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Efficacy of Traumatic Brain Injury Rehabilitation: Interventions of QEEG-guided Biofeedback, Computers, Strategies, and Medications

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Abstract The onset of cognitive rehabilitation brought with it a hope for an effective treatment for the traumatic brain injured subject. This paper reviews the empirical reports of changes in cognitive functioning after treatment and compares the relative effectiveness of several treatments including computer interventions, cognitive strategies, EEG biofeedback, and medications. The cognitive functions that are reviewed include auditory memory, attention and problem solving. The significance of the change in cognitive function is assessed in two ways that include effect size and longevity of effect. These analyses complement the previously published meta-reviews by adding these two criteria and include reports of EEG biofeedback, which is shown to be an effective intervention for auditory memory.

Keywords EEG biofeedback · Traumatic brain injury · Cognitive rehabilitation · Neurocognitive rehabilitation · QEEG · Activation QEEG · Memory rehabilitation

Traumatic brain injury (TBI) is associated with impairments in cognitive functioning. Rehabilitation is designed to restore cognitive functions such as memory, attention, and problem-solving. Many research studies report statistically significant effects for treatments, with the recommendations that the treatments are effective and beneficial. However, many research findings are not more effective than placebo, and many of the improvements in test scores from pre-treatment to post-treatment are no different than the improvements in scores due to repeated administrations of the test as shown by the changes in scores of the placebo control groups. In this paper, we describe the neuropsychological evaluation of TBI including brain electrophysiology. In addition, we assess the effectiveness of interventions designed to restore cognitive functions. The assessment includes an analysis of the effect size (ES) of the intervention, which is a method that quantifies the efficacy of a particular intervention relative to a reference and answers the question of how well does the intervention work. Clinical recommendations for treatment based on the efficacy are provided.

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The Neuropsychological Evaluation of Traumatic Brain Injury

The NIH (1998) consensus statement indicated that "… rehabilitation of persons with traumatic brain injury (TBI) should include cognitive and behavioral assessment and intervention" (p. 23). Neuropsychological assessment has long provided these cognitive diagnostic tests for the TBI patient, and the cognitive measures that are typically evaluated in the case of TBI include memory, attention, and problem-solving. The associations between neuropsychological measures and outcome measures have attracted considerable attention. Outcome measures of interventions include neuropsychological revaluations, employment status, self reports, and reports by significant others. However, several of these basic measures do not indicate if cognitive abilities are restored. For example, employment status does

not directly measure ability, as the person may be employed on the basis of a variety of factors unrelated to cognitive function, such as the workplace tolerance of the employee with TBI, as well as returning to work in a less skilled position. In addition, self-reports and reports of others are fraught with issues of subjectivity. The advantages of neuropsychological measures reside in the objection quantification of the changes in specific cognitive abilities.

An additional issue with this patient population is severity. Severity is commonly thought of in terms of mental status immediately following the injury or in the emergency room and is judged by employing scales such as Ranchos Los Amigos or Glasgow Coma Scale (GCS) at the scene of the accident or in the emergency room. Other measures would include (1) description of accident; (2) period of retro- and antero-grade amnesia; or (3) results of magnetic resonance imaging (MRI) and computed tomography (CT). However, severity can also be conceived of in terms of neuropsychological deficits independent from mental status and medical imaging methods. The three assessment techniques do not always coincide. Wallesch et al. (2001) found only 3 of 13 measures had significant correlations ranging from −.54 to .45 between initial GCS ratings and neuropsychological measures of memory, reaction time, executive functions administered 8–21 days post injury. The sample included subjects with documented diffuse axonal injury (DAI) on CT and MRI scans. Only 4 of the 13 measures were significantly different between the patients with documented DAI and those without. It can be reasonably argued, given our limited understanding of the association between severity and outcome in the mild-moderate TBI range, that severity issues are best ecologically understood in terms of neuropsychological measures and their relation to everyday functioning.

A review of the literature on the associations between neuropsychological measures and outcomes concludes that "many neuropsychological tests have a moderate level of ecological validity when predicting everyday cognitive functioning" (Chaytor and Schmitter-Edgecombe (2003), p. 181). Specifically, high scores on tests predicted full-time employment 62% of the time while low scores predicted unemployment 67% of the time (Fabiano and Crewe 1995). While neuropsychological testing does predict return to work, the relationship is moderate and other non-cognitive factors are relevant. Although problematic in many respects, neuropsychological measures remain our best measure of rehabilitation success.

Many of the research studies we review in this article employed the same or similar standardized measures of memory, attention, and problem-solving, lending credibility to this comparison of the effectiveness of interventions. Memory ability is assessed by either paragraph recall or by list learning. Standardized tests of memory are the paragraph recall subtest of the Wechsler Memory Test III (Wechsler 1945), the Rey Auditory Verbal Learning Task (RAVLT; Rey 1941), the California Verbal Learning Test (CVLT; Delis et al. 1987), a well-standardized variation of the RAVLT for list learning, and the Luria (Christensen 1975) memory for word list task. Several standardized tests of attention ability are the digit span of various forms of the Wechsler Adult Intelligence Scale (WAIS; Wechsler 1955); the Paced Auditory Serial Addition Test (PASAT; Gronwall 1977); and variations of the continuous performance test (CPT) such as the Conner's CPT (Mental-Health Systems), the Tests of Variables of Attention (1992), the Trail Making Test (Reitan and Wolfson 1993) and the Integrated Visual and Auditory Continuous Performance Test (IVA; Brain Train). Attentional resources are assumed to be involved in other cognitive tasks, such as cancellation tasks, Trail Making tasks (Reitan and Wolfson 1993), and the Stroop Test (Stroop 1935). Standardized tests of problem solving include the Category Test (Psychological Assessment Resources, Inc., PAR), which measures concept formation, and the Wisconsin Card Sorting Test (1993) which measures perseveration.

The current standard practice for the diagnosis of TBI is to conduct the clinical interview, assess the specifics of the injury, and assess standardized test performance. However, issues with respect to malingering, pre-existing status, appropriate norms, cultural background and, more recently, effort (Gavett et al. 2005) have rendered the diagnostic accuracy of these tests problematic in many cases. It is then important to have a measure of physiologic functioning which can be correlated with the cognitive problems.

The Quantitative EEG as a Supplemental Physical Diagnostic Tool for TBI

Modern medical diagnostic techniques such as MRI, CT, positron emission tomography (PET), and diffusion tensor imaging (DTI) have been used to identify differences in brain states between groups of patients with TBI and normal controls. However, conventional MRI and CT scans are not reliable assessments of mild TBI (McAllister et al. 2001). A recent review of neuroimaging techniques in TBI concluded that some imaging techniques may be more sensitive in the assessment of structural and functional abnormalities following mild TBI than are conventional MRI and CT (Belanger et al. 2007). The techniques that show promise include structural or chemical techniques such as DTI, magnetization transfer imaging (MTI), and magnetic resonance spectroscopy (MRS), as well as functional techniques such as functional MRI (fMRI), PET, and single photon emission computed tomography (SPECT). In

addition, MRS (Babikian et al. 2006) and DTI (Ashwal et al. 2006) have shown value in detection of pediatric brain injury. Thatcher (2000) asserts that MRI and CT medical diagnostic techniques are generally not used in the identification of TBI cases due to their low sensitivity in individual and group cases.

In contrast, there has been an increase in the use of quantitative electroencephalography (QEEG) in TBI evaluations to supplement neuropsychological testing. Traditional analog electroencephalography (EEG) employs an immediate paper printout of the waveforms, while the QEEG digitizes the signal and saves mathematical information regarding the waveform to a hard disk, thus enabling mathematical analysis rather than employing human judgment and classification. The QEEG analysis generates two types of variables. The first type of variable measures the strength of the brainwaves in terms of microvolt, peak amplitude, spectral power, peak frequency, and relative power at specific scalp locations in frequency ranges (delta, theta, alpha, and beta). The second type of variable addresses the relationship between pairs of locations in terms of coherence and phase, which assess the coordination of brain activity across separate brain regions within different frequencies.

Thatcher and others (Thatcher et al. 1989) provided the initial research demonstrating the reliability of a discriminant function analysis that distinguished TBI patients and normals in three independent samples. The QEEG showed a sensitivity of 95.4% of TBI cases and a specificity of 97.4% (Thatcher et al. 1989). While Nuwer (Nuwer 1997), representing the American Academy of Neurology (AAN), argued that the "… QEEG remains investigational for clinical use in post-concussion syndrome, mild or moderate head injury" (p. 9), rebuttals of the AAN position paper have been published (Hoffman et al. 1999; Hughes and John 1999; Thatcher et al. 1999). Furthermore, the QEEG has been identified as an appropriate diagnostic tool for TBI by the *Electrodiagnostic and Clinical Neuroscience Society* (Hughes and John 1999) and by the *Veteran's Administration* (Salazar et al. 2000).

However, the use of QEEG data in the rehabilitation of cognitive functions is not necessarily concerned with diagnostic issues. *The International Society for Neuronal Regulation* has stated (Hammond et al. 2004) that: "Unlike neurology and psychiatry, where QEEG is principally used for purposes of diagnosing medical pathology, neurotherapists who use QEEG primarily do so to guide EEG biofeedback training" (p. 6). One of the purposes of this paper is to assess the efficacy of the QEEG-guided biofeedback in the rehabilitation of brain function and assess the effectiveness of QEEG-guided biofeedback relative to other interventions including computers, cognitive strategies and medications.

Definition of Cognitive Rehabilitation

The National Academy of Neuropsychology (NAN 2002) adopted the American Congress of Rehabilitation Medicine's definition of cognitive rehabilitation as:

> "… a systematic, functionally oriented service of therapeutic cognitive activities, based on an assessment and understanding of the person's brain-behavior deficits. Services are directed to achieve functional changes either by reinforcing, strengthening, or reestablishing previously learned patterns of behavior or by establishing new patterns of cognitive activity or compensatory mechanisms for impaired neurological systems." (Harley et al. 1992), p. 63)

In 1990 there were over 700 programs for cognitive rehabilitation (Ashley et al. 1990). The majority of programs are grouped into two classes of interventions. The first are those interventions that are introduced from "outside" the patient, which include three cognitive rehabilitation models; restorative cognitive rehabilitation, which employs computers; strategy cognitive rehabilitation, which employs instructions in strategies; and compensatory rehabilitation, which employs external aids. The second class includes programs based on interventions that work from "inside" the patient, which include medications and EEG biofeedback. We describe the programs, their assessment and their relative effectiveness.

The "Outside" Approach—Three Cognitive Rehabilitation Models

There are three general "outside" approaches to cognitive rehabilitation. Restorative cognitive rehabilitation (RCR), which employs stimulation and practice, is based upon the concept that repetition can restore function. RCR is an attempt to reinforce, strengthen, or reestablish previously learned patterns of behavior (NAN 2002). This approach generally employs computer interventions as the intervention tool. An example is a vigilance task designed to improve attention in which the patient views a computer screen and taps the space bar on the keyboard whenever a large red circle is displayed (Gray and Robertson 1992). Feedback to the patient is contingent upon their response speed, with increases in frequency of feedback following increases in response speed. However, there is evidence that simple repetitive practice is of minimal or no aid in improving memory for recall (Glisky and Schacter 1986; McKinlay 1992). On a physiological level, reestablishing previously learned patterns of behavior should translate to reestablishing previous EEG and blood flow patterns. Thornton (2000) established that "time does not heal". The

brain does not spontaneously repair the damage caused by the TBI but instead allocates different resources to accomplish the task with less efficient results (Thornton 2002). This physical compensatory pattern of results was also demonstrated in a PET study showing that while both TBI patients and controls engaged frontal, temporal, and parietal regions known to be involved in memory retrieval, the TBI patients showed relative increases in frontal, anterior cingulate, and occipital activity (Levine et al. 2002). The hemispheric asymmetry that is a typically evident in controls was also attenuated in patients with TBI.

The second approach, strategy cognitive rehabilitation (SCR), focuses on developing conscious cognitive processes that involve visualizing, creating associations, and structuring concepts with the expectation that improvement will generalize to activities of daily living by establishing new patterns of cognitive activity (NAN 2002). This approach can be administered with instructors or through use of the computers. However, researchers in the field generally agree that these approaches face the problem that the subject does not continue to use the strategy after treatment terminates (Freeman et al. 1992).

The third approach, compensatory cognitive rehabilitation (CCR), provides external, prosthetic assistance for dysfunctions (Wehman et al. 1989) and is considered to be a compensatory mechanism (NAN 2002). This approach has received positive recommendations (Cappa et al. 2003; Cicerone et al. 2000). However, there is no evidence that indicates use of compensatory devices results in meaningful improvement in core cognitive skills (Ricker 1998). This article included only the articles which employed traditional neuropsychological measures and not more global measures such as the Mini-Mental State Inventory or rating scales.

The "Inside" Approach—Medication and Quantitative Electroencephalography Medication

Depression often accompanies TBI with over 50% comorbidity (Moldover et al. 2004). ADHD drugs such as Ritalin (Methylphenidate) and Focalin® (dexmethylphenidate HCl) have been recommended due to their effectiveness with attention deficit disorder (Plenger et al. 1996). Bromocriptine® (2 bromo-alpha-ergocryptin) has been recommended due to effects on working memory and executive functions, which are two of the affected cognitive abilities in TBI (McDowell et al. 1998). Other medications that have been used historically include Symmetrel® (amantadine), Dexedrine (D-Amphetamine™), Sinemet® (Carbidopa-Levodopa), Larodopa® (levodopa), and Provigil (Modafinil) (Napolitano et al. 2005). This review covers medication interventions with an antidepressant (Zoloft), anti-Parkinson medications (Citicholine and Parlodel) and stimulants (Ritalin).

EEG Biofeedback Interventions—An Alternate "Inside" Approach

EEG biofeedback interventions are the latest approaches to the rehabilitation problem. This method involves operant conditioning of brainwave patterns through the use of reinforcement. A goal of the feedback is to return the underlying electrophysiological functioning of the brain to a normative, preexisting level. The four current approaches in the implementation of EEG biofeedback in the TBI situation are (a) the Flexyx system, (b) the standard quantitative EEG approach (SQ), and use of (c) an eye closed QEEG database (EcQ) and d) an activation database QEEG (ActQ) in guiding the biofeedback interventions. The Flexyx system provides extremely low energy electromagnetic stimulation based on the dominant EEG amplitude, and is designed to reduce EEG amplitudes (Schoenberger et al. 2001).

Historically, the initial "standard" QEEG-guided (SQ) biofeedback with the ADHD and learning disabled population focused on increasing the amount of beta microvolt activity (13–20 Hz) and decreasing the amount of theta microvolt activity (4–8 Hz) along the sensorimotor strip, which is located on the top central portion of head (scalp locations C3, CZ, C4) (Lubar and Lubar 1984; Tansey 1991; Othmer and Othmer 1992). The next advance in the field was to compare the patient's resting, eyes closed QEEG to a reference database (EcQ) leading to more customized protocols for patients (Tinius and Tinius 2000).

The most recent logical development of electroencephalography techniques is the use of an activation database QEEG-guided biofeedback (ActQ) approach that examines brain activity while patients engage in specific cognitive tasks (Thornton 2001). This contrasts with the EcQ approach, which assesses brain activity while patients are resting with their eyes closed. In addition, the ActQ assesses brain activity over the frequency range of 0 to 64 Hz, in contrast to the 0–32 Hz range of the EcQ approach. The addition of the high frequency range (32–64 Hz), which involves the gamma frequency (40 Hz), has been a widely studied phenomenon in cognition. A normative database was developed by measuring the QEEG variables with a group of subjects who had no history of TBI (Thornton 2001). This serves as an empirical reference to compare the QEEG measures on patients. The QEEG variables that are measured on patients while engaged in the tasks are compared to the normative database values for attention, memory and problem-solving. The results of

these comparisons are the deviations of the individual patient from the normal group in each cognitive task. In particular, the method analyzes the variables that are related to success at the task. Treatment protocols are selected that address the deficits indicated by the comparisons. The approach is based upon a coordinated allocation of resources (CAR) model, which states that each cognitive task requires a set of specific locations and frequencies for success (Thornton and Carmody in press). Treatment consists of the operant conditioning of the task relevant QEEG variables while the subject is engaged in the cognitive task. Elaboration on the approach is provided in a companion report (Thornton and Carmody 2007).

Assessment of Cognitive Rehabilitation Programs for the TBI patient

In this section, we review and summarize the evidence for the effectiveness of the interventions in three ways. First, we summarize the conclusions from reviews of the literature completed in the last two decades (Cappa et al. 2003; Chestnut et al. 1998; Cicerone et al. 2000). Second, we use an effect size (ES) analysis, which is a statistical approach to summarize the data available in published reports (Cohen 1969; Hedges and Olkin 1985). We included in this review only those research articles that supplied the statistical data required to calculate the effect size. These data include pre- and post-treatment means and standard deviations of the measures of cognitive processes when available.

A Medline search for cognitive rehabilitation and traumatic brain injury rehabilitation was conducted to include in the analyses articles published since 2000. The search employed the following terms: cognitive rehabilitation, traumatic brain injury rehabilitation. Articles published in well-known rehabilitation journals in the United States prior to 2000 were available to the authors via subscriptions. This review presents the journal articles up to 2007 that satisfied the criteria of providing means and standard deviations for pre and post measures.

Third, we report the methodology of the studies in terms of use of control groups to provide the reader with information on the quality of the research reported. The use of a control group (wait list, alternate treatment) is considered to be methodologically superior to research reports which do not employ a control group. However, many of the published studies have methodological weaknesses in terms of a lack of randomization to treatment and control groups, small sample sizes, and a lack of control groups and similarity of measures. This article attempted to address the similarity of measures problem by examining studies which employed the same or similar outcome measures. Some equivalency of outcome measures was obtained with the auditory memory measures of paragraph, word list recall and problem solving. However, attention measures have a history of diverse instruments. The reader will need to keep these qualifications in mind when reviewing the data. Relevant methodological information reported in the research articles are provided in this paper.

Position Statements and Literature Reviews on Effectiveness of Cognitive Rehabilitation

One of the initial reviews of memory rehabilitation, using strategy instruction, indicated inconsistent results of the interventions, adding that the identification of specific treatment effects is hindered by methodological inadequacies (Benedict 1989). Since that review, four additional reviews of the literature on cognitive rehabilitation have been completed in the past decade (Cappa et al. 2003; Chestnut et al. 1998; Cicerone et al. 2000; Cicerone et al. 2005).

The Agency for Healthcare Research and Quality (AHRQ) investigated whether the application of cognitive rehabilitation enhanced outcomes for people who sustain TBI (Chestnut et al. 1998). The AHRQ report is a review of 2,603 studies published from 1982 to 1997 and, via reviews of abstracts, reduced the list to 114 studies that met the eligibility requirements of Class I, II, or III studies. Well-designed randomized controlled trials (RCTs) were rated as Class I. Studies rated as Class II were RCTs with design flaws; well-done, prospective, quasi-experimental or longitudinal studies; and case-control studies. Case reports, uncontrolled case series, and expert or consensus opinion were generally rated Class III. A "gray zone" exists between Class II and definite Class III articles. Much of the research in rehabilitation uses quasi-experimental designs, which lack control over the constitution of the compared groups. Addressing cognitive rehabilitation, 16 randomized controlled trials and comparative studies that met specified inclusion criteria were placed into evidence tables. Within all these studies there was only sufficient evidence from two studies (Class I and III) that a compensatory approach reduced everyday memory failures in the TBI patient and two studies (Class I and II) that support restorative cognitive rehabilitation with computer assisted interventions for memory rehabilitation. The AHRQ report concluded that there is evidence from three Class I studies using randomized controlled trials that the restorative technique of practice, both with and without the aid of a computer, operates to improve short-term recall on laboratory tests of memory for people with TBI, thus providing some evidence for the restorative cognitive rehabilitation approach. It should be noted that 70% of the research studies focused on the three specific cognitive skill areas of attention and concentration, memory, and concept formation.

Table 1 Studies of the effectiveness of cognitive rehabilitation programs to improve cognitive skills

Types of studies		Attention and orientation	Memory	Verbal and language	Construction	Concept formation	Executive function and motor	Global tests (WAIS)	Total
RCT[a]	Number	12	13	1	2	1	0	1	30
	Percentage[c]	0	8	100	50	0	0	0	10%
Comparative between groups	Number	16	8	3	3	6	3	5	44
	Percentage	31	12	33	67	50	0	20	29%
Correlational studies[b]	Number	16	14	5	3	9	5	10	62
	Percentage	56	57	0	67	44	40	60	50%
Total studies		44	35	9	8	16	8	16	136

Source of studies: Chestnut et al. 1998

[a] RCT: Randomized control trials studies

[b] The number of correlational studies that report a significant correlation between the test and a health outcome or employment

[c] Percentage figures reflect the percentage of positive studies divided by total number of studies for each category

Table 1 presents a comparison of the effectiveness of cognitive rehabilitation programs to improve cognitive skills by reporting the number of positive and negative outcome studies for the three types of evidence (RCT, Comparative, Correlational). Comparative studies examined pre and post treatment employment outcomes or performance measures on neuropsychological instruments. Correlational outcome reports involve a significant relationship between a test and a health outcome or employment. In addition, the percentage is obtained showing positive results of studies relative to the total number of studies.

While the AHRQ report presented favorable results for cognitive rehabilitation programs, a different conclusion was reported in a review of 171 studies that addressed specific cognitive deficits in TBI (Cicerone et al. 2000). Using evidence-based clinical practice criteria, Practice Guidelines were recommended for interventions for (1) attention during the post acute stage with the caveat that the effects can be relatively small or task specific and there is insufficient evidence to indicate improvement over spontaneous recovery during the acute recovery stage; (2) memory, using memory notebooks as compensatory aide with mild memory deficits; and (3) problem solving. It was acknowledged that "no evidence exists to support the effectiveness of cognitive rehabilitation to restore memory functioning in subjects with severe memory impairment" (p. 1605). Practice Guideline criteria were based on well-designed class II studies (prospective cohort studies, retrospective case-control studies or clinical series with well-designed controls) with adequate samples that directly address the effectiveness of the treatment reviewed. The report from the European Federation of Neurological Sciences (Cappa et al. 2003) also concluded that "no evidence is available concerning effective restoration of memory functioning in patients with severe memory impairment" (p. 7). The authors concluded that there is enough overall evidence to recommend some forms of cognitive rehabilitation in patients with neuropsychological deficits after TBI. These include attention training after TBI in the post-acute stage and memory rehabilitation with compensatory training in patients with mild amnesia (Cappa et al. 2003). Not included in any of the three previous reviews was a Veteran's Administration review of their cognitive rehabilitation program which showed improvements on an attention measure (PASAT) but failed to find any statistical significant difference from the control group (a home treatment strategy training group) with their cognitive rehabilitation methods in a group of moderate to severe TBI patients (Salazar et al. 2000).

In conclusion, all reviewers agreed upon the use of memory aides and two of the three reviews agreed upon attention interventions in the post-acute stage (Cappa et al. 2003; Cicerone et al. 2000). However, problematic in this memory recommendation is the long-term follow up in one study that failed to find positive long term effects of this approach at 6 months compared to supportive psychotherapy (Chaytor and Schmitter-Edgecombe 2003; Schmitter-Edgecombe et al. 1995). These recommendations, however, must be viewed in light of the totality of research as well as the magnitude and longevity of the effects. Although no intervention is successful 100% of the time, the ratio figures presented in the AHRQ report are not encouraging (Chestnut et al. 1998).

Effect Size Analyses

We will evaluate the effectiveness of the rehabilitation interventions using effect sizes and include QEEG-guided biofeedback research which was not available at the time of the earlier reviews (Cappa et al. 2003; Chestnut et al. 1998; Cicerone et al. 2000), Cicerone et al. 2005). In order

to obtain an effect size statistic (*ES*), it is necessary to have the mean scores on standardized tests from both the pre-treatment and post-treatment assessments, as well as the measures of the standard deviations of the treatment group on the standardized test. The *ES* for the treatment is calculated using the formula: the post-treatment mean score minus the pre-treatment mean score, divided by the standard deviation of the pre-score and post treatment score (Cohen 1969). It was judged that the *ES* approach was the most appropriate in comparing alternate treatment interventions. This provides a change score in cognitive functioning from pre-treatment to post-treatment in standard deviation units, thus allowing a comparison of changes in functioning due to the treatment. In addition, the *ES* is bias-adjusted for the size of the sample (Hedges and Olkin 1985). Appendix A presents the rationale for the effect size analysis as well as the details and examples of the effect size calculation.

The analysis of effect sizes is organized by the cognitive functions of memory, attention and problem-solving and subsequently by a review of the effect size of follow-up studies. This manuscript is limited to publications with reported effect sizes or with the statistics required to obtain effect sizes, specifically the pre- and post-treatment (when available) means and standard deviations. Medline searches for medication interventions for TBI that met the inclusion criteria yielded articles for the effects of anti-depressants, methylphenidate and Bromocriptine but not for amantidine, Focalin, D-amphetamine, levodopa, and Modafinil.

Description of Table Format and Clinical Effectiveness Rating Criteria

The tables present the individual research results across the four cognitive tasks of paragraph recall, word list recall, attention and problem solving. Each study is analyzed for effect size and confidence intervals and classified whether it is pre-post (PP) or control group (CG) data. In some studies there is the appearance that the ES is significant; however, due either to small sample sizes or large variability of the test scores, the confidence interval suggests that the intervention is no different than 'no effect'. The average *ES* is indicated in the table with the number of studies contributing to the value. An overall average *ES* (separately for both PP and CG data) is also calculated and presented.

An overall clinical effectiveness (CE) value was categorized based on the results of the effect size analysis. The lowest level of CE was zero. The zero category includes those studies that had a value of zero in the ES confidence interval. A decision is rendered (indicated by an asterisk) regarding which data is employed in determining the clinical effectiveness value. The control group studies were the preferred choice. Studies for which confidence intervals could not be calculated were reported but not included in the clinical effectiveness ratings or averaging value. Appendix B provides the sample sizes, and the number of sessions for each study. The overall CE rating is based upon all of the studies within a group (computers, strategies, etc.) and methodology type (control group, pre-post) with the control group studies being the preference when available.

The four categories of clinical effectiveness were defined as follows. If the confidence interval included 0 or below, the measure was assigned a CE rating of 0 and averaged in with the standard deviation effect size measures whose confidence interval was above 0:

CE 0 rating: standard deviation effect size less than .50,
CE 1 rating: standard deviation effect sizes between .50 and 1.00
CE 2 rating: standard deviation effect sizes between 1.00 and 2.00
CE 3 rating: standard deviation effect sizes between 2.00 and 3.00
CE 4 rating: standard deviation effect sizes greater than 3.00

Recommendations for clinical use follow the following criteria.

1. Not Recommended—CE ratings of 0
2. Mild Recommendation—CE ratings of 1 or 2
3. Moderate Recommendation—CE ratings of 3 or 4
4. Strong Recommendations—CE ratings are 3 or 4 with strong methodology such as placebo control groups. There was no research report which met this criterion.

Effect Size Analysis of Rehabilitation of Memory

The effect sizes of studies that addressed auditory memory are presented for paragraph recall in Table 2 and word list recall in Table 3. The 'outside approaches' (computers, strategies) had an average ES of 0.37 across both auditory memory tasks, while 'inside approaches' (QEEG-guided biofeedback, medications) averaged .62 ES. Two restorative (computer) intervention studies averaged 0.44 *ES* for paragraph recall (Table 2) and one study obtained a 0.72 *ES* for word lists (Table 3). Strategy instruction showed improvements averaging 0.32 *ES* for paragraphs (Table 2) and 0.00 *ES* for word list recall (Table 3). Antidepressant medications showed a +.52 *ES* improvement in paragraph recall (Table 2) (Fann et al. 2001) and a 0.00 *ES* effect on word lists. The Flexyx approach scores on the RAVLT had an ES of 0.00 on immediate post treatment evaluation. A 0.90 *ES* at a 2–3 month reevaluation time period was reported with the same word list, which suggests a probable

Table 2 A comparison of interventions to improve memory for paragraph recall

Intervention, reference and type CG: control group PP: pre versus post Computer	Comparison type Control group studies	Effect size and (95% confidence interval) Significant effects in bold
Kerner and Acker (1985)	**3 groups**	
CG—severity-NA	*CMRG-computer memory training group*	
	CCG-computer control group	
	NECG-no exposure control group	
	30 day CMRG post-test scores versus pretest scores	
	Memory scaled score	.26 (−.55 to 1.06)
	Same effect for standard score	.26 (−.55 to 1.06)
	CMRG-TX versus NECG-control	**1.33 (.44 to 2.21)***
	CMRG outperformed computer control group	**1.16 (.29 to 2.02)**
Gray and Robertson (1992)	*Post- versus pre-treatment scores from treatment group*	
CG—severity-NA	Immediate memory	.12 (−.55 to .79)
	Delayed memory	−.05 (−.72 to .63)
	Post- versus pre-treatment scores from control group	.06 (−.68 to .80)
	Post-treatment group versus post-control group	−.16 (−.90 to .58)
	Immediate	−.01 (−.72 to .70)*
	Delayed	−.02 (−.73 to .69)*
	Summary & average for control group studies computer interventions for paragraph recall	**CG effect = .44 (N = 2, 3 measures)**
Strategies	Control group studies	Effect size
Freeman et al. (1992)	**Post- versus pre-treatment scores**	
CG—severity-NA	Control group	.45 (−.70 to 1.59)
	Treatment group	1.15 (−.07 to 2.37)*
Kaschel et al. (2002)	**Post-treatment versus post-baseline scores**	
CG	Rivermead memory behavioral test (RBMT) immediate	
Treatment group:	Pragmatic control group	−.10 (−.91 to .70)
5 CHI, 3 CVA,	Imagery treatment	.71 (−.24 to 1.67)
1 arachnoid cyst	**Using change scores in RMBT**	
Control group:	**Imagery treatment versus pragmatic control**	**.95 (.04 to 1.87)***
7 CHI, 4 CVA,	This uses the change in score from post-baseline	
1 encephalitis	to post-treatment and uses the SD of the post-baseline scores	
	RMBT delayed	
	Pragmatic control group	−.14 (−.95 to .66)
	Imagery treatment	.77 (−.12 to 1.67)
Fasotti et al. (2000)	RMBT	
CG—severe closed head injury	Post- versus pre-treatment group	.26 (−.54 to 1.06)
	Post-treatment versus post-control	.46 (−.39 to 1.31)*
	Post- versus pre- control group	−.20 (−1.08 to .68)
	Summary & average for control group studies strategy interventions for paragraph recall	**CG effect = +.32 (N = 3, 3 measures)**
Strategies	Pre post assessment studies	Effect size
Ryan and Ruff (1988)	Post- versus pre-treatment scores from treatment group	
Mild-Moderate TBI—PP	**Immediate memory**	**.79 (.05 to 1.53)***
	Delayed memory	.74 (.00 to 1.48)*

Table 2 continued

Strategies	Pre post assessment studies	Effect size
Cicerone et al. (1996)	**Post- versus pre-treatment scores**	
PP—mild TBI	Immediate logical memory	.35 (−.56 to 1.25)*
	Delayed logical memory	.66 (−.26 to 1.58)*
Laatsch and Stress (2000)	**Post- versus pre-treatment scores**	
PP 16% mild TBI—remaining moderate to severe; 46% had closed head injuries; remaining had CVAs, tumors, multiple sclerosis, seizures	Immediate verbal memory	.46 (0.0 to .93)*
	Delayed verbal memory	**.71 (.22 to 1.19)***
Quemada et al. (2003)	Post- versus pre-treatment scores RBMT	.29 (−.51 to 1.10)*
PP—posttraumatic amnesia		
Greater than 28 days; Initial GCS score 5.7(SD = 2.2) Severe TBI		
	Summary & average pre-post studies strategy interventions for paragraph recall	**PP effect = +.21 (*N* = 4, 7 measures)**
Antidepressants	**Pre-post study**	**Effect size**
Fann et al. (2001)	**Post- versus pre-treatment scores for treatment group**	
PP	Immediate logical memory	.70 (−.03 to 1.44)*
Mild TBI—Zoloft (Sertraline) (anti-depressant)	**Delayed logical memory**	**1.05 (.29 to 1.82)***
	Summary & average pre-post study medications for paragraph recall	**PP effect = .52 (*N* = 1, 2 measures)**
Activation QEEG	**Control group study**	**Effect Size**
Thornton and Carmody, this article	**Post- versus pre-treatment scores for treatment group**	
CG—mild TBI	**Paragraph recall—combined STM & LTM**	**2.61 (1.74 to 3.47)***
	Immediate memory treatment group PP	**2.05 (1.27 to 2.84)**
	Delayed recall treatment group PP	**2.92 (2.01 to 3.83)**
	Compare treatment to control group	
	Pre-treatment group starts with lower score than control group	−2.48 (−3.43 to −1.53)
	Post-treatment group ends with higher score than control group	**2.04 (1.16 to 2.92)***
	Control group	
	Compared recall Last 8 versus first 7 stories	.21 (−.81 to 1.22)
	Summary & average for control group study QEEG activation method for paragraph recall	**CG effect = + 2.61 (*N* = 1, 1 measure)**

All QEEG references refer to QEEG guided biofeedback

Effect size and confidence intervals were calculated using the methods of Hedges and Olkin (1985)

See Appendix B for details on the number of subjects and length of treatment

NA = not available

* Employed in calculation of effect size (*N* = number of studies used, number of measures used)

practice effect (Schoenberger et al. 2001). Due to the practice effect problem the 0.90 *ES* was not included in the analysis. A SQ approach (Stephens 2006) obtained a 0.00 *ES* on word list recall.

The activation QEEG-guided biofeedback treatment for the improvement of paragraph recall performance obtained gains in paragraph recall of 2.61 *ES* (with 95% confidence interval of 1.74 to 3.47). This represents an improvement in memory scores of 185%. Treatment effectiveness was assessed by comparing the treated group to a control group of paid volunteers, with no history of TBI, recruited through advertising. The pretreatment TBI group ($N = 19$, $M = 8.59$, $SD = 4.31$) had lower scores then the control group ($N = 15$, $M = 18$, $SD = 2.45$) for an *ES* of −2.54 (−3.45 to −1.63). Post-treatment scores for the QEEG-guided biofeedback group ($M = 24.50$, $SD = 7.25$)

Table 3 A comparison of interventions to improve memory for word lists

Intervention and reference Computer	Comparison Pre-post study	Effect size and (95% confidence interval)
Ruff et al. (1994)	Pre post-test scores treatment group	
mild-moderate TBI—PP	Rey	.72 (.02 to 1.46)*
	Summary & average pre-post study computer intervention for word list recall	**PP effect = .72 (*N* = 1, 1 measure)**
Strategies	Control group studies	Effect size
Ryan and Ruff (1988)	Post- versus pre-treatment scores treatment group	
CG—mild to moderate TBI	RAVLT	−.02 (−.64 to .60)*
Niemann et al. 1990	Post- versus pre-treatment scores	
CG—moderate to severe TBI	RAVLT-M sum	
	Attention training group	.24 (−.53 to 1.01)*
	Memory training group—served as control	.41 (−.37 to 1.19)
Milders et al. (1998)	Post- versus pre-treatment scores	
CG—severe to very severe TBI defined by PTA length	Dutch version Rey AVLT	.57 (−.22 to 1.35)*
	Treatment group post versus pre	.57 (−.22 to 1.35)
	Treatment group follow-up versus pre	.15 (−.62 to .92)
	Control group—PP	.78 (−.02 to 1.57)
Fasotti et al. (2000)	Rey	
CG—severe closed head injury	Post- versus pre-treatment group	.43 (−.38 to 1.24)
	Treatment pre versus Control pre	.18 (−.66 to 1.02)
	Post-treatment versus post-control	.30 (−.55 to 1.14)*
	Control post versus pre	.42 (−.46 to 1.31)
	Summary control group studies strategies for word list recall	**CG effect = 0 (*N* = 4, 4 measures)**
Strategies	Pre-post studies	Effect size
Cicerone et al. (1996)	Post- versus pre-treatment scores Rey	.33 (−.56 to 1.21)*
PP—mild TBI	Post- versus pre-treatment scores CVLT	.08 (−.82 to .98)*
	Combined 20 subjects	
Quemada et al. (2003)	Post- versus pre-treatment scores Rey	.45 (−.36 to 1.26)*
PP—PTA greater than 28 days		
Stephens (2006)	Post- versus pre-treatment scores Rey total	.39 (−.49 to 1.28)*
PP—moderate to extremely severe	Cognitive rehab	
	Summary & average pre-post studies strategies for word list recall	**PP effect = 0 (*N* = 3, 4 measures)**
Antidepressants	Pre post study	Effect size
Fann et al. (2001)	Selective reminding Long Term Recall	.49 (−.23 to 1.22)*
PP—mild TBI Zoloft (Sertraline)		
León-Carrión et al. (2000)	Luria memory words list	
CG (citicholine) $N = 7$; Glasgow coma scale <8—severe	Post versus pre for placebo group	−.06 (−1.30 to 1.18)
	Post versus pre for medication treatment group	.46 (−.80 to 1.72)
	Summary & average pre-post study medications for word list recall	**PP effect = 0 (*N* = 1, 1 measure)**

Table 3 continued

Flexyx	Control group study	Effect size
Schoenberger et al. (2001)	Immediate treatment versus wait list	
CG—9 Mild and 3 moderate TBI	Post- versus pre- treatment	.23 (−.57 to 1.04)*
	AVLT combined immediate and delayed 12 Ss	
6 immediate treatment compared to 6 wait-list treatment	Immediate treatment group $n = 6$	
	AVLT immediate recall	0.00 (−1.13 to 1.13)
	AVLT delayed recall	.63 (−.53 to 1.79)
	Delayed treatment waitlist group $n = 6$	
	AVLT immediate recall	.64 (−.52 to 1.79)
	AVLT delayed recall	0.00 (−1.13 to 1.13)
	Summary & average for control group study Flexyx for word list recall	**CG effect = 0 ($N = 1$, 1 measure)**
Standard QEEG	Pre-post studies	Effect size
Stephens (2006)	Post- versus pre-treatment scores Rey total	−.34 (−1.23 to .54)*
PP—moderate to extremely severe	Neurotherapy group	
	Summary & average pre-post study standard QEEG for word list recall	**PP effect = 0 ($N = 1$, 1 measure)**

Effect size and confidence intervals were calculated using the methods of Hedges and Olkin (1985)

See Appendix B for details on the number of subjects and length of treatment

NA = not available

* Employed in calculation of effect size (N = number of studies used, number of measures used)

compared to the control group obtained an *ES* of 1.12 (95% CI = .39 to 1.85). Thus the treatment group was now performing significantly better than the control group. In order to determine if there was a practice effect for the control group, a comparison was made on performance for the first 8 stories ($M = 17.75$, $SD = 2.91$) and the last 7 stories ($M = 18.30$, $SD = 1.98$). There is no evidence in the control group that practice with the memory test has an effect on performance, $ES = 0.21$ (−.81 to 1.22).

Effect Size Analysis of Rehabilitation of Attention

Table 4 presents the comparisons of the different approaches for improvement of attention. Outside interventions (using CG results) averaged an *ES* of 0.00 while inside approaches averaged 0.46 *ES*.

Combined EEG biofeedback and computer training approaches (Tinius and Tinius 2000) resulted in improvements in attention (0.94 ES) in the experimental group. Keller (2001) employed the standard QEEG-guided biofeedback approach (increase beta microvolts, decrease theta microvolts) at the Fz location rather than commonly used Cz location. This intervention was compared to a standard computerized cognitive attention training, which focused on speed of information processing and selective attention for 10 sessions of 30-minutes (COGPACK; Marker 1996; Siegmund 1999). Superior results were found for the standard QEEG-guided biofeedback group (2.09 ES) compared to the group receiving standard computerized training only for the letter cancellation. The Flexyx system (Schoenberger et al. 2001) improved one attention measure immediately following treatment (0.86 ES) and 3 attention measures at a 3 month follow (average 1.02 ES). In summary, the 3 QEEG-guided biofeedback interventions averaged improvements of 0.61 *ES* on attention measures. The medication studies on attention showed an *ES* of 0.00.

Effect Size Analysis of Rehabilitation of Problem Solving

Table 5 presents the treatment effect comparison across the different approaches to problem solving abilities. Outside interventions averaged 0.11 *ES* while a combined inside (Ecq) and outside approach (strategies) obtained a 0.84 *ES*.

Effect Size Analysis of Long Term Effects

As shown in Table 6, there are five studies that included data on the follow-up effectiveness of interventions. For computer interventions, there is an average improvement in memory and problem-solving of 0.00 *ES* for both the

Table 4 A comparison of interventions to improve attention

Intervention and reference	Comparison	Effect size and (95% confidence interval)
Computer	Control group studies	
Gray and Robertson 1992	**Post-treatment versus control**	
CG Severity-NA	PASAT	.46 (−.26 to 1.17)*
	Digit span-forward	−.02 (−.73 to .69)*
	Letter cancellation (cx)-errors	.33 (−.38 to 1.04)
	Control group—recreational computing	
	Control group	
	PASAT post versus pre	.23 (−.51 to .98)
	Digit span post versus pre	0.00 (−.74 to .74)
	Letter cx post versus pre	−.08 (−.82 to .66)
	Treatment group	
	PASAT post versus pre	.57 (−.11 to 1.26)*
	Digit span post versus pre	.28 (−.39 to .96)
	Letter cx Post versus pre	−.24 (−.92 to .43)
Park et al. 1999	PASAT	
CG—severity-NA	Post- versus pre-intervention	3.06 (2.21 to 3.92)
	Post- versus pre-control	4.01 (3.01 to 5.01)
	Post-intervention versus post-control	**−2.62 (−3.43 to −1.85)***
	Summary & average for control group studies computer interventions for attention	**CG effect = 0 (N = 2, 4 measures)**
	Pre post studies	**Effect size**
Ruff et al. (1994)	Pre post-test scores treatment group	
PP—severity-NA	Digit symbol & continuous performance test	.32 (−.40 to 1.05)*
Keller (2001)	Post versus pre-intervention (reverse sign)	
PP—severity-NA	**Cog Rehab**	
	Letter cancellation—post intervention	.49 (−.40 to 1.38)*
	Sustained attention errors post intervention	**1.19 (.24 to 2.14)***
	Choice RT—post intervention	**.97 (.05 to 1.90)***
	Summary & average of pre post studies computer intervention for attention	**PP effect = .44 (N = 2, 4 measures)**
Strategies	Control group studies	Effect size
Niemann et al. (1990)	**Post- versus pre-treatment scores**	
CG—moderate to severe TBI	**PASAT-R**	
Control group is memory training group	Attention training group	.58 (−.20 to 1.37)*
	Memory training group	.66 (−.13 to 1.45)
	Trail-making test B	
	Attention training group	.73 (−.06 to 1.53)*
	Memory training group	.25 (−.53 to 1.02)
	Divided attention test	
	Attention training group	.61 (−.18 to 1.40)*
	Memory training group	.57 (−.22 to 1.35)
	Test d2	
	Attention training group	.61 (−.17 to 1.40)*
	Memory training group	.39 (−.39 to 1.16)
	Average over tasks	
	Attention training group	.63
	Memory training group	.47

Table 4 continued

Strategies	Control group studies	Effect size
Fasotti et al. (2000)	Post- versus pre-treatment group	
CG—severe closed head injury	PASAT	.66 (−.17 to 1.48)
	Visual simple RT	.09 (−.75 to .93)
	Post-treatment versus post-control	
	PASAT	.17 (−.67 to 1.01)*
	Visual simple RT	.32 (−.53 to 1.16)*
Kaschel et al. (2002)	Post- versus pre-treatment scores	
CG—treatment group: 5 CHI, 3 CVA, 1 arachnoid cyst	d2 test of concentration endurance	
	Pragmatic control group	27 (−.54 to 1.07)
Control group: 7 CHI, 4 CVA, 1 encephalitis	Imagery treatment	.69 (−.26 to 1.64)*
Schoenberger et al. (2001)	Immediate treatment versus wait list	
CG—9 mild and 3 moderate TBI	Post- versus pre- treatment	.23 (−.57 to 1.04)*
	Trails b test; (negative ES means faster time)	
6 immediate treatment compared to 6 wait-list treatment	Immediate treatment group $n = 6$	−.26 (−1.40 to .87)
	Delayed treatment waitlist group $n = 6$	−.29 (−1.43 to .85)
	Summary & average for control group studies strategies for attention	**CG effect = 0.00 ($N = 3$, 8 measures)**
Strategies	**Pre post studies**	**Effect size**
Cicerone et al. (1996)	**Post- versus pre-treatment scores**	
PP—mild TBI	**Combined 20 subjects**	
	Digit span forward	.01 (−.87 to .88)*
	Digit span backward	.25 (−.65 to 1.14)*
	Trail making test B errors	−.17 (−1.07 to .74)*
	PASAT	.46 (−.60 to 1.52)*
	CPTA errors	−.38 (−1.28 to .53)*
	Average for all tasks—reverse sign for errors	.25
Laatsch and Stress (2000)	Stroop speed	
PP—16% mild TBI; remaining moderate to severe; 46% had closed head injuries; remaining had CVAs, tumors, multiple sclerosis, seizures	**Post- versus pre-intervention**	**.56 (.07 to 1.04)***
Salazar et al. (2000)	2 groups—home training versus hospital training	
PP	PASAT	
Moderate to severe CHI	**Post- versus pre-home**	**.85 (.45 to 1.25)**
GCS <13 or PTA >25 h	**Post- versus pre-hospital**	**.79 (.44 to 1.14)***
Or CT/MRI positive	Post-hospital versus post-home	.04 (−.32 to .40)
Stephens (2006)	**Cog rehab group**	
PP—moderate to extremely severe	Symbol Search	.10 (−.78 to .98)*
	Trails A	.00 (−.88 to .88)*
	Trails B	.07 (−.81 to .94)*
	TOVA	
	Omissions	.19 (−.69 to 1.07)*
	Commissions	.00 (−.88 to .88)*
	Response time	.17 (−.70 to 1.05)*

Table 4 continued

Strategies	Pre post studies	Effect size
		This means longer RT in post than pre
	PASAT	−.01 (−.89 to .86)*
	Summary & average pre-post studies strategies for attention	**PP effect = .09 (*N* = 4, 14 measures)**
EcQ QEEG & strategies interventions	Control group study	Effect size
Tinius and Tinius (2000)	**Integrative visual and auditory continuous performance test**	
CG—mild TBI	**Post- versus pre-treatment scores**	**.94 (.21 to 1.67)***
Employing classification criteria of American Congress of Rehabilitation Medicine	Post-treatment versus control group	−.46 (−1.13 to .20)
	The treatment group POST mean of 97.1 is lower than control score of 104;	
	The treatment group post score of 97.1 is higher than the treatment group pre score of 74.3:	
	The treatment group shows improvements from pre to post:	
	The treatment group post-score does not differ from controls post-score: Control group—shows no change pre to post	
	Post versus pre IVA	.35 (−.27 to .98)
	Summary & average for control group study EC QEEG & strategies for attention	**CE effect = .94 (*N* = 1, 1 measure)**
Standard QEEG Interventions	Pre post studies	Effect size
Keller (2001)	Post versus pre-intervention (reverse sign)	
PP—severity-NA	**EEG intervention**	
	Letter cancellation—post intervention	**3.92 (2.56 to 5.29)***
	Sustained attention errors—post intervention	**1.09 (.23 to 1.94)***
	Choice RT—post intervention	**.97 (.05 to 1.90)***
	Compare EEG intervention to Cog Rehab intervention	
	Letter cancellation—post intervention	**2.09 (1.05 to 3.13)**
	Sustained attention errors—post intervention	.74 (−.13 to 1.61)
	Choice RT—post intervention	.47 (−.38 to 1.32)
Stephens (2006)	Neurotherapy group	
PP—moderate to extremely severe	Symbol Search	−.12 (−1.00 to .75)*
	Trails A	.23 (−.65 to 1.11)*
	Trails B	−.75 (−1.65 to .16)*
	TOVA	
	Omissions	−.70 (−1.60 to .20)*
	Commissions	−.82 (−1.73 to .09)*
	Response time	−.30 (−1.18 to .58)*
	PASAT #4 This means shorter RT in post than pre	−.22 (−1.10 to .66)*
	Summary & average pre-post studies standard QEEG for attention	**PP effect = .60 (*N* = 2, 12 measures)**
Flexyx	Control group study	Effect size
Schoenberger et al. (2001)	Post- versus pre- treatment all 12 Ss	
CG—9 Mild and 3 moderate TBI	**PASAT trial 4**	**.86 (.02 to 1.69)***
6 Immediate treatment; compared to 6 wait list controls	Digit span backward	.83 (0.0 to 1.67)*
	Digit symbol	.67 (−.16 to 1.49)*
	Delayed treatment waitlist group $n = 6$	

Table 4 continued

Flexyx	Control group study	Effect size
	PASAT trial 4	.11 (−1.02 to 1.25)
	Digit span backward	−.09 (−1.23 to 1.04)
	Digit symbol	−.09 (−1.23 to 1.04)
	Immediate treatment group $n = 6$	
	PASAT trial 4	1.28 (.04 to 2.53)
	Digit span backward	1.22 (−.01 to 2.45)
	Digit symbol	1.03 (−.17 to 2.24)
	Summary & average for control group study Flexyx for attention	**CG effect = .28 ($N = 1$, 3 measures)**
Antidepressants	**Control group study**	**Effect size**
León-Carrión et al. (2000)	Attention	
CG Placebo + Neuropsych	Post- versus pre-intervention	.66 (−.61 to 1.93)
(CogRehab) Vs CDPc (citicholine) & Neuropsych Glasgow coma scale <8—severe	Post- versus pre-placebo	1.21 (−.13 to 2.56)
	Post-intervention versus post- placebo	1.01 (−.31 to 2.32)*
	Summary & average for control group study medications for attention	**CG effect = 0 *($N = 1$, 1 measure)***
Medications	**Control group study**	
Whyte et al. (2004)	Speed of information processing (average effect across 8 measures)	.26**
Ritalin—(Methylphenidate) .3 mg/kg/dose—CG	Sustained attention to response task	.20**
Moderate to severe TBI	Divided attention	0
	Sustained attention	0
	Susceptibility to Distraction	0
	Summary & average control group study medications for attention	**Not calculable due to lack of SD data**
Medications	**Pre post studies**	**Effect size**
McDowell et al. (1998)	Stroop	.7**
TBI GCS <8 PP Placebo versus Parlodel (bromocriptine)	Trails	.35**
Fann et al. 2001	Post- versus pre-intervention	
PP—mild TBI	Digit Span	−.12 (−.84 to .60)*
Zoloft (Sertraline) (anti-depressant)	Digit symbol	.42 (−.30 to 1.14)*
	Trail making—composite	.58 (−.15 to 1.31*
	Summary & average pre-post study medications for attention	**PP effect = 0 ($N = 1$, 3 measures)**

Effect size and confidence intervals were calculated using the methods of Hedges and Olkin (1985)

See Appendix B for details on the number of subjects and length of treatment

** author gave effect size and means; lack of SD prevented CI calculations

NA = not available

* Employed in calculation of effect size (N = number of studies used, number of measures used)

treatment group and the control group. All effect sizes include zero in the confidence intervals, suggesting the interventions do not have an effect that is statistically reliable. The strategies intervention used by Kaschel et al. (2002) shows a follow-up *ES* for memory improvement (RBMT) of 1.24 (immediate) and 1.16 (delayed) compared to a control group *ES* of .00. The strategies intervention is clearly effective and differs from the improvements expected on repeated test administrations. In contrast, the strategies program by Milders et al. (1998) showed an *ES* of 0.00 at 6 month follow-up on the Rey word list task. The Flexyx (Schoenberger et al. 2001) showed an *ES* of 1.02 for 3 measures of attention, indicating that the subjects maintained their gains. The lack of a control group for

Table 5 A comparison of interventions to improve problem solving

Intervention and reference	Comparison	Effect size and (95% confidence interval)
Computer	Control group study	
Gray and Robertson (1992)	Post- versus pre-treatment scores from treatment group	
CG Severity-NA	WCST errors	.56 (−.13 to 1.24)*
	WCST perseverative	.42 (−.30 to 1.13)*
	Post- versus pre-treatment scores from control group	
	WCST errors	.63 (−.10 to 1.35)
	WCST perseverative	.61 (−.08 to 1.30)
	Summary & average for control group study computer interventions for problem solving	**CG effect = 0 (N = 1, 2 measures)**
Strategies	Pre post studies	Effect size
Cicerone et al. (1996)	Post- versus pre-treatment scores	
PP—mild TBI	WCST—perseveration score	.20 (−.60 to 1.00)*
	Category test- error score	.11 (−.91 to .69)*
Laatsch and Stress (2000)	WCST perseverative errors or category test errors	
PP—6% mild TBI—remaining moderate to severe; 46% had closed head injuries; remaining had CVAs, tumors, multiple sclerosis, seizures	**Post- versus pre-treatment**	**.67 (.17 to 1.16)***
	Summary & average pre-post studies strategies for problem solving	**PP effect = .22 (N = 2, 3 measures)**
EcQ & strategies	Control group study	Effect size
Tinius and Tinius (2000)	Post- versus pre-treatment scores from treatment group	
Severity—CG	**WCST trials**	**.91 (.18 to 1.64)***
	WCST perseverative	**.77 (.05 to 1.49)***
	Post- versus pre-treatment scores from control group	
	WCST trials	.16 (−.46 to .78)
	WCST perseverative	.12 (−.50 to .74)
	Summary & average for control group study EcQ & strategies for problem solving	**CG effect = .84 (N = 1, 2 measures)**
Medication		
McDowell et al. 1998	Bromocriptine versus placebo	
CG Severity-NA	WCST perseveration	.55**

Effect size and confidence intervals were calculated using the methods of Hedges and Olkin (1985)

See Appendix B for details on the number of subjects and length of treatment

** Author gave effect size and means; lack of SD prevented CI calculations

NA = not available

* Employed in calculation of effect size (N = number of studies used, number of measures used)

follow-up precludes a comparison to ensure that the improvements are not attributed to repeat testing. There was a stronger long term effect for the attention measures with the Flexyx approach because the subject's values continued to improve after the cessation of the treatment. This effect could either be a practice effect or the effect of the improvement building upon itself.

Summary of Effect Size Analyses and Recommendations

Figure 1 presents the results of the comparisons of the 28 studies. Overall there were five QEEG-guided biofeedback studies, five computer intervention studies, eleven studies which involved strategy interventions and three studies

Table 6 A Comparison of Long Term Effects of Interventions

Intervention and reference	Comparison—control group studies	Effect size and (95% confidence interval)
Gray and Robertson (1992)	6 month follow-up versus pre-intervention for intervention group	
Computer intervention	LM immediate memory	.43 (−.25 to 1.11)*
CG Severity-NA	LM delayed memory	.51 (−.17 to 1.19)*
LM = Logical memory of Wechsler memory scale	6 month follow-up versus pre-intervention for control group	
	LM immediate memory	.30 (−.45 to 1.04)
	LM delayed memory	.26 (−.48 to 1.01)
WCST = Wisconsin card sorting test	6 month follow-up versus pre-intervention for intervention group	
	WCST errors	−.57 (−1.25 to .12)*
	WCST perseverative	−.51 (−1.19 to .18)*
	6 month follow-up versus pre-intervention for control group	
	WCST errors	−.70 (−1.47 to .06)
	WCST perseverative	−.62 (−1.38 to .14)
Kerner and Acker (1985)	Memory index	
Computer intervention CG severity	30-day follow-up versus pre-intervention	.35 (−.46 to 1.16)
CHI unspecified	45-day follow-up versus pre-intervention	.19 (−.61 to .99)*
	Summary & average for control group studies—computer interventions for memory and problem solving	**CG effect = 0 (N = 2, 5 measures)**
Strategies	**Control group studies**	**Effect size**
Milders et al. (1998)	6 month follow-up versus baseline Rey memory	
CG Severe CHI with mean PTA 36 days	Intervention group	.15 (−.62 to .92)*
	Control group	.78 (−.04 to 1.59)
Kaschel et al. (2002)	Follow-up versus pre-treatment scores	
CG	Pragmatic group—control	
Treatment group:	**RBMT immediate**	**.40 (−.41 to 1.20)**
5 CHI, 3 CVA,		
1 arachnoid cyst		
Control group:	**RBMT delayed**	**.49 (−.33 to 1.30)**
7 CHI, 4 CVA,	Imagery group—treatment group	
1 encephalitis		
RBMT = Rivermead behavioral memory test	**RBMT immediate**	**1.89 (.78 to 3.00)**
	RBMT delayed	**2.10 (.87 to 3.14)**
	Follow-up versus 2nd-baseline scores	
	Pragmatic group	
	RBMT immediate	12 (−.68 to .92)
	RBMT delayed	.06 (−.74 to .86)
	Imagery group	
	RBMT immediate	**1.24 (.23 to 2.25)***
	RBMT delayed	**1.16 (.16 to 2.16)***
	Concentration endurance	
	Post-treatment versus post-baseline	
	Experimental group	.36 (−.58 to 1.29)*
	Control group	.23 (−.57 to 1.03)
	Summary & average for control group studies strategies for memory & attention	**Memory: CG Effect = .80 (N = 2, 3 measures) attention: CG Effect = 0 N = 1, 1 measure)**
Schoenberger et al. (2001)	3 month follow-up versus post-intervention score	

Table 6 continued

Strategies	Control group studies	Effect size
Flexyx	Attention	
9 Mild and 3 moderate TBI	PASAT #4	.36 (−.44 to 1.17)
6 immediate treatment compared–6 wait-list treatment—CG	Digit span	.18 (−.62 to .98)
	Digit symbol	.18 (−.62 to .98)
	3 month follow-up versus pre-intervention score	
	Attention	
	PASAT #4	**1.22 (.35 to 2.09)***
	Digit span	**1.01 (.16 to 1.86)***
	Digit symbol	**.85 (.01 to 1.68)***
	Summary & average for control group study Flexyx method for attention	**CG effect = +1.02 (*N* = 1, 3 measures)**

Effect size and confidence intervals were calculated using the methods of Hedges and Olkin (1985)

See Appendix B for details on the number of subjects and length of treatment

NA = not available

* Employed in calculation of effect size (*N* = number of studies used, number of measures used)

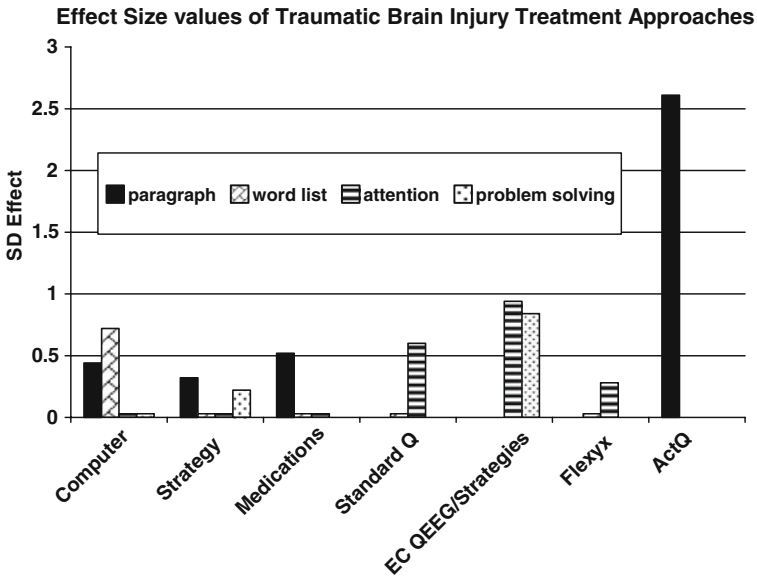

Fig. 1 Effect size values of traumatic brain injury treatment approaches. Sq = Standard QEEG Ecq = Eyes Closed QEEG; Flexyx; Actq = Activation QEEG; Small (.03) effect sizes are 0, included to indicate data was available. Used control group data for Fig. 1 when both values available and pre-post when only pre-post available

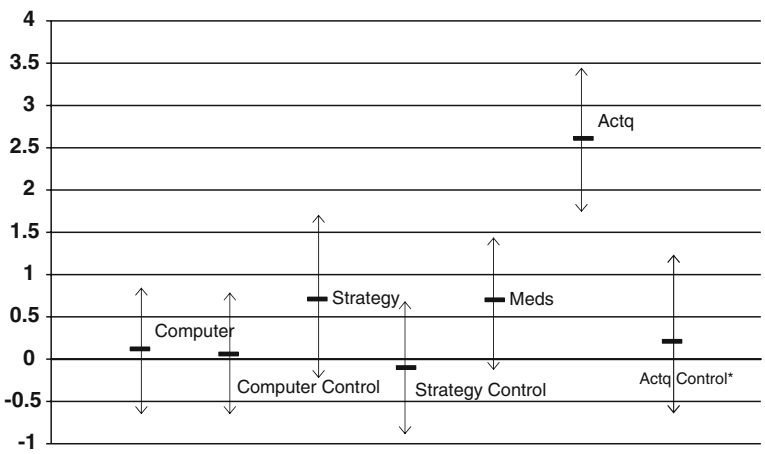

Fig. 2 The effect size and 95% confidence intervals for immediate memory. The references for the interventions are: Computer—Gray and Robertson 1992; Strategy—Kaschel et al. 2002; Medications—Fann et al. 2001; Activation Q—Thornton, this article. Note that the Fann study provided only pre- and post-treatment means; there was no control group. For the interventions where the confidence interval includes the zero value, the intervention is not reliable

* Actq values employed total recall values.

Table 7 Recommendation Criteria

Levels of recommendation	Memory for paragraph recall	Memory for word lists	Attention	Problem solving
1 Not recommended CE = 0	Strategies—CG (.32) PP (.21) Computers—CG (.44)	Strategies—CG (0) PP (0) Flexyx—CG (0) Sq—PP (0) Medications—PP (0)	Computer—CG (0) PP (.44) Strategies—CG (0) PP (.09) Meds—CG (0) PP (0) Flexyx—CG (.28)	Computer CG (0) Strategies PP (.22)
2 Mild recommendation CE = 1 (not labeled) or CE = 2 (labeled)	Medications—PP (.52)	Computers—PP (.72)	Ecq & Strategies—CG (.94) Sq—PP (.60) ***CE = 2—Flexyx	Ecq & Strategies PP (.84)
3 Moderate recommendation CE = 3	Activation QEEG—CG (2.61)			

CE = Clinical effectiveness

*** long term effectiveness rating

CG = Control group comparisons

PP = pre versus post testing comparisons

() = SD value of treatment effect

involving the effect of medication. For paragraph recall mild recommendations could be made for medications and imagery and moderate recommendations for the ActQ intervention model. For word list recall only a mild recommendation for computer intervention could be rendered. For attentional abilities, the combined eyes-closed QEEG-guided biofeedback and strategies and the standard QEEG-guided biofeedback approaches both received mild recommendations. For problem solving only the eyes closed QEEG-guided biofeedback and Strategies approach obtained a mild recommendation. Thus, overall across all tasks and all methods, the outside approach averaged .21 SD across all tasks while the inside approach averaged .51 SD. Long term results and the combined approach (Tinius and Tinius 2000) were excluded in this analysis because the Tinius and Tinius (2000) combined different treatment approaches (strategies and Ecq) and long term results, although of some value, are problematic to include in this type of analysis.

Figure 2 presents a graphic comparison of the different approaches employing the SD effect size and confidence intervals for paragraph recall. This figure is illustrative of the value of employing confidence intervals in the analysis of the data. The Actq approach is superior in this analysis. The control condition for the Actq is the comparison between the recall scores of the first 7 stories compared to the subsequent 8 stories.

Additional Considerations

Additional effectiveness issues involve generalization to other cognitive abilities, rehabilitation time, cost and long term effects. The additional issue of degree of severity of initial injury has been previously discussed in this paper.

Since most interventions did not obtain clinically significant results, generalization becomes impossible to meaningfully measure. Only three approaches demonstrated any long term effects; imagery for paragraph recall and the Flexyx approach for attention. The auditory memory improvements were maintained from 1 month to 11 months on repeat testing for the four subjects that were available for retesting in the ActQ treated TBI sample (Thornton and Carmody 2005). The QEEG-guided biofeedback literature indicates that the effects of QEEG-guided biofeedback can last up to ten years (Lubar et al. 1995; Tansey, 1993).

Severity issues, from a neuropsychological perspective, can be revealed by the raw scores for paragraph recall across the studies. The raw initial scores (immediate and delayed recall) on the Wechsler Memory scale were provided in three studies using interventions of computers (Gray and Robertson 1992) and strategies (Cicerone et al. 1996; Ryan and Ruff 1988). The mean recall score for the three studies was 13.9 (average *SD* of 3.38; *M*s range from 11.1 to 16.8). The ActQ TBI group reported in this research had memory scores averaging 8.59 ($SD = 4.31$), reflecting a more severe memory impairment in this group. The ActQ group was 1.39 *SD* below the mean of the 3 comparison studies at the onset of treatment (employing *SD* of both groups). Improvement in memory in the three comparison research studies was 19% compared to 186% of TBI ActQ group. Intervention times ranged from 10 to 132 sessions. The correlation between the *ES* effect (ignoring issues of confidence intervals) and number of sessions was 0.09 (9

studies) for paragraph recall and −.17 for attentional abilities (12 studies).

It should be kept in mind, however, that to expect any significant change in 10 sessions is overly optimistic for a brain injured subject. While cost is always a factor, the long term costs of failure to rehabilitate far outweigh the type of cost structures evident in this analysis. The four QEEG-guided biofeedback approaches dominate the recommendation results in Table 7 and appear to be the most promising to obtain meaningful results.

Cost Issues

A cost-benefit analysis reported that for the 9,744 long-term disability claims over a 6-year period at Northwestern National Life, there was an average savings of $35 in disability reserves for every dollar spent on rehabilitation services (Cherek and Taylor 1995). It was also estimated that medical case management savings for NWNL increased from about $500,000 in 1987 to 8.1 million in 1993. The financial value, as well as the humanitarian value, of continuing to search for improvements in rehabilitation services is self-evident.

Conclusions

The mild to moderate traumatic brain injured subject represents a formidable challenge to the rehabilitation profession. The initial interventions have not proven to fulfill the original hopes. The activation QEEG database guided biofeedback has demonstrated effectiveness in this area, as evidenced in this research article. While it is axiomatic that more research needs to be conducted, at least there appears to be a potential to have a positive impact upon the TBI patient whether they come from auto accidents, slip and falls or our soldiers returning from war.

Appendix A. Calculation of Effect Size

Effect size is a way of quantifying the size of the difference between two groups (Coe 2000). It quantifies the effectiveness of a particular intervention relative to some comparison and answers the question of how well does the intervention work. An effect size (*ES*) of zero means that the mean scores of two groups are identical, while an *ES* of 1 indicates that the mean scores of one group are superior to a second group by a value of one standard deviation. Some examples of other effect sizes show the overlap in the distributions of scores. An *ES* of 0.20 indicates that the treatment moved a subject from the 50th percentile to the 58th percentile, while an *ES* of 0.50 means that the subject is now performing at the 69th percentile, and an *ES* of 0.80 means that the subject is now performing at the 79th percentile.

Olejnik and Algina (2000) describe the history of methods for calculating effects size. Cohen's effect size (1969), *d,* was the first commonly recognized effect size. It represented mean differences in units of common population standard deviation. Glass et al. (1981) proposed a modification of the Cohen *d* where the common standard deviation was replaced with the standard deviation of the control group. Hedges (1981) suggested that a better estimate of effect size would use the pooled variance and standard deviation rather than the standard deviation of one of the groups. There are also differences in the literature on which estimate of variance to use. Typically the variance of the control group is used, which represents the population. Others argue for a pooled estimate when there is no control group but rather two treatment groups and the population variance is unknown. As indicated by Coe (2000), when using the pooled standard deviation to calculate the effect size, which generally gives a better estimate than the control group *SD*, it is slightly biased and gives a value slightly larger than the true population value. This bias is corrected using a formula (Hedges and Olkin 1985), p. 80).

While Cohen (1988), p. 25) warned that he arbitrarily chose values to classify the interpretation of size of the effect, many studies continue to interpret an effect size of .2 as a small effect, a .5 as a medium effect, and a .8 is a large effect (Coe 2000). The interpretation is improved by using confidence intervals that provide a range of values around the effect size to determine the likelihood of the effect size occurring due to chance. Greater accuracy of the effect size is more likely when based on a large sample rather than a small sample. If the confidence interval includes the value of zero, then the effect size is statistically equivalent to no effect. If the confidence interval does not include the value of zero, then the effect size is statistically significant.

In the effect size analysis of the interventions for TBI, we included research reports that provided the statistics necessary to obtain an effect size. These statistics included the means and standard deviations of the treatment and control groups. In the studies where there was no control group, then we used the means and standard deviations of the pre-treatment and post-treatment scores of the treatment group.

We provide an example of how we obtained the effect size and confidence intervals for three interventions that addressed memory. Kerner and Acker (1985) treated 12 subjects with TBI using a memory retraining software and showed improved memory scores for the treatment group ($M = 34.75$, $SD = 12.53$) compared to 12 subjects in a control group ($M = 30.42$, $SD = 11.41$). The pooled standard deviation is 11.98. The effect size, using Hedge's bias correction for sample size, is 0.35 with a 95% confidence interval of −0.46 to 1.16. Using Cohen's terms, the effect size of 0.35 is small to moderate. However, the confidence interval includes the value of zero, making the effect size

not statistically different from zero. The conclusion, using the effect size and 95% confidence interval, is that the memory retraining software intervention is no different than the control group treatment.

In a second example, Schoenberger et al. (2001) treated 12 TBI subjects with 25 sessions of Flexyx Neurotherapy System. Immediate and delayed memory scores were obtained using the Rey's Auditory Verbal Learning Test (AVLT). Six subjects were treated first for five to six weeks while six were in a wait-list control group. Then the six subjects in the wait-list group received treatment. We can assess the effect size for the treatment by using pre- and post- treatment scores for the entire group of 12 subjects. There was no significant effect size for immediate memory score. The pre-treatment scores ($M = 10.50$, $SD = 2.11$) were no different than the post-treatment scores ($M = 10.17$, $SD = 1.90$), $ES = -0.16$ with a 95% confidence interval of −0.96 to 0.64. The authors reported a significant effect ($p < .10$) for treatment with a significant improvement in the delayed memory scores between pre-treatment ($M = 9.67$, $SD = 2.39$) and post-treatment scores ($M = 11.08$, $SD = 2.54$); however the ES was 0.55 with a 95% confidence interval ranging from −0.26 to 1.37.

In the third example, on data reported in this paper, 19 subjects with TBI were given QEEG treatment. Their pre- and post-treatment scores were compared to a control group of 15 subjects. The TBI subjects improved their scores on paragraph recall from pre-treatment ($M = 8.75, SD = 4.51$) to post-treatment ($M = 24.46$, $SD = 7.25$), in addition the ES was 2.61 with a 95% confidence interval ranging from 1.87 to 3.47. The confidence interval does not include the value of zero. Clearly the treatment was effective.

Appendix B Sample sizes and durations of interventions

Intervention	Reference	Number subjects	Number sessions
Computer	Kerner and Acker (1985)	12	12
	Gray and Robertson (1992)	31	17.5
	Ruff et al. (1994)	15	20
	Park et al. 1999	23	20
	Niemann et al 1990	29	36
Strategies	Ryan and Ruff, (1988)	20	132
	Freeman et al. (1992)	6	15
	Cicerone et al. (1996)	20	6 months
	Novak et al. 1996	22	20
	Milders et al. (1998)	13	12
	Fasotti et al. (2000)	12	7.4
	Laatsch and Stress (2000)	16	Mean of 32
	Quemada et al. (2003)	12	120
	Kaschel et al. (2002)	12	30
	Stephens (2006)	10	20
	Salazar et al. (2000)	120	32
		67 in hospital treatment	
		53 home treatment	
Medications	McDowell et al. (1998)	24	Subjects tested twice—with placebo and with Bromocriptine
	Whyte et al. (2004)	19 Ss completed some tasks	Subjects tested twice—with placebo and with Methylphenidate
		9 Ss completed all tasks	
	León-Carrión et al. (2000)	10	Cytidinediphosphocholine for 3 months
	Fann et al. (2001)	15	Sertraline for 8 weeks
Eyes Closed QEEG	Tinius and Tinius (2000)	16	20
Standard QEEG	Stephens (2006)	6	20
Modified QEEG	Keller (2001)	12	10
	Schoenberger et al. (2001)	12	25
Activation QEEG	Thornton and Carmody (2005)	7	80
	Thornton and Carmody, this article, paragraph recall	19	54

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