASAT	–	Auditory Concentration Test: Detection Score	–	–
McMillan	PASAT	Trail Making Test B	TEA Lottery	–	–
Tiersky	PASAT	–	–	–	–
Butler	–	Trail Making Test B	CPT: Omissions	–	Stroop Color Word Test Trial
Ferguson	–	Trail Making Letter-Number Trial	–	–	Color-Word Interference Trial

PASAT, Paced Auditory Serial Addition Test; TAP; Test for Attentional Performance; IVA; Integrated Visual and Auditory; CPT, Continuous Performance Test; TEA, Test of Everyday Attention; RT, reaction time.

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