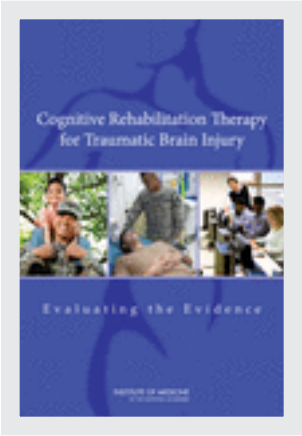

Cognitive Rehabilitation Therapy for Traumatic Brain Injury: Evaluating the Evidence

DETAILS

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Cognitive Rehabilitation Therapy for Traumatic Brain Injury

Evaluating the Evidence

Committee on Cognitive Rehabilitation Therapy for Traumatic Brain Injury

Rebecca Koehler, Erin E. Wilhelm, Ira Shoulson, *Editors*

Board on the Health of Select Populations

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"Knowing is not enough; we must apply.
Willing is not enough; we must do."
—Goethe

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Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

Charles H. Bombardier, University of Washington School of Medicine
Diana D. Cardenas, University of Miami
Keith Cicerone, JFK-Johnson Rehabilitation Institute
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Mark Sherer, TIRR Memorial Hermann
McKay Moore Sohlberg, University of Oregon

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions

or recommendations nor did they see the final draft of the report before its release. The review of this report was overseen by **Dan G. Blazer,** Duke University Medical Center, and **Nancy E. Adler,** University of California, San Francisco. Appointed by the National Research Council and Institute of Medicine, they were responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Preface

Traumatic brain injury (TBI) is a too common and disabling occurrence in civilian and military life, estimated to annually affect 10 million people worldwide. The Institute of Medicine (IOM) has a long-standing role of providing guidance to the Department of Defense (DoD) on the health and well-being of services members and their families. At the request of DoD, the current study represents a concentrated endeavor by the Committee on Cognitive Rehabilitation Therapy for Traumatic Brain Injury to comprehensively evaluate the value of cognitive rehabilitation therapy (CRT) as a therapeutic intervention for traumatic brain injury.

The United States military is currently engaged in ongoing operations in Afghanistan (Operation Enduring Freedom) and Iraq (Operation Iraqi Freedom). Conflicts in these war zones have been characterized by more explosive weaponry and other aggressive tactics, placing members of the military at greater risk for TBI, the "signature wound" of these wars. Recovering and returning service members with TBI may face long-term challenges in rehabilitation and reintegration to everyday life. These challenges to injured individuals also affect their families and communities. Survivors of TBI require ongoing support systems to care for and cope with physical injuries, cognitive impairment and coexisting disabilities such as posttraumatic stress disorders. An effective and reliable health care infrastructure and evidence-based treatment and rehabilitation policies must be in place to achieve effective recovery and a return to optimal functioning and productivity. The public increasingly is confronted with and better recognizes the often enduring and serious consequences of TBI and the need for providing the most effective treatments for those who serve our country in harm's way.

The committee sought to provide a scientific framework to evaluate current research and practices related to CRT. To evaluate the value of CRT for TBI, the committee iteratively developed criteria for inclusion of published scientific reports and reviewed and analyzed some 88 studies to inform our findings on specific domains such as attention, executive function, language and social communication, and memory, as well as multimodal or comprehensive CRT programs.

We are honored to have been of service in providing DoD with a comprehensive evidence-based review of CRT for TBI. This was a timely review, both in terms of the relevance of the topic and relatively brief time allocated to complete the review and our report. I am deeply appreciative of the expert work of our dedicated committee members and their extraordinary commitment and contributions to the task at hand. Over a course of about 6 months, we convened six in-person committee meetings, two open meetings including scientific presentations, and an abundance of teleconferences and email exchanges. We trust that this report assists not only DoD in its efforts to care for recovering and returning service members, but also informs the broader research community about the value of cognitive rehabilitation therapy for TBI sustained in both military and civilian settings.

The committee extends its appreciation to the many people who presented information at its open meeting and to our dedicated IOM staff: Rebecca Koehler, Erin Wilhelm, Alicia Jaramillo-Underwood, and Jon Sanders. We also thank Mary Ferraro and Andy Packel at the Moss Rehabilitation Institute (Philadelphia), who expertly abstracted information from reviewed research reports. We also thank consultants to the committee, Jennifer Vasterling and Barbara Vickrey, for their contributions in the development of several chapters of the report. A special appreciation is due to the patients, their families, and clinicians who strive together to combat and recover from the disabling and often devastating consequences of TBI.

Ira Shoulson, *Chair*
Committee on Cognitive Rehabilitation Therapy for Traumatic Brain Injury

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Tables, Figures, and Boxes

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BOXES

Acronyms and Abbreviations

AAD	Assessment of awareness of disability
AANN	American Association of Neuroscience Nurses
ACBIS	Academy of Certified Brain Injury Specialists
ACFI	Assessment of Client Functioning Inventory
ACOTE	Accreditation Council for Occupational Therapy Education
ACRM	American Congress of Rehabilitation Medicine
ADHD	Attention deficit hyperactivity disorder
ADL	Activities of daily living
AIM	Assessment of Intentional Memory
AIP	Awareness Intervention Program
AMPS	Assessment of Motor and Process Skills
ApoE	Apolipoprotein E
APT	Attention Process Training
ARN	Association of Rehabilitation Nurses
ASHA	American Speech-Language-Hearing Association
BI-ISIG	Brain Injury Interdisciplinary Special Interest Group
BINT	Blast-induced neurotrauma
BRISS–R	Behaviorally Referenced Rating System of Intermediary Social Skills–Revised
bTBI	Blast-induced traumatic brain injury
BVRT	Benton Visual Retention Test
CAA	Council on Academic Accreditation
CACR	Computer-assisted cognitive rehabilitation

CAMG	Computer-Assisted Memory Training Group
CAPTE	Commission on Accreditation of Physical Therapy Education
CBIS	Certified Brain Injury Specialist
CBT	Cognitive behavioral therapy
CDC	Centers for Disease Control and Prevention
CDE	Common data element
CFT	Rey-Osterrieth Complex Figure Test
CG	Control group
CHART–R	Craig Handicap Assessment and Reporting Technique–Revised
CHART–SF	Craig Handicap Assessment and Reporting Technique–Short Form
CIQ	Community Integration Questionnaire
CNRN	Certified Neuroscience Registered Nurse
CO	Cognitive orthosis
COPM	Canadian Occupational Performance Measure
COWAT	Controlled Oral Word Association Test
CP	Clinical psychologist
CPT	Continuous Performance Test
CRBC	Cognitive Retraining Behavior Checklist
CRRN	Certified Rehabilitation Registered Nurse
CRT	Cognitive Rehabilitation Therapy
CS	Constraint seeking
CSG	Cognitive skills group
CT	Computed tomography
CVLT	California Verbal Learning Test
DARE	Database of Reviews of Effects
DASS	Depression, Anxiety and Stress Scale
DMDC	Defense Manpower Data Center
DO	Diary only
DoD	Department of Defense
DRS	Disability Rating Scale
DSIT	Diary and Self-Instructional Training
DTI	Diffusion Tensor Imaging
DVBIC	Defense and Veterans Brain Injury Center
ECRI	Emergency Care Research Institute
EEG	Electroencephalogram
EL	Errorless learning
EMF	Everyday memory failures
EMQ	Everyday Memory Questionnaire

ERIC	Education Resources Information Center
FAM	Functional assessment measure
FANCI	First Steps Acute Neurobehavioral and Cognitive Intervention
FCSUS	Frequency of Cognitive Strategy Usage Scale
FIM	Functional independence measure
FITBIR	Federal Interagency Traumatic Brain Injury Research
fMRI	Functional magnetic resonance imaging
FNM	Face-name method
FRsBe	Frontal Systems Behavior Scale
GAS	Goal Attainment Scaling
GCS	Glasgow Coma Scale
GMT	Goal Management Training
GOS	Glasgow Outcome Scale
GOS-E	Extended Glasgow Outcome Scale
GST	General Stimulation Training
HKLLT	Hong Kong List Learning Test
HRTB	Halstead-Reitan Neuropsychological Test Battery
HVLT–R	Hopkins Verbal Learning Test–Revised
IADL	Instrumental activities of daily living
ICF	International Classification of Functioning, Disability, and Health
ICIDH	International Classification of Impairments, Disabilities and Handicaps
IED	Improvised explosive device
IRB	Institutional review board
IOM	Institute of Medicine
ISMT	Interactive strategy modeling training
IT	Information Technology
IVA-CPT	Integrated Visual and Auditory Continuous Performance Test
KAS	Katz Adjustment Scale
KAS–R	Katz Adjustment Scale–Relative Report Form
KAS-R1	Katz Adjustment Scale, modified form R1
LAP	Learning activities packet
LCFS	Levels of Cognitive Functioning Scale
LCSW	Licensed Clinical Social Worker

LM	Logical memory
LOC	Loss of consciousness
LTM	Long-term memory
MAC–F	Memory Assessment Clinics ratings scales–Family
MAC–S	Memory Assessment Clinics ratings scales–Self
MANOVA	Multivariate analysis of variance
MCI	Mild cognitive impairment
MCQ	Memory Compensation Questionnaire
MEPSM	Means-Ends Problem-Solving Measure
MHS	Military Health System
MI	Metacomponential Interview
MOL	Method of loci
MPAI-3	Mayo-Portland Adaptability Inventory III
MRI	Magnetic resonance imaging
MTBI	Mild traumatic brain injury
MSW	Master of Social Work
NART	National Adult Reading Test
NCLEX-RN	National Council Licensure Examination for Registered Nurses
NCSE	Neurobehavioral Cognitive Status Examination
NFI	Neurobehavioral Functioning Inventory
NICHD	National Institute of Child Health and Human Development
NIDRR	National Institute on Disability and Rehabilitation Research
NIH	National Institutes of Health
NR	Neurorehabilitation program
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
ORM	Orientation Remedial Module
OT	Occupational therapist
OTR	Occupational therapist registered
PASAT	Paced Auditory Serial Addition Test
PASAT–R	Paced Auditory Serial Addition Test–Revised
PCS	Post-concussion syndrome
PCSS	Personal Conversational Style Scale
PDA	Personal digital assistant
PDBS	Partner Directed Behavior Scale
PET	Positron emission tomography

PFIC	Profile of Functional Impairment in Communication
PQOL	Perceived Quality of Life
PQRST	Preview, Question, Repeat, State, and Test
PROM	Patient Reported Outcome Measures
PRPP	Perceive, Recall, Plan, and Perform
PSQ	Problem Solving Questionnaire
PTA	Posttraumatic amnesia
PTSD	Posttraumatic stress disorder
QCIQ	Quality of Community Integration Questionnaire
RAPS	Rapid Assessment of Problem Solving
RAVLT–M	Rey Auditory Verbal Learning Test–Modified
RBMT	Rivermead Behavioural Memory Test
RCT	Randomized controlled trial
RIS	Ridiculously imaged story
RITS	Rehabilitation Intensity of Therapy Scale
RLTLT	Ruff-Light Trail Learning Test
RN	Registered nurse
RPM	Raven's Progressive Matrices
SADI	Self Awareness of Deficits Interview
SART	Sustained Attention to Response Test
SCL–90 R	Symptom Checklist–90 Revised
SCSQ–A	Social Communication Skills Questionnaire–Adapted
SES	Socioeconomic status
SIT	Self-instruction training
SLP	Speech-language pathologist
SPRS	Sydney Psychosocial Reintegration Scale
SPRS–Relative	Sydney Psychosocial Reintegration Scale–Relative Ratings
SPRS–Self	Sydney Psychosocial Reintegration Scale–Self Ratings
SPSS	Social Performance Survey Schedule
SPSVM	Social Problem-Solving Video Measure
SR	Spaced Retrieval
SRSI	Self-regulation skills interview
SS/MB	Single-subject, multiple baseline
SUD	Substance use disorders
SWLS	Satisfaction with Life Scale
TAI	Traumatic axonal injury
TAMG	Therapist Administered Memory Training Group
TAP	Test for Attentional Performance
TASIT	The Awareness of Social Interference Test

TBI	Traumatic brain injury
TMS	Transcranial magnetic stimulation
TPM	Time Pressure Management
TOT	Temporal Orientation Test
UCSS	Usefulness of Cognitive Strategy Scale
USUHS	Uniformed Services University of the Health Sciences
VA	Department of Veterans Affairs
VAMC	Veterans Affairs' Medical Center
VHA	Veterans Health Administration
VPA	Visual paired associates
WA	Working alliance
WAIS	Wechsler Adult Intelligence Scale
WAIS–R	Wechsler Adults Intelligence Scale–Revised
WCST	Wisconsin Card Sorting Test
WHO	World Health Organization
WHO-ICF	World Health Organization's International Classification of Functioning, Disability, and Health
WMS–R	Wechsler Memory Scale–Revised
WMT	Working Memory Training
WRAMC	Walter Reed Army Medical Center

Summary

Traumatic brain injury (TBI) affects an estimated 10 million people worldwide and causes significant physical, emotional, and cognitive disabilities among those affected (CDC 2010; WHO 2011). Conflicts in Iraq (Operation Iraqi Freedom [OIF]) and Afghanistan (Operation Enduring Freedom [OEF]) have put members of the U.S. military at high risk for TBI, largely due to repeated and prolonged deployments, increasing injuries to the head and neck, and attacks with improvised explosive devices (IEDs), which may cause blast-induced neurotrauma (BINT) (Terrio et al. 2009; Warden 2006). More individuals live with the consequences of these injuries due to advances in life-saving measures such protective equipment, emergency care and medical evacuation systems, and treatment and care of TBI (Martin et al. 2008). Individuals with TBI often require some form of treatment for their condition. One form of treatment for the cognitive and behavioral deficits associated with TBI is cognitive rehabilitation therapy (CRT), a systematic, goal-oriented approach to overcoming cognitive impairments. Recognizing that TBI is the signature war wound of OIF/OEF conflicts, the U.S. Department of Defense (DoD) saw the importance of ensuring adequate treatment for personnel who have sustained service-related TBI. Therefore, DoD asked the Institute of Medicine (IOM) to evaluate CRT for TBI to guide its use and coverage in the Military Health System (MHS).

SCOPE AND STRUCTURE OF THE REPORT

To complete its task (see Box S-1 for the Statement of Task), the IOM formed an ad hoc committee of experts from a range of disciplines

BOX S-1
Statement of Task

A consensus committee shall design and perform a methodology to review, synthesize, and assess the salient literature and determine if there exists sufficient evidence for effective treatment using cognitive rehabilitation therapy (CRT) for three categories of traumatic brain injury (TBI) severity—mild, moderate, and severe—and will also consider the evidence across three phases of recovery—acute, subacute, and chronic. In assessing CRT treatment efficacy, the committee will consider comparison groups such as no treatment, sham treatment, or other non-pharmacological treatment. The committee will determine the effects of specific CRT treatment on improving (1) attention, (2) language and communication, (3) memory, (4) visuospatial perception, and (5) executive function (e.g., problem solving and awareness). The committee will also evaluate the use of multi-modal CRT in improving cognitive function as well as the available scientific evidence on the safety and efficacy of CRT when applied using telehealth technology devices. The committee will further evaluate evidence relating CRT's effectiveness on the family and family training. The goal of this evaluation is to identify specific CRT interventions with sufficient evidence base to support their widespread use in the MHS, including coverage through the TRICARE benefit.

The committee shall gather and analyze data and information that addresses

1. A comprehensive literature review of studies conducted, including but not limited to studies conducted on MHS or VA wounded warriors;
2. An assessment of current evidence supporting the effectiveness of specific CRT interventions in specific deficits associated with moderate and severe TBI;
3. An assessment of current evidence supporting the effectiveness of specific CRT interventions in specific deficits associated with mild TBI;
4. An assessment of (1) the state of practice of CRT and (2) whether requirements for training, education and experience for providers outside the MHS direct-care system to deliver the identified evidence-based interventions are sufficient to ensure reasonable, consistent quality of care across the United States; and
5. An independent assessment of the treatment of traumatic brain injury by cognitive rehabilitation therapy within the MHS if time or resources permit.

including neurology, psychology, psychiatry, rehabilitation medicine, neuropsychology, neuropharmacology, nursing, speech-language pathology, epidemiology and neurocognitive study design, and disability and long-term care. The committee developed a strategy for reviewing the evidence, including a comprehensive review of the literature on CRT for TBI. After reviewing the statement of task and meeting with a representative from the Department of Defense to clarify intent, the committee interpreted its charge as assessing the state of the evidence. The committee acknowledges the goal of evidence assessments is to inform policy, upon which clinical

practice guidelines are developed. Those at the Department of Defense are the only ones in position to make policy judgments for the Military Health System. After extensive deliberation, the committee determined it was beyond its charge to interpret its assessment of the evidence with respect to policy recommendations or clinical practice guidelines.

In addition to reviewing the literature, the committee heard from experts in the fields of cognitive rehabilitation research and practice, investigators of major research studies of traumatic brain injury in military and civilian settings, and advocates for the role of families and communities in providing ongoing support to injured members of the military and veterans. The committee also received statements from stakeholders from various organizations and members of the public. Over the course of the study, the committee met six times, engaged the public through two workshops, and participated in a number of ongoing activities organized by working groups. The committee did not complete an independent assessment of the treatment of TBI by cognitive rehabilitation within the MHS (Subtask 5). This exclusion was due to constrained resources, including a lack of access to available data and time limitations.

TRAUMATIC BRAIN INJURY

In broad terms, a TBI is an injury to the head or brain caused by externally inflicted trauma. DoD defines TBI as a "traumatically induced structural injury and/or physiological disruption of brain functions as a result of an external force." TBI may be caused by a bump, blow, or jolt to the head, by acceleration or deceleration forces without impact, or by penetration to the head that disrupts the normal function of the brain (CDC 2011b; Katz 1997; VA/DoD 2009a). The events that lead to TBI vary by population. Among civilians, motor vehicle accidents are the leading cause of TBI-related deaths; among young children and older adults, falls are a major cause of TBI (CDC 2010); and among soldiers and veterans, the most common source of TBI is a blast (i.e., BINT), followed by falls, motor vehicle accidents, and lastly, assault (DVBIC 2009). Chapter 2 provides a more complete description of TBI, including mechanisms of injury and classification schemes, which may aid in short- and long-term prognosis.

Across time, incidence of TBI has risen among the military population as an all-volunteer force has been engaged in the longest war (OEF) in U.S. history, and service members are exposed to longer and more frequent deployments. While in-theater, service members are increasingly attacked by more explosive weaponry. Approximately 22 percent of wounded soldiers from OEF/OIF theaters experienced wounds to the head, face, or neck (Okie 2005). From 2000 to 2010, the number of military service members diagnosed with TBI has nearly tripled (DVBIC 2011). Mild TBI, also called

concussion, often goes underreported since period of unconsciousness may be negligible and medical attention may not be sought. Therefore the actual annual incidence of TBI is thought to be higher than currently estimated.

TBI is a major public health concern for civilians as well as members of the military. Each year, an estimated 1.7 million individuals in the United States sustain a TBI (CDC 2010). Of those, approximately 52,000 individuals die each year from their injuries. According to the U.S. Centers for Disease Control and Prevention (CDC), each year an estimated 124,626 people with TBI experience long-term impairment or disability from their injury (CDC 2011a).

TBI Classification Schemes

Head injuries have historically been classified using various clinical indexes that include pathoanatomical features, severity of injury, or the physical mechanisms of the injury (i.e., causative forces). Different classification systems may be used for clinical research, clinical care and management, or prevention. The classification systems most relevant to rehabilitation deal with severity as it relates to pace of recovery or expected degree of impairment. These include the Glasgow Coma Scale (GCS), posttraumatic amnesia (PTA), and others. Chapter 2 includes descriptions of these scales. One classification system is severity of the injury. TBI severity is generally graded in degree, from mild to moderate or severe. Severity can be graded in multiple ways, and each measure has different predictive utility, including determining mortality, morbidity, or long-term or functional outcomes. Determining severity is often based on the acute effects of the injury such as the individual's level of arousal or duration of amnesia; these are measured by GCS, duration of unconsciousness, and PTA. It is important to note that severity of injury does not always correspond with severity of one or more impairments.

The majority of TBIs are mild, consisting of a brief change in mental status or unconsciousness. Mild TBI is also referred to as a concussion. While most people fully recover from mild TBI, individuals may experience both short- and long-term effects. Moderate to severe TBIs are characterized by extended periods of unconsciousness or amnesia, among other effects. The distinction between moderate and severe injuries is not always clear; as such, individuals with moderate and severe injuries are often grouped for research purposes. Throughout the remainder of this report, the committee refers to more severe injuries as moderate-severe TBI. The more severe the injury, the more severe and persistent the cognitive deficits—though clinical measurements do not always concur. Severity measures graded during the acute phase sometimes reflect variance due to medications used during resuscitation, substance use, and communication

issues. However, the relationship between clinical severity measures (e.g., GCS, LOC, and PTA) and various types of outcome measures (e.g., neuropsychological or functional disability) has been well established (Cifu et al. 1997; Dikmen et al. 2003; Sherer et al. 2002; Temkin et al. 2003). The utility of these measures depends on how long after the injury a patient is evaluated. Measures obtained later in time are generally better predictors of long-term outcomes; specifically, duration of PTA is more predictive than duration of LOC, which is more predictive than GCS at the time of injury (Katz and Alexander 1994).

Consequences of TBI

The consequences of TBI include short- and long-term effects which likely impact the individual's family or primary caregiver. These may include disruptions to everyday life and work, changes in family and social functioning, and potentially burdensome financial costs. Recovering from TBI, therefore, may be a slow, long, and painful process for individuals and their families, requiring unique and specific medical, vocational, and rehabilitative therapy (Sayer et al. 2008).

The biological and structural impairments caused by TBI are far reaching and include physical, emotional, and cognitive impairments (Cernak and Noble-Haeusslein 2010). Cognitive impairments resulting from TBI can affect multiple domains, including attention, language and communication, memory, visuospatial, and executive function.[1] Cognitive impairments may limit daily activities (Temkin et al. 2009; Wise et al. 2010) and restrict participation in their community (Hoffman et al. 2007), employment, recreation, and social relationships (Temkin et al. 2009). The extent of disability from cognitive impairment is shaped by personal factors, such as age and cognitive reserve (Green et al. 2008), and environmental factors, such as family support (Sady et al. 2010). Chapter 3 provides a more in-depth description of the factors that may affect recovery and outcome.

TREATMENT

Determining the appropriate method and timing of treatment for an individual with TBI depends on a number of factors, including severity of injury, stage in recovery, and premorbid, comorbid, and environmental conditions, unique to every individual. The focus of treatment changes as a patient progresses from the acute, immediate phase after injury to more

[1] The term "executive function" represents a set of integrated cognitive processes necessary to perform or accomplish everyday life activities. Chapter 8 provides a detailed description of these cognitive processes.

chronic, long-term stages of recovery. In the acute phase, treatment may primarily focus on increasing the patient's chances of survival while reducing the long-term impact of the sustained injury or injuries (Meyer et al. 2010). Though effects of TBI often coincide shortly after injury, long-lasting effects of TBI do not always appear immediately after injury; likewise, the acute-stage impairments may recover with or without treatment and rehabilitation (Lovell et al. 2003). (Also known as spontaneous recovery, this type of recovery can occur at any time and is difficult to predict or control for in research.) In the chronic stage of recovery, the goals of rehabilitation are functional recovery of long-lasting physical, cognitive, and emotional impairments.

Cognitive Rehabilitation Therapy

CRT is a collection of treatments, generally tailored to an individual depending on the pattern of the impairments and activity limitations, related disorders (e.g., preexisting conditions or comorbidities), and the presence of a family or social support system. The modern practice of CRT began in the late 1970s, and evolved as a means to treat patients with acquired brain injuries, including those due to stroke, infection, multiple sclerosis or traumatic injury. A more complete description and the state of practice and providers of CRT are discussed in Chapters 4 and 5, respectively.

Some forms of CRT are directed toward impairments in specific cognitive processes such as attention or memory. Within these focused treatments, there are two roughly distinguished approaches: (1) restorative approaches that seek to enhance the overall operation of a cognitive system with the goal of improving performance of a wide range of activities that depend on that system, and (2) compensatory approaches that seek to provide internal mental strategies (e.g., mnemonics) or external devices or aides (e.g., memory notebooks) to support activity performance despite the presence of a cognitive impairment. In addition, a number of different treatment components may be combined into a comprehensive CRT treatment program, often referred to as comprehensive, holistic, or multi-modal CRT. Such approaches are more likely to be used for patients with multiple cognitive or behavioral impairments and may include a combination of focused approaches as above, coupled with psychotherapy, pharmacotherapy, behavior modification, occupational therapy, vocational rehabilitation, and other therapies (e.g., nutrition, art or music therapy, acupuncture).

CRT is offered in a wide range of settings, including rehabilitation hospitals, community-care centers, and individuals' homes and workplaces. Due to the range of services offered, CRT providers also vary widely. They represent a number of fields and professions including rehabilitation medicine, nursing, physical therapy, speech-language pathology, occupational

therapy, psychology, psychiatry, neuropharmacology, neuropsychology, and vocational rehabilitation. Moreover, members of these disciplines may deliver services indistinguishable from CRT under the disciplinary headings of "physical therapy," "occupational therapy," or "counseling," such that the correspondence between treatment *label* and *contents* is imprecise. While there has been some movement to standardize CRT, wide variations between the expectations of practitioners within different professions still exist, reflecting the fact that the respective accreditation organizations for these professions separately determine the educational and licensing requirements for these practitioners.

EVALUATION OF THE EVIDENCE

The IOM committee iteratively developed a protocol to address the following questions:

- *Do cognitive rehabilitation interventions improve function and reduce cognitive deficits in adults with mild, or moderate to severe TBI?*
- *Are any cognitive rehabilitation interventions associated with risk for adverse events or harm?*
- *Are cognitive rehabilitation interventions delivered through telehealth technology proven safe and efficacious?*

Methods

The committee reviewed published systematic reviews (Cicerone et al. 2000, 2005, 2011; ECRI 2009; Kennedy et al. 2008) and worked with a research librarian to develop search strategies to identify pertinent evidence. The strategies included searches in the following electronic bibliographic databases: Medline, EMBase, PsycInfo, ERIC, and Cochrane (e.g., Cochrane DB of Systematic Reviews, Database of Reviews of Effects [DARE] and Cochrane Central Register of Controlled Trials). Strategy parameters included limiting the search to human subjects, the English language, and results published between January 1991 and April 2011. The time period was chosen to include articles prior to Operation Desert Storm, which began in 1991. Setting time parameters allowed for the evaluation of the most recent research of relevance, acknowledging that more recent studies build on the evidence base created by older literature. The committee also culled references from previously published systematic reviews (Cicerone et al. 2000, 2005, 2011; ECRI 2009; Kennedy et al. 2008) to identify studies meeting selection criteria including any such studies published prior to 1991. Per its charge, the committee considered CRT for TBI across all severities (mild

and moderate-severe) and across all stages of recovery (acute, subacute, and chronic). The searches limited the scope of terms to traumatic brain injury, and did not consider other forms of acquired brain injury, such as those due to stroke, ischemia, infection, or malignancy. Similarly, the committee did not review literature on the effects of CRT for non-TBI cognitive disorders or injuries, such as schizophrenia, dementia, or learning disabilities. Chapter 6 provides a complete description of the committee's methods for selecting relevant evidence.

The committee categorized CRT interventions as either (1) modular strategies aimed at attention, language and communication, memory, visuospatial deficits, or executive function, or (2) multi-modal/comprehensive strategies. The intent of the therapy was categorized as restorative or compensatory and the goals and setting of therapy as decontextualized or contextualized. Compensatory strategies that targeted brain function but either did or did not involve changes to the environment were categorized as external or internal, respectively. These categorizations provided useful ways to dissect the literature and analyze findings across studies.

FINDINGS

The committee identified 90 studies that met selection criteria. These studies signal there is benefit from some forms of CRT for TBI. However, the evidence for the therapeutic value of CRT is variable across domains and is currently insufficient overall to provide definitive guidance for the development of clinical best practice, particularly with respect to selecting the most effective treatment(s) for a particular patient.

The committee found the insufficiency of the evidence was due to a number of identified limitations in the research designs, commonly seen among studies evaluating rehabilitation strategies, including the heterogeneity and lack of operational definitions of different forms of CRT; small sample sizes; the variety of premorbid conditions, comorbidities, and environmental factors that may moderate the value of a given form of CRT across patients; and the range of outcomes that may be targeted. Some of the studies did not identify injury severity or recovery phase for included participants, or there was a lack of uniformity across studies in defining these criteria. Another limitation is that objective measures sensitive to the cognitive complaints of patients with mild TBI are lacking in many instances and the use of subjective self-report measures as an alternative is problematic when studying treatments that cannot be blinded. Also, studies of subacute treatments require relatively large samples because the ability to gauge the impact of a treatment regimen in individual patients is diminished in the context of rapid and variable natural recovery. Thus, in practice clinicians may defer substantial resource investment in CRT to

later stages of TBI when it becomes clear which problems and impairments will persist long term.

The committee focused on studies that used one or several forms of CRT to ameliorate the effects of TBI, and evaluated the outcomes of these studies to determine the short-term, long-term, or patient-centered (i.e., real-world functioning) outcomes, when reported, of the therapies. To determine efficacy, the committee relied on studies that compared the primary CRT treatment to either no treatment or a non-CRT treatment. To determine effectiveness, the committee evaluated studies comparing CRT treatment to another form of CRT. In other words, varying comparators were not considered more or less useful, only that they answer different questions about the value of CRT for TBI.

In an interactive and collaborative process, the committee graded the overall body of evidence for each CRT category (by domain, TBI severity, and recovery phase [for example, CRT interventions for attention deficits in moderate-severe TBI patients in the chronic phase of recovery]). To draw conclusions about treatment efficacy or effectiveness, the committee qualitatively assessed the strength of individual studies, as well as the consistency of treatment effect among studies. The strength of each study was based on an iterative quality assessment, considering study design, size of the sample, reported characteristics of the sample (e.g., injury severity) and treatment (e.g., dosage, frequency, and timing), control for potentially confounding factors, magnitude of the treatment effect, statistical significance of the findings, and the length of follow-up. The committee gave more weight to controlled designs than uncontrolled (e.g., results of RCTs were given more weight than results from pre-post single group designs). Conclusions were not based solely on findings from uncontrolled studies, however the committee included pre-post single group designs and single subject, multiple baseline experiments in the review because uncontrolled studies may include useful information about nascent interventions or lend support to a controlled design with similar results. Where evidence was informative, the committee specifically identifies the treatment mode and cites the one or more studies that led to its conclusion. Box S-2 provides the description of evidence grades used to judge the sufficiency of the evidence. It is important to note that evidence ruled "limited" does not mean the intervention was inadequate; it may simply mean a better-designed or -executed study is necessary to show meaningful short- or long-term treatment effect. In reviewing the evidence regarding the efficacy and effectiveness of CRT, the committee found no studies addressing cognitive deficits in the acute phase of recovery following TBI, few studies addressing cognitive treatment for individuals with mild injuries—of those, only in the chronic phase—and few studies addressing treatment of those with moderate to severe injuries in the subacute phase. The committee did not identify any

BOX S-2
Evidence Grades

- **None or not informative (0):** No evidence because the intervention has not been studied or uninformative evidence because of null results from flawed or otherwise limited studies.
- **Limited (+):** Interpretable result from a single study or mixed results from two or more studies.
- **Modest (++):** Two or more studies reporting interpretable, informative, and largely similar result(s).
- **Strong (+++):** Reproducible, consistent, and decisive findings from two or more independent studies characterized by the following: (1) replication, reflected by the number of studies in the same direction (at least two studies); (2) statistical power and scope of studies (N size of the study and single or multisite); and (3) quality of the study design to measure appropriate endpoints (to evaluate efficacy and safety) and minimize bias and confounding.

relevant literature for treatment of visuospatial perception deficits, which are more common after stroke than TBI. Table S-1 summarizes the committee's conclusions for CRT, reflected in Chapters 7 through 11 in narrative form following detailed descriptions of individual studies.

In its conclusions, the committee separated evidence grades by cognitive domain and multi-modal/comprehensive CRT, further subdividing by reported injury severity, recovery phase, and the treatment approach (i.e., restorative or compensatory). Evidence grades were based on the breadth of literature assessed for each cognitive domain and multimodal/comprehensive CRT; the table does not reflect the grades for individual studies.

Telehealth Technology

The committee found that a small evidence base demonstrates that telehealth technologies, including the telephone and two-way messaging, are feasible means of providing at least part of CRT for some patients. No studies evaluated the use of telemedicine, defined by the Centers for Medicare & Medicaid Services as two-way audio and video interactive communication. Overall evidence is insufficient to clearly establish whether telehealth technology delivery modes are more or less effective or more or less safe than other means of delivering cognitive rehabilitation. However, when combined as part of a broader CRT program, telehealth technologies, including telephone calls, can contribute to outpatient treatment programs

TABLE S-1 Conclusions by Cognitive Domain and Multi-Modal/Comprehensive CRT

Domain	Attention		Executive Function		Language and Social Communication	Memory					Multi-Modal/ Comprehensive CRT		
Subdomain			Awareness	Non-Awareness									
TBI Severity	Moderate-Severe		Moderate-Severe		Moderate-Severe	Mild	Moderate-Severe				Moderate-Severe	Mild	Moderate-Severe
Recovery Phase	Subacute	Chronic	Chronic		Chronic	Chronic					Subacute	Chronic	
Approach	R	R	R	R/IC/EC	R	IC	EC	R	IC	EC	M	M	M
Patient-Centered Outcomes	0	+	0	+	0	0	N/A	0	+	++	0	+	0
Long-Term Treatment Effect	+	0	0	0	+	+	N/A	0	+	N/A	0	+	0
Immediate Treatment Benefit	+	+	+	+	++	+	N/A	0	++	++	0	+	0

NOTES: EC = external compensatory strategy; IC = internal compensatory strategy; M = mixture of treatment approaches; R = restorative strategy.

with comparable results to inpatient programs for selected individuals. Chapter 12 provides details on relevant studies and the committee's assessments leading to these conclusions.

Adverse Events or Harm

The committee found that evidence indicating any potential adverse event and risk for harm associated with CRT is scant. Although the limited available evidence suggests no great concern regarding risk for harm, future studies that evaluate cognitive rehabilitation should include and report measures that assess such risks. Chapter 13 provides details on relevant studies and the committee's assessments leading to these conclusions.

RECOMMENDATIONS

Considering the dearth of conclusive evidence identified to date, the committee recommends an investment in research to further develop CRT. As reflected in Table S-1, the evidence provides limited, and in some cases modest, support for the efficacy of CRT interventions. However, the limitations of the evidence do not rule out meaningful benefit. The committee defined *limited* evidence as "Interpretable results from a single study or mixed results from two or more studies" and *modest* evidence as "Two or more studies reporting interpretable, informative, and largely similar results" (see Box 6-2 for all evidence grades and definitions). **The committee emphasizes that conclusions based on the limited evidence regarding the effectiveness of CRT does not indicate that the effectiveness of CRT treatments are "limited"; these the limitations of the evidence do not rule out meaningful benefit.** ***In fact, the committee supports the ongoing clinical application of CRT interventions for individuals with cognitive and behavioral deficits due to TBI.*** One way policy could reflect the provision of CRT is to facilitate the application of best-supported techniques in TBI patients in the chronic phase (where natural recovery is less of a confound), with the proviso that objectively measurable functional goals are articulated and tracked and that treatment continues only so long as gains are noted.

To acquire more specific, meaningful results from future research the committee has laid out a comprehensive research agenda to overcome challenges in determining efficacy and effectiveness. These recommendations are therefore possible because the evidence review signals some promise. However, to improve future evaluations of efficacy and effectiveness of CRT for TBI, larger sample sizes and volume of data are required, particu-

larly to answer questions about which patients benefit most from which treatment(s). This requires more extensive funding of experimental trials and a commitment to mining clinical practice data in the most rigorous way possible. For such approaches to be most informative, the variables that characterize patient heterogeneity, the outcomes that are used to measure impact of treatment, and the treatments themselves need to be defined and standardized. In addition, more rigorous review of potential harm or adverse events related to specific CRT treatments is necessary.

Nascent efforts at standardization are underway across multiple civilian and military funding agencies. These efforts should take place in collaboration. The National Institutes of Health (NIH) common data element (CDE) initiative, a National Institute on Disability and Rehabilitation Research (NIDRR)–supported center on treatment definition, and several practice-based evidence studies are helping to better characterize TBI patients, treatments, and relevant outcomes. Practice-based evidence studies include the Congressionally Mandated Longitudinal Study on TBI, DVBIC Study on Cognitive Rehabilitation Effectiveness for Mild TBI (SCORE!), Millennium, and TBI Model Systems. These cohorts involve collaborative efforts between DoD and the VA via the Defense and Veterans Brain Injury Center (DVBIC). The committee recognizes the ongoing emphasis from both government agencies to enhance collaboration for TBI and psychological health of service members and veterans through the VA/DoD Joint Executive Council Strategic Plan to integrate health care services (VA/DoD 2009b). This collaboration is especially important in evaluating and maintaining transitions in care and long-term treatment for injured soldiers as they move out of the MHS and into the VA's health care system, the Veterans Health System.

Because CRT is not a single therapy, questions of efficacy and effectiveness need to be answered for each cognitive domain and by treatment approach. Nevertheless, within a specific cognitive domain, there must be sufficient research and replication for conclusions to be drawn. Standard definitions for intervention type, content, and key ingredients will be critical to developing evidence-based practice standards. The documentation of interventions in practice and more frequent use of manual-based interventions in research will help validate measures of treatment fidelity. For example, while there is evidence from controlled trials that internal memory strategies are useful for improving recall on decontextulized, standard tests of memory, there is limited evidence that these benefits translate into meaningful changes in patients' everyday memory either for specific tasks/activities or for avoiding memory failures. Therefore, an increased emphasis on functional patient-centered outcomes would allow for a more meaningful translation from cognitive domain to patient functioning.

The committee recommends DoD undertake the following:

Recommendation 14-1: The DoD should work with other rehabilitation research and funding organizations to

1. **Identify and select uniform data elements characterizing TBI patients including cognitive impairments (to supplement measures of injury severity) and key premorbid conditions, comorbidities, and environmental factors that may influence recovery and treatment response;**
2. **Identify and select uniform TBI outcome measures, including standard measures of cognitive and global/functional outcomes; and**
3. **Create a plan of action to**
   a. **Identify currently feasible methods of measuring the delivery of CRT interventions;**
   b. **Advance the development of a taxonomy for CRT interventions that can be used for this purpose in the future; and**
   c. **Advance the operationalization of promising CRT approaches in the form of treatment manuals and associated adherence measures.**

Recommendation 14-2: The DoD should convene a conference to achieve consensus among a multi-agency (e.g., VA, NIH, and NIDRR), multi-disciplinary team of clinicians and researchers to finalize the selection of patient characteristic and outcome variables to be included in experimental and observational CRT research, and to plan a strategy to advance the common definition and operationalization of CRT interventions.

Recommendation 14-3: The DoD should incorporate the selected measures of patient characteristics, outcomes, and defined CRT interventions into ongoing studies (e.g., DVBIC: SCORE!, Millennium, TBI Model System) and develop a comprehensive registry encompassing the existing cohorts and de-identified MHS medical records to allow ongoing evaluation of CRT interventions.

Recommendation 14-4: Using these data sources, the DoD should plan to prospectively evaluate the impact of any policy changes related to CRT delivery and payment within the MHS with respect to outcomes and cost-effectiveness.

Recommendation 14-5: The DoD should collaborate with other research and funding organizations to foster all phases of research and

development of CRT treatments for TBI, from pilot phase, to early efficacy research (safety, dose, duration and frequency of exposure, and durability), to large-scale randomized clinical trials, and ultimately, effectiveness and comparative effectiveness studies.

CONCLUSION

The current evidence for CRT does not point a clear path to *conclusive findings* regarding CRT efficacy or effectiveness in the treatment of TBI-related deficits. The committee thoughtfully considered the challenges it faced throughout the study process. The committee's recommendations aim to aid the Department of Defense in addressing a significant problem: Members of the military (and civilians) experience high rates of TBI, and TBI often causes significant cognitive, physical, or psychosocial deficits requiring rehabilitation. In light of the lack of conclusive evidence, either because interventions or approaches are new and still being studied, or study designs were flawed, the committee has identified these recommendations as a way forward for the Military Health System.

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PART I: BACKGROUND

1

Introduction

Traumatic brain injury (TBI) affects an estimated 10 million people worldwide and causes significant physical, emotional, and cognitive disabilities among those affected, including soldiers, veterans, and civilians. Conflicts in Iraq (Operation Iraqi Freedom [OIF]) and Afghanistan (Operation Enduring Freedom [OEF]) have put members of the U.S. military at high risk for TBI, largely due to repeated and prolonged deployments, increasing injuries to the head and neck, and attacks with improvised explosive devices (IEDs) (Taber et al. 2006; Terrio et al. 2009). The high rate of TBI resulting from current combat operations directly impacts the health and safety of service members and their families and subsequently the level of troop readiness and retention. In addition, advances in life-saving measures have increased survival from TBI, leading to more individuals living with the consequences of these injuries. These advances include improved protective equipment, such as helmets and body armor; more responsive emergency care and improved medical evacuation systems; and innovations in treatment and care of TBI, such as better understanding of the effects of trauma and more sensitive and specific capabilities in diagnosing acute injury (Martin et al. 2008). Moreover, individuals living with TBI in military and civilian populations often require treatment for their condition. One form of treatment for TBI-related deficits is cognitive rehabilitation therapy (CRT), a systematic approach to functional recovery of cognitive or behavioral deficits and participation in related activities; however, the effectiveness of this treatment remains uncertain. Recognizing that TBI is the signature war wound of OIF/OEF and that there is a responsibility to care for individuals who serve in the military, the Department of Defense (DoD)

saw the need to ensure personnel have adequate treatment for wounds sustained in relation to military service. Therefore, DoD asked the Institute of Medicine (IOM) to evaluate the efficacy and effectiveness of CRT for TBI to guide its use and coverage in the Military Health System (MHS).

SCOPE OF THE REPORT

To complete its task, the IOM formed an ad hoc committee of experts from a range of disciplines to conduct a 15-month study aimed at evaluating the efficacy of CRT for TBI. The Committee on Cognitive Rehabilitation Therapy for Traumatic Brain Injury (hereafter referred to as "the committee") comprised members with expertise in epidemiology and study design, disability and long-term care, neurology, neuropharmacology, neuropsychology, nursing, psychiatry, psychology, rehabilitation medicine, and speech-language pathology. To address its Statement of Task (see Box 1-1), the committee developed a workplan and strategy for reviewing the evidence, including a comprehensive review of the literature on CRT for TBI. In addition to reviewing the literature, the committee conducted an assessment of recently completed or ongoing clinical trials; invited input from experts in the fields of cognitive rehabilitation research and practice, investigators of major research studies in both military- and civilian-related TBI, and advocates for the role of families and communities in providing ongoing support to injured members of the military and veterans; and received statements from stakeholders from various organizations and members of the public.

After reviewing the Statement of Task and meeting with a representative from the Department of Defense to clarify its intent, the committee interpreted its charge as assessing the state of the evidence. The committee acknowledges the goal of evidence assessments is to inform policy, upon which clinical practice guidelines are developed. Those at the Department of Defense are the only ones in position to make policy judgments for the Military Health System. After extensive deliberation, the committee determined it was beyond its charge to interpret its assessment of the evidence with respect to policy recommendations or clinical practice guidelines.

Over the course of the study, the committee met six times, engaged the public through two public workshops and participated in a number of ongoing activities organized by working groups. The committee did not complete an independent assessment of the treatment of TBI by cognitive rehabilitation within the MHS (subtask 5 of the Statement of Task). To accomplish this subtask, the committee determined it would need a substantial amount of data and submitted relevant questions as well as a request for data to the Department of Defense. The committee did not receive answers or data in response to the specific request. Due to constrained resources, including a lack of available data and time constraints, the committee was

BOX 1-1
Statement of Task

A consensus committee shall design and perform a methodology to review, synthesize, and assess the salient literature and determine if there exists sufficient evidence for effective treatment using cognitive rehabilitation therapy (CRT) for three categories of traumatic brain injury (TBI) severity—mild, moderate, and severe—and will also consider the evidence across three phases of recovery—acute, subacute, and chronic. In assessing CRT treatment efficacy, the committee will consider comparison groups such as no treatment, sham treatment, or other non-pharmacological treatment. The committee will determine the effects of specific CRT treatment on improving (1) attention, (2) language and communication, (3) memory, (4) visuospatial perception, and (5) executive function (e.g., problem solving and awareness). The committee will also evaluate the use of multi-modal CRT in improving cognitive function as well as the available scientific evidence on the safety and efficacy of CRT when applied using telehealth technology devices. The committee will further evaluate evidence relating CRT's effectiveness on the family and family training. The goal of this evaluation is to identify specific CRT interventions with sufficient evidence-base to support their widespread use in the MHS, including coverage through the TRICARE benefit.

The committee shall gather and analyze data and information that addresses

1. A comprehensive literature review of studies conducted, including but not limited to studies conducted on MHS or VA wounded warriors;
2. An assessment of current evidence supporting the effectiveness of specific CRT interventions in specific deficits associated with moderate and severe TBI;
3. An assessment of current evidence supporting the effectiveness of specific CRT interventions in specific deficits associated with mild TBI;
4. An assessment of (1) the state of practice of CRT and (2) whether requirements for training, education and experience for providers outside the MHS direct-care system to deliver the identified evidence-based interventions are sufficient to ensure reasonable, consistent quality of care across the United States; and
5. An independent assessment of the treatment of traumatic brain injury by cognitive rehabilitation therapy within the MHS if time or resources permit.

not able to complete the assessment. In addition, early in the course of the study, the Department of Defense indicated that completing this subtask was of lesser importance than other requirements in the Statement of Task.

TRAUMATIC BRAIN INJURY

In broad terms, TBI is an injury to the head or brain caused by externally inflicted trauma. DoD defines TBI as a "traumatically induced structural injury and/or physiological disruption of brain function as a result

of an external force" (see Box 1-2). TBI may be caused by a bump, blow, or jolt to the head, by acceleration or deceleration without impact, or by penetration to the head that disrupts the normal function of the brain (CDC 2010; Katz 1997; VA/DoD 2009). The events that lead to the trauma vary by population. Among civilians, motor vehicle accidents are the leading cause of TBI-related deaths; among young children and older adults, falls are a major cause of TBI (CDC 2010); and among soldiers and veterans, the most common source of TBI is a blast, followed by falls, motor vehicle accidents, and assault (DVBIC 2011).

In recent years, incidence of TBI has risen among the military population, as an all-volunteer force has been engaged in the longest war in U.S. history (OEF) and service members are exposed to longer and more frequent deployments. While in-theater, service members are increasingly attacked with more explosive weaponry. In 1991, during Operation Desert Storm, commonly referred to as the "first Gulf War," approximately 20

BOX 1-2
Department of Defense Definition of Traumatic Brain Injury

A traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:

- Any period of loss of or a decreased level of consciousness
- Any loss of memory for events immediately before or after the injury (i.e., posttraumatic amnesia [PTA])
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.)
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient
- Intracranial lesion

External forces may include any of the following events:

- Head being struck by an object
- Head striking an object
- Brain undergoing an acceleration/deceleration movement without direct external trauma to the head
- Foreign body penetrating the brain
- Forces generated from events such as blast or explosion, or other force yet to be defined

SOURCE: DoD 2007.

percent of treated wounds were head injuries (Carey 1996; Leedham and Blood 1992). Approximately 22 percent of wounded soldiers from OEF/OIF theaters have experienced wounds to the head, face, or neck (Okie 2005). From 2000 to 2010, the number of military service members diagnosed with TBI has nearly tripled (see Figure 1-1) (DVBIC 2011).

In 2000, 10,963 cases of TBI were diagnosed. Of these, 58 percent were mild, 38 percent were moderate, 2 percent were severe, 3 percent were penetrating, and the remainder not classifiable (< 1 percent). Chapter 2 provides information about the characteristics and definitions of mild, moderate, and severe TBI. In 2010, 30,703 TBIs were diagnosed, but a larger proportion were mild (81 percent) compared to 2000, followed by moderate (12 percent), severe (1 percent), penetrating (1 percent), and not classifiable (5 percent).

However, the actual annual incidence of TBI among service members is thought to be higher than currently estimated. Mild TBI, also called concussion, often goes underreported since recovery of consciousness is rapid and medical attention may not be sought. In addition, due to stigma associated with seeking medical treatment and appearing physically or psychologically vulnerable, or the desire to stay with their unit instead of leaving for treat-

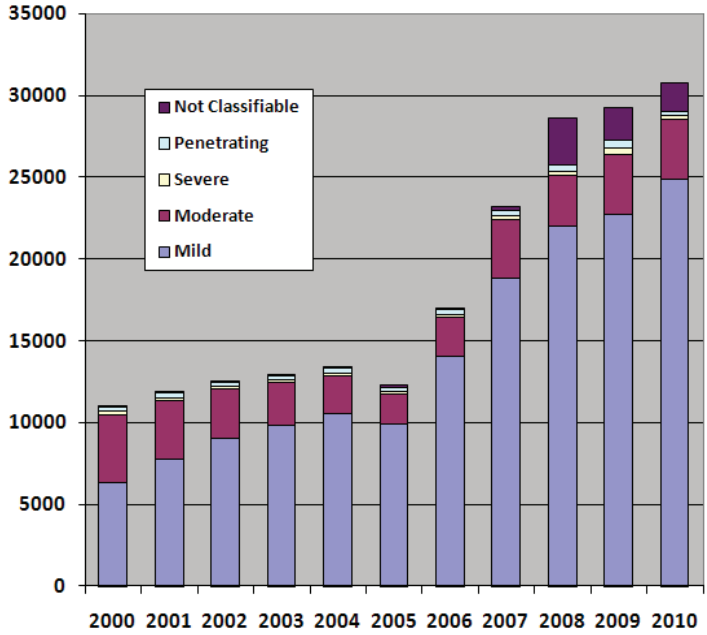

FIGURE 1-1 Number of U.S. service members with TBI, by severity.
DATA SOURCE: DVBIC 2011.

ment or medical discharge, service members who need treatment may be hesitant to report or seek care for mild TBI or related symptoms. Perhaps for this reason, much more is known about the effects of moderate to severe TBI than mild TBI.

TBI is a major public health concern for civilians as well as members of the military. Each year, an estimated 1.7 million individuals in the United States sustain a TBI and either receive care in an emergency department, are hospitalized, or die from their injuries (Faul et al. 2010). Of those, approximately 52,000 individuals die each year from their injuries. According to the U.S. Centers for Disease Control and Prevention (CDC), each year an estimated 124,626 people with TBI experience long-term impairment or disability from their injury (CDC 2011). Overall, 75 percent of all TBIs occur among men, with higher rates among men than women across age groups. Very young children (0–4 years of age), adolescents (15–19 years of age), and older adults (> 65 years of age) are more likely to sustain TBI than other age groups (CDC 2011).

CONSEQUENCES OF TBI

The consequences of TBI include short- and long-term effects, and often impact the individual's family or primary caregiver as well. These effects may include disruptions to everyday life and work, changes in family and social functioning, and potentially burdensome financial costs. Recovering from TBI may be a slow, long, and painful process for individuals and their families, requiring unique medical, vocational, and rehabilitative therapy (Sayer et al. 2009; VA/DoD 2009). Symptoms of mild TBI may include

- Disorientation,
- Diminished arousal or alertness,
- Headaches,
- Dizziness,
- Loss of balance,
- Ringing in the ears,
- Blurred vision,
- Nausea or vomiting,
- Irritability or other changes in behavior or mood,
- Sensitivity to light or noise,
- Sleep disturbances, and
- Difficulty with attention/memory and other cognitive problems.

Individuals with moderate-severe TBI may show similar symptoms, but may also experience seizures, an altered level of consciousness, cranial nerve abnormalities, and paralysis or loss of sensation. With any severity of TBI, acute and persistent symptoms can have a profound impact on the survivor.

Biological and structural changes caused by TBI are far reaching and may lead to physical, emotional, and cognitive impairments (Cernak and Noble-Haeusslein 2010). Cognitive impairments resulting from TBI can affect multiple domains, including attention, language and communication, memory, visuospatial perception, and executive function. Cognitive impairments may limit activities of daily living (Temkin et al. 2009; Wise et al. 2010) and restrict participation in community, employment, recreation, and social relationships (Temkin et al. 2009). The extent of disability from cognitive impairment is shaped by many personal factors, such as age and cognitive reserve (Green et al. 2008), and environmental factors, such as family support (Sady et al. 2010). Chapter 3 provides a more in-depth description of the factors that may affect recovery.

Following a disabling illness or injury such as TBI, activity and participation may be increased by reducing impairments, modifying the environment, or both. These goals are part of rehabilitation strategies, including CRT, as depicted in the framework proposed by the World Health Organization (WHO) International Classification of Functioning, Disability, and Health (ICF) (see Figure 1-2). The WHO-ICF framework recognizes impairments in *body structures and functions* (e.g., impaired memory) as a result of disease or injury, and limitations in *activities and participation*, i.e., the ability to carry out important daily activities (e.g., remembering weekly appointments) and the ability to participate in society (e.g., potential impact of the impairment on employment, home, school, or community). Importantly, activity and participation limitations result from an interaction between the person with impairment(s) and the physical and social environment. For example, an individual with TBI may have difficulty learning and remembering new information. With repeated training, she may be able learn some basic routines, such as writing appointments and

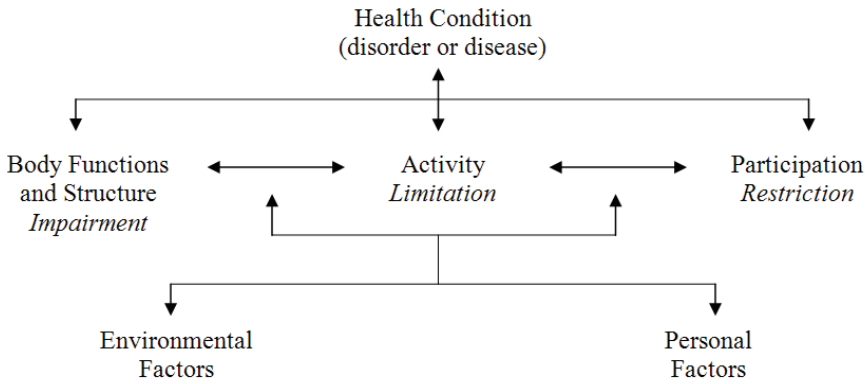

FIGURE 1-2 WHO-ICF Model of Disablement.
SOURCE: WHO 2001.

other important information down in her daily planner and consulting it frequently, allowing her to keep track of her schedule and other important tasks despite her memory impairment.

TREATMENT

Determining the appropriate method and timing of treatment for an individual with TBI depends on a number of factors, including severity of injury, stage in recovery, and factors unique to the individual. At any stage of recovery, treatment success can be moderated by a number of factors including time since injury, etiology, and age. Some long-term consequences of TBI, such as seizures or depression, may not appear immediately after injury; likewise, the acute impairments may recover with or without treatment and rehabilitation, also known as spontaneous or natural recovery. Natural recovery typically occurs more quickly soon after injury and decelerates gradually over time, but the degree and duration of natural recovery is highly variable across individuals (Lovell et al. 2003). In general, the focus of treatment changes as a patient progresses from the acute/immediate phase after injury to more chronic stages of recovery. In the acute phase, treatment may primarily focus on increasing the patient's survival while preventing or minimizing long-term consequences of injury and facilitating recovery (Meyer et al. 2010).

Once medically stable, those with more severe impairments may receive hospital or outpatient rehabilitation services typically focusing on overall return of activity and independence, as well as near-term necessities such as performing daily activities and mobility. As natural recovery slows in the subacute and chronic periods, rehabilitation typically narrows its focus to the areas likely to be persistent problems and to the specific activities of importance to the individual. Rehabilitation treatment may include a mixture of pharmacologic and nonpharmacologic interventions. Nonpharmacologic treatments include, but are not limited to, physical therapy, occupational therapy, speech-language therapy, and psychotherapy. Often, pharmacologic therapies supplement the overall rehabilitation program and aim to reduce specific impairments or effects of the injury. While no approved prescribed drug exists to treat the effects of TBI, many agents can be used to aid patients in their recovery. For example, patients who experience seizures may benefit from anticonvulsants (e.g., phenytoin, valproate), which allow patients to focus on recovery from existing impairments, unimpeded by intermittent and unpredictable seizures. Comorbid conditions such as pain, fatigue, or posttraumatic stress disorder (PTSD) may present additional challenges and may also require pharmacologic intervention.

An earlier IOM report, *Gulf War and Health, Volume 7* (IOM 2009), identified important causal and associative effects of both mild and moder-

ate to severe TBI on short- and long-term outcomes following injury. However, neither this report nor a recent IOM report on nutrients to support recovery following TBI, *Nutrition and Traumatic Brain Injury: Improving Acute and Subacute Health Outcomes in Military Personnel* (IOM 2011), examined the role of rehabilitation on recovery and outcome following mild or moderate to severe TBI.

Cognitive Rehabilitation Therapy

The goal of CRT is to increase individuals' ability to process and interpret information, thereby enhancing their capacity to function in everyday life. Treating individuals with cognitive deficits began early in the 19th century, as medical advancements allowed better understanding of cognitive processes and led to more individuals surviving previously life-ending events. The late 1970s ushered in the modern era of CRT, for the treatment of patients with acquired brain injuries, including those due to stroke, infection, multiple sclerosis, or traumatic injury. The therapy is a collection of treatments, generally tailored to individuals depending on the pattern of their impairments and activity limitations, related disorders (e.g., preexisting conditions or comorbidities), and the presence of a family or social support system. These factors all contribute to how, and perhaps how effectively, the treatment can be applied. CRT focuses on restoring impaired functions or compensating for residual impairments in areas such as attention, executive function, memory, and language or social communication, as well as the application or use of these functions during activities. Treatment may also include related comorbidities or secondary results of TBI. The application and practice of CRT varies in a number of ways, as described in Chapters 4 and 5.

CRT is offered in a wide array of settings, including rehabilitation hospitals, community-care centers, and individuals' homes and workplaces. Due to the range of services offered, providers of cognitive rehabilitation also vary widely. They represent a number of fields and professions including rehabilitation medicine, nursing, physical therapy, speech-language pathology, occupational therapy, psychology, psychiatry, neuropharmacology, neuropsychology, and vocational rehabilitation. Moreover, members of these disciplines may deliver CRT services under disciplinary headings such as "physical therapy," "occupational therapy," or "counseling," such that the correspondence between a treatment's *label* and its *contents* is imprecise. While there has been some movement to standardize CRT, wide variations between expectations of practitioners from different professions still exist, reflecting how accreditation organizations separately determine educational and licensing requirements for practitioners within individual professions.

Due to the individualization of CRT, the appropriate timing and duration of the treatment is not known. These factors depend on the individual, severity of injury, and response to treatment, as well as health insurance coverage. The therapy may evolve throughout the course of treatment in response to feedback from the patient and caregivers. Although individualization is clinically useful, it presents challenges to researchers who attempt to study standardized CRT practices and discover what is effective, what could be improved, and what could be harmful to patients.

Assessments of the efficacy of CRT for TBI to date have utilized various methodologies and yielded mixed results. Systematic reviews published in peer-reviewed journals have generally found evidence for the benefits of CRT (Cicerone et al. 2000, 2005, 2011; Kennedy et al. 2008; Rohling et al. 2009). According to Cicerone et al. (2011), there is substantial evidence to support CRT for TBI, including interventions for attention, memory, language and communication, executive function, and for comprehensive (i.e., multi-modal or holistic) neuropsychological rehabilitation. A recent health care "technology assessment" (i.e., systematic review) commissioned by DoD found evidence of benefit from specific aspects of CRT, but generally found a small evidence base for the therapy, leading to inconclusive results about CRT's efficacy (ECRI 2009). Ongoing needs for TBI survivors, especially service members and veterans cared for within the MHS, combined with inconsistent findings in prior evaluations of CRT for TBI, necessitated the current assessment. The literature evaluation is described in Part II of this report.

THE MILITARY HEALTH SYSTEM

The MHS is the agency of the Department of Defense that provides health care for uniformed service members, military retirees, and their families. The VA health care system, the Veterans Health Administration (VHA), is separate from the MHS; however, these two organizations share many common goals and characteristics.[1] TRICARE is the MHS health care program for active duty personnel, military retirees, and family members of the seven uniformed services: the Army, the Air Force, the Navy, the Marine Corps, the Coast Guard, the Commissioned Corps of the Public

[1] Individuals who formerly served in the military are "veterans." Individuals who serve in the military for 20 years or more are "military retirees"; in some cases, those who are medically discharged from service prior to 20 years may qualify as military retirees. It is important to note that all former military members are veterans, but not all are military retirees. Military retirees and their dependents may access benefits through TRICARE, either through the direct care or purchased care systems. The military retiree may also access care through the VHA. Veterans who are not military retirees may be eligible for care through the VHA. In certain circumstances, the VHA may send a veteran for health care at an MHS or civilian facility (OPM 2009).

Health Service, and the Commissioned Corps of the National Oceanic and Atmospheric Administration, as well as the National Guard and Reserves. TRICARE is a single-payer system, encompassing direct care services at military treatment facilities and purchased care from civilian professional providers and health care services, suppliers, and facilities. In 2010, TRICARE served 9.4 million beneficiaries. Of these, 20 percent were active duty members of the various uniformed services, 26 percent were family members of an active duty member, and 54 percent were retirees and their families (TRICARE 2010).

The effects of TBI are felt within each branch of the service and throughout both DoD and the VA. In 1992, DoD and the VA collaborated to establish the Defense and Veterans Brain Injury Center (DVBIC) to address the increasing incidence of TBI (DVBIC 2009). The DVBIC is specifically designed to provide services for active duty military, their beneficiaries, and veterans with TBI. It is a multi-site network of services, including clinical care, research initiatives, and educational programs. Since 2008, the DVBIC has also provided TBI surveillance and a registry of TBI survivors, as well as predeployment neuropsychological testing to service members. Ongoing and future research on acute and chronic recovery from TBI, including CRT, is facilitated through the DVBIC. Appendix C provides an overview of future and ongoing CRT clinical trials, including those sponsored through the DVBIC.

Current Coverage

Regarding the general subject of *rehabilitation*, TRICARE states coverage includes "any therapy for the purpose of improving, restoring, maintaining, or preventing deterioration of function. The treatment must be medically necessary and appropriate medical care. The rehabilitation therapy must be rendered by an authorized provider, necessary to the establishment of a safe and effective maintenance program in connection with a specific medical condition, provided at a skilled level and must not be custodial care or otherwise excluded from coverage (e.g., exercise or able to be provided at a non-skilled level)" (TRICARE 2010).

TRICARE does not state explicitly its coverage policy for CRT. In addition to coverage for rehabilitation generally, services such as speech, occupational, and physical therapy are provided; telemedicine is also covered under the policy. For *speech therapy*, TRICARE provides coverage when prescribed and provided or supervised by a physician to treat speech, language, and voice dysfunctions resulting from birth defects, disease, injury, hearing loss, and pervasive developmental disorders, with exclusions (e.g., TRICARE does not cover the following: disorders resulting from occupational or educational deficits, myofunctional or tongue thrust therapy,

videofluroscopy evaluation, maintenance therapy that does not require a skilled level after a therapy program has been designed, or special education services from a public educational agency to beneficiaries age 3 to 21). For *occupational therapy*, TRICARE covers therapy when prescribed and supervised by a physician to improve, restore, or maintain function, or to minimize or prevent deterioration of function. TRICARE covers *physical therapy* when prescribed by a physician and professionally administered to aid in the recovery from disease or injury by helping the patient attain greater self-sufficiency, mobility, and productivity through exercises and other modalities intended to improve muscle strength, joint motion, coordination, and endurance. Specific exclusions to physical and occupation therapy apply by region. In terms of *telemedicine*, TRICARE covers the use of interactive audio/video technology to provide clinical consultations and office visits when appropriate and medically necessary, including clinical consultations, office visits, and telemental health (e.g., individual psychotherapy, psychiatric diagnostic interview examination, and medication management).

According to a statement from TRICARE Management Activity, the organizing institution of TRICARE, CRT interventions for service members currently are available at medical treatment facilities through DoD's supplemental health care program and through VA programs. Under the supplemental health care program, active duty service members may receive care that is excluded under TRICARE's basic program if necessary to ensure adequate availability of health care services. DoD may also authorize reimbursements for CRT for service members or veterans under this supplemental program. However the therapy must be considered medically or psychologically necessary for the recovery of the injury and subsequent impairments for service members to receive these benefits.

CONCLUSION

TBI affects approximately 1.7 million people in the United States, and due to advanced lifesaving measures, more individuals are surviving their injuries and living with long-term disabilities. Among affected populations, members of the military and veterans, with their families, are impacted most (Faul et al. 2010). Given the rising burden of TBI and remaining questions regarding the efficacy of CRT, the goal of this report is to identify CRT interventions with sufficient evidence base to support widespread use in the MHS.

The remainder of the report is organized to inform the reader about unique aspects of TBI that may affect recovery; these aspects are described in relation to the injury (Chapter 2) and the specifics of the affected individual (Chapter 3). Chapter 4 describes the history and evolution of CRT,

including the current definitions endorsed by professional and research organizations; Chapter 5 describes the state of practice and the role of various providers. Chapter 6 details the committee's methodology for reviewing the literature and making assessments about the quality of studies, as well as the hierarchy of evidence grading the committee used to make judgments. Chapters 7 through 12 provide the summary analysis of the evidence by cognitive domain, multi-modal/comprehensive CRT, and the therapy's application through telehealth technologies. A discussion of possible adverse effects or harm is provided in Chapter 13. Chapter 14 discusses directions for research and clinical practice. The committee identified these directions throughout the report process, and many of the conclusions and recommendations in the final chapter aim to address the lack of methodological rigor among studies, while acknowledging the history of the therapy's development, the unique features of the injury being addressed, and how future research may strive to compensate for these many challenges.

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2

Traumatic Brain Injury

The multifaceted characteristics of traumatic brain injury (TBI) complicate the evaluation of therapeutic interventions, including rehabilitation. The intensity, direction, and duration of external forces that cause TBI, coupled with a range of factors specific to the individual and early medical management, affect the pattern and extent of damage and the degree of recovery (Maas et al. 2008). These combined factors may determine the type and effectiveness of the rehabilitation therapy. In this chapter, the pathophysiology of TBI, injury complications, and person-specific variables are discussed in relation to outcome. Chapter 3 addresses other factors related to recovery after TBI. These chapters provide the relevant background for interpreting the cognitive and neurobehavioral sequelae of TBI. Research indicates that TBI may manifest differently depending on the mechanism of injury. For example, blast-induced neurotrauma (BINT) shows significantly more changes in brain matter versus TBI caused by other forces. Because active duty members of the military and veterans have higher exposure to blasts than civilians, TBI incurred by military and veteran populations may determine different outcomes than non-blast-related TBI. However, civilians may be exposed to blasts due to terrorism, occupational hazards, or other acts of violence. The committee assumes civilian versus military populations respond similarly to TBI, unless otherwise noted.

TBI causes both direct, immediate physical damage and delayed, secondary changes that contribute to subsequent tissue impairment and related neuropsychiatric dysfunction. Injury may be focal or diffuse; due to closed impact or penetrating insults; and if severe, may include other complicating factors such as hemorrhage, hypoxia, reduced blood flow, or metabolic

alterations (Jeremitsky et al. 2003; Saatman et al. 2008). These early, acute events are highly relevant to long-term outcomes, as they can critically affect an individual's degree of disability and need for rehabilitation. The following chapter does not contain exhaustive descriptions of the many factors related to TBI. The reader may refer to *Gulf War and Health, Volume 7: Long-Term Consequences of Traumatic Brain Injury* (IOM 2009) for more in-depth discussion of TBI biology.

The response to injury and subsequent treatment varies by multiple factors unique to the affected individual, such as age, gender, genetics, cognitive reserve, polytrauma, multiple concussions from the same impact, and history of prior brain injury (Colantonio et al. 2008; Loane and Faden 2010; Perel et al. 2008). Such variability influences long-term functional outcomes, including cognitive processes. The ultimate degree of recovery likely reflects individual variability with regard to neuroplasticity, or the ability of undamaged brain regions or pathways to take over irreparably damaged cells or brain regions (Cramer et al. 2011). Although most mild injuries appear to recover completely within weeks to months after trauma, a small but not insignificant subset of mild TBIs cause longer-term symptoms, and these also may be associated with sustained or progressive neuroimaging abnormalities (Vannorsdall et al. 2010). Secondary injury processes may continue for months or years, particularly with moderate or severe injuries, which may lead to progressive long-term tissue loss (Greve and Zink 2009; Werner and Engelhard 2007). Thus, characteristics of the injury and the individual contribute to the heterogeneity of TBI, which has implications for treatment options.

CLASSIFICATION SCHEMES

Head injuries have historically been classified using various clinical indexes that include pathoanatomical features, severity of injury, or the physical mechanisms of the injury (i.e., causative forces). Different classification systems may be used for clinical research, clinical care and management, or prevention. Additional classification schemes include those that address secondary injury. The classification systems most relevant to rehabilitation help determine pace of recovery or expected degree of impairment. These systems include the Glasgow Coma Scale (GCS), posttraumatic amnesia (PTA), duration of loss of consciousness (LOC), and degree of altered consciousness.

Pathoanatomical Classification

Sometimes known as the "where and what" of TBI classification, pathoanatomical classification describes the location and the pathological

features (i.e., pathoanatomy) of tissue damage induced by the injury. Pathoanatomical features influence outcomes for individuals with brain injuries (Saatman et al. 2008) and indicate the likelihood of developing certain secondary problems (e.g., cerebral edema) (Saatman et al. 2008). Pathoanatomical classification may aid with prognosis (Saatman et al. 2008), which helps determine the appropriate timing and type of rehabilitation. The injury is classified based on the presence or absence of a mass lesion, which is found using diagnostic tools such as computed tomography (CT) and magnetic resonance imaging (MRI) (Olson-Madden et al. 2010). Imaging helps with location of injury, which can be useful in understanding localization of deficits (e.g., frontal lobe injuries are associated with problems with attention, initiating activity) (Kringelbach and Rolls 2004).

Severity Scales

Severity of TBI is generally graded from mild to moderate or severe. Severity can be classified in multiple ways, and each measure has different predictive utility, including determining morbidity, mortality, or long-term functional outcomes. Patients with more severe head injuries demonstrate lower cognitive functioning and have more gradual cognitive improvements following the initial injury (Novack et al. 2000). Degree of severity is often based on the acute effects of the injury, such as an individual's level of arousal or duration of amnesia, and these are measured by the GCS, PTA, duration of LOC (Ptak et al. 1998) and degree of altered consciousness.

The majority of TBIs are mild, consisting of a brief change in mental status or unconsciousness. Mild TBI is also referred to as a concussion. While most people fully recover from mild TBI, individuals may experience both short- and long-term effects. Moderate-severe TBI is characterized by extended periods of unconsciousness or amnesia, among other effects. The distinction between moderate and severe injuries is not always clear; as such, individuals with moderate and severe injuries are often grouped for research purposes. Throughout the remainder of this report, the committee refers to more severe injuries as moderate-severe TBI. Chapter 1 provides epidemiological statistics on TBI by severity.

These classification systems not only determine the severity of TBI, but also may be indicative of the degree of long-term disability. The more severe the injury, the more severe and persistent the cognitive deficits—though clinical measurements do not always concur. Severity measures graded during the acute phase sometimes reflect variance due to medications used during resuscitation, substance use, and communication issues. However, the relationship between clinical severity measures (e.g., GCS, LOC, and PTA) and various types of outcome measures (e.g., neuropsychological, functional disability, levels of handicap) has been well established (Cifu et

al. 1997; Dikmen et al. 2003; Sherer et al. 2002; Temkin et al. 2003). The utility of these measures depends on factors such as how long after the injury a patient is evaluated. Measures obtained later in time are generally better predictors of long-term outcomes; specifically, duration of PTA is more predictive than duration of LOC, which is more predictive than GCS at the time of injury (Katz and Alexander, 1994). Table 2-1 includes the mild, moderate, and severe classifications.

The most common classification scheme for TBI injury severity is the GCS, which has been in use since the 1970s. It provides a numerical index of level of consciousness that is used to grade injury severity. The 15-point scale is based on ratings of eye opening, verbal behavior, and motor behavior (Teasdale and Jennett 1976). A score of 13 to 15 is classified as mild, 9 to 12 as moderate, and 3 to 8 as severe. Though well known and widely used, this classification scheme is most useful in predicting acute survival and gross outcome, and performs more poorly in predicting later and more detailed functional outcomes, particularly in cognitive and emotional realms. Valid scoring has also become more difficult with earlier intubation and sedation for individuals with more severe injuries. However, more recent studies have found that the motor component of GCS may be more useful in predicting outcomes than the verbal data, which has not been found useful (Healey et al. 2003).

Other postinjury conditions contribute to the spectrum of severity, such as posttraumatic amnesia. PTA is defined as the interval between injury and return of day-to-day memory. It is a state of confusion that occurs immediately following TBI, in which the injured person is disoriented and unable to remember events after the injury. PTA can be directly assessed during the subacute stage of recovery using a brief examination that tests orientation and memory for circumstances of the injury and events prior to and following the injury. In addition, duration of PTA can be estimated retrospectively by asking the patient memory-related questions concerning

TABLE 2-1 Classification of Mild, Moderate, and Severe Traumatic Brain Injury

Severity of Injury/Measure	Mild	Moderate	Severe
Glasgow Coma Scale	13 to 15	9 to 12	3 to 8
Loss of Consciousness	< 30 minutes	> 30 minutes < 24 hours to 24 hours	> 24 hours
Posttraumatic Amnesia	< 24 hours	> 24 hours < 7 days	≥ 7 days
Altered Consciousness	≤ 24 hours	> 24 hours	> 24 hours

SOURCES: Helmick et al. 2007; Kay et al. 1993.

events immediately postinjury and estimating the postinjury interval prior to restoration of memory. In contrast to the brief duration of PTA after mild TBI—typically 5 to 10 minutes and less than 30 minutes—PTA could extend for days to weeks after severe TBI. Beginning rehabilitation prior to the end of PTA may be problematic since the patient is less likely to transfer learning across sessions.

Retrograde amnesia may also be present after injury, but its duration is typically shorter than PTA. Retrograde amnesia is "partial or total loss of the ability to recall events that have occurred during the period immediately preceding brain injury" (Cartlidge and Shaw 1981). In contrast, anterograde amnesia is difficulty forming new memories after the trauma, and it can sometimes lead to a decreased attention span and inaccurate perception. After a loss of consciousness, anterograde memory is often one of the last cognitive functions to return (Cantu 2001).

Natural History of Recovery

The natural process of recovery following TBI depends upon the initial injury severity, as described with the GCS, though there can be considerable variability even within categories. With most injuries there is a gradual resolution of symptoms. For most mild, single concussive injuries, the majority of patients are symptom-free within several weeks (Belanger and Vanderploeg 2005; Carroll et al. 2004; Lovell et al. 2003; McCrea et al. 2003). Several meta-analyses indicate the path to preinjury symptom levels following a mild TBI is 2 weeks, approximately, and no more than 3 months (Iverson 2005; McCrea et al. 2009). Development of new symptoms following resolution of the initial symptoms in civilians with mild TBI occurs infrequently. However, with multiple mild TBIs, both the number and duration of symptoms are likely to increase.

The course of recovery from severe TBI is more prolonged, with greatest function recovery occurring within 1 to 2 years of injury. One study (Corrigan et al. 1998) reported that following rehabilitation, an increasing number of people were independent at 6 to 12 months, and up to 5 years, postinjury. In another study assessing recovery in people with severe TBI, approximately 22 percent of individuals were found to have improved from year 1 to year 5; however, 14 to 15 percent declined, and approximately 62 percent remained unchanged (Millis et al. 2001). At the present time, the course and pattern of recovery following blast-related TBI is not well characterized, with no published longitudinal studies. However, the congressionally mandated Longitudinal Study on Traumatic Brain Injury Incurred by Members of the Armed Forces in Operation Iraqi Freedom and Operation Enduring Freedom (H.R. 5122) is currently ongoing and should provide details on the natural recovery in this population.

HETEROGENEITY

Heterogeneity of the injury is important to consider because it may help determine those who will benefit from cognitive rehabilitation therapy (CRT). Participation in CRT generally requires patients to be stable and recovered well enough to participate effectively in goal-oriented treatment programs. This generally occurs after the acute care phase. The unique, heterogeneous nature of an individual's TBI should be taken into account when designing or delivering a CRT program. Some of the most important heterogeneous factors to consider are physical mechanisms, pathobiology, severity, presence of polytrauma, multiple impacts, and other factors including age, gender, cognitive reserve, and genetic variation.

Physical Mechanisms of Injury

The physical mechanism of TBI, which determines the forces involved in the injury, represents an alternate way of classifying head injury based on the causative forces of the injury. Injuries can be classified according to whether the head makes contact with an object (also called impact loading) and whether the brain moves within the skull due to acceleration or deceleration forces (inertial loading) (Gennarelli 1983). Lesions can form when the brain is brought into contact with the skull, when an object strikes the head, or as a result of acceleration or deceleration. Medical records often only indicate the acute injury classification of a trauma, not its cause. This challenge must be overcome in clinical practice, where the event's preceding conditions must be estimated from incomplete details (Saatman et al. 2008). In addition to severity, anatomical features of the injury (i.e., pathobiology) and the mechanism of causative forces are important factors to consider, especially for rehabilitation purposes, as explained in the following sections. Mechanisms of injury may manifest in different ways, and include focal versus diffuse injuries as well as penetrating versus closed head injuries. Another way to characterize the physical mechanisms of TBI is to compare those that are commonly seen in military populations with those most commonly seen in civilian populations. These physical mechanisms of injury may occur in various combinations.

Focal Versus Diffuse

Whether an injury is focal, diffuse, or both contributes to the degree of heterogeneity of the resulting damage. A focal injury refers to a wound at a specific location, which affects the grey matter of the brain; a diffuse injury refers to more widespread damage, causing degeneration of white matter. Focal injuries most commonly reflect cerebral contusion resulting

from impact, with or without a fracture to the skull (Povlishock and Katz 2005). Features of focal injury may include lacerations, contusions, and/or hemorrhage (Morales et al. 2005). Diffuse injuries often result from rapid rotations of the head, which cause tissue distortion, typical in automobile accidents. Diffuse axonal injury, now superseded by the term traumatic axonal injury (TAI), can occur with either focal or diffuse brain injury, most commonly following rapid acceleration or deceleration of the head. TAI, which is often caused by blasts (Mac Donald et al. 2011), is characterized by shearing forces that cause axonal stretching, often with swelling of the brain and fiber degeneration. TAI can serve as a predictor of outcome (Graham et al. 2002; Hurley et al. 2004), though the long-term implications on treatment in humans are still not well understood (Greer et al. 2011).

Focal and diffuse injuries also may occur in combination (Povlishock and Katz 2005), which is often the result of a penetrating brain injury caused by severe whiplash or blast (Hynes and Dickey 2006); these features are commonly seen in military wounded with moderate-severe TBI. Blunt injuries can be either focal or diffuse—or, in some cases, mixed. Both static and dynamic forces cause blunt head injuries. Static loading occurs in crush-type injuries (e.g., avalanche, landslide) and is relatively uncommon (Graham et al. 2006). This type of injury generally causes skull fracture, and in more severe cases can cause brain laceration and coma. More often, blunt force injuries to the head are caused by dynamic forces: direct impact or rapid acceleration, deceleration, or rotational movement, which significantly strain the brain tissue (Graham et al. 2006).

Penetrating Versus Closed

Penetrating injuries involve an object entering or lodging within the cranial cavity. In civilian populations, these most often result from projectile or knife wounds; in the military setting, blast-related shrapnel or missile injuries are the most common causes (Warden 2006). Penetrating injuries have been less studied than closed models. Closed head injuries occur due to a nonpenetrating injury to the brain, usually resulting from a rapid rotation or shaking of the brain within the skull, or by impact to the skull. The most frequent causes of closed head injury are motor vehicle accidents or falls, resulting in either diffuse or focal injury. When not accompanied by penetrating wounds, a blast may also cause closed head injury. Common symptoms of nonpenetrating TBI include TAI, contusion, and subdural hemorrhage.

Military Versus Civilian

TBI has been the signature injury in the conflicts in Afghanistan and Iraq (Operation Enduring Freedom [OEF] and Operation Iraqi Freedom

[OIF]), with blast-induced neurotrauma (BINT) the most common cause due to increased use of improvised explosive devices (IEDs). It has been estimated that approximately 22 percent of military personnel in these war zones may sustain a TBI, and that as many as 60 percent of injured soldiers may have a TBI as part of their clinical spectrum (Terrio et al. 2009). Previous military campaigns have seen much lower rates of TBI-related injuries and mortality. In the Vietnam War, approximately 40 percent of the 58,000 U.S. combat fatalities were due to head and neck wounds and 14 percent survived a head injury (Schwab et al. 2003). In 1991, only about 20 percent of the military wounded in Operation Desert Storm were treated for head injuries (Carey 1996; Leedham and Blood 1992). The mortality and morbidity patterns during the OIF/OEF years still await full analysis.

BINT is often mild and may occur in combination with physical injuries, which may mask symptoms of TBI, causing true incidence to be underestimated. While body armor improvements have increased survival rates, they may also increase TBI prevalence either by preventing death from organ trauma or by potentially reflecting the blast waves (Phillips et al. 1988; Warden 2006). Blast injuries themselves are highly heterogeneous, and may result in primary, secondary, tertiary, quaternary, or quinary effects. Injuries that occur as a direct result of blast wave–induced atmospheric pressure changes, also called barotraumas, are referred to as the *primary* blast injury; these injuries may result in organ and tissue damage due to the forces of acceleration and deceleration. *Secondary* injuries may occur from the impact of blast-energized debris, producing penetrating or nonpenetrating injuries. *Tertiary* injuries can result from the blast victim being thrust against an immovable object, such as a wall or heavy machinery. *Quaternary* injuries can come from exposure to heat or fire generated by the blast. *Quinary* injuries may result from exposure to toxic agents released by the blast. In the military population, exposure to multiple blast injuries is common and may increase subsequent TBI-related symptoms and disability (Belanger et al. 2009). A recent study of active duty military with primary blast exposure plus another blast-related mechanism of injury (e.g., a motor vehicle collision or being struck by a blunt object) demonstrated the unique nature of military blast TBI (Mac Donald et al. 2011). The study found that patients demonstrated substantial numbers of abnormalities in the brain; civilian cases consistent with TAI do not commonly share these abnormalities. Although BINT may be unusually high compared to head injuries sustained by civilians, the risk of exposure to explosive devices exists in nonmilitary settings due to landmines, explosive weaponry used in terrorist incidents, or industrial or recreational accidents (Bilukha et al. 2008). Blast-related injuries are only in the beginning stages of study; pend-

ing development of further research, the true impact of these injuries on short- and long-term outcomes for survivors are unknown.

Pathobiology

As detailed above, the consequences of TBI depend in part on which areas of the brain are injured. The "primary injury," not to be confused with primary blast injury, refers to the immediate mechanical damage to brain cells and tissue that occurs at the moment of impact. This damage is nonreversible and therefore untreatable. In contrast, "secondary" or delayed injury occurs after the trauma and may progress for days, months, or even years; the damage from this injury is potentially treatable. Secondary injury is a complex, multifactorial process that includes metabolic and physiological changes related to biochemical alterations at the molecular and cellular level. In addition, secondary insults, such as hypoxia, hypotension, hypercarbia, and hyponatremia have long been recognized as influencing the outcome of TBI. It is well known that chronic inflammation occurs after TBI, but recent experimental and clinical studies indicate that persistent activation of the brain's resident immune cells (microglia) may continue for months to years after more severe injuries and lead to continuing progressive degeneration (Amor et al. 2010; Gavett et al. 2010; IOM 2009; Iwata et al. 2005).

Severity Continuum

The severity of brain injuries, described earlier in this chapter, also contributes to the heterogeneity of TBI, as the residual impact of TBI can increase as injury severity increases. The initial effects of TBI may range from mild, with a brief change in mental status or consciousness, to severe, with an extended period of unconsciousness. Ultimately, clinical severity is the result of both primary and secondary injury. Research shows a dose–response relationship between acute brain injury severity and cognitive deficits; when acute injuries are severe as measured by the GCS or PTA duration, the residual cognitive deficits are severe, may involve more cognitive domains, and are more persistent (Dikmen et al. 1995; Rohling and Demakis 2010; Schretlen and Shapiro 2003). Prospective, longitudinal studies of mild TBI have shown that by 3 months after injury, performance on cognitive tests generally does not differ from uninjured control subjects or patients who sustained mild orthopedic injury (Dikmen et al. 1995; Levin et al. 1987). Although some studies have reported more persistent cognitive deficits in a subgroup of patients with mild TBI (Kraus et al. 2007; Niogi and Mukherjee 2010), the literature is unclear about what percent of prospective patients may fall into this category.

Polytrauma

TBI can occur as part of a polytraumatic event, meaning that other organs or body parts are injured in addition to the brain. In recognition of the multifaceted nature of physical and psychological trauma exposure to members of the military and veterans, the Department of Defense (DoD) and the U.S. Department of Veterans Affairs (VA) health care systems frequently use the term polytrauma to refer to the combination of extreme physical injuries affecting two or more organ systems, which may include emotional trauma. Polytrauma means concurrent injuries to the brain and other organ systems resulting in physical, cognitive, and psychosocial impairments (Lew et al. 2007; Sayer et al. 2009), which may complicate treatment. Concomitant injury to body regions other than the head occurs in both military and civilian trauma patients. In service members, polytrauma may result in loss of limbs and burns, complications that are less common in civilians with TBI. However, civilians with mild TBI complicated by multiple trauma have shown more frequent disability than those recovering from isolated, mild TBI (Stulemeijer et al. 2008).

Multiple TBIs

In certain instances, a head injury may be followed by additional impacts to the head. Sometimes these injuries go unnoticed or unreported, as is often the case with mild TBI. Risk for repeated TBI is generally more common among military populations due to war zone characteristics, such as frequent exposure to blasts. For civilians, exposure to multiple TBIs may occur in contact sports or among those in active war zones alongside the military. Apart from developing posttraumatic dementia, the effects of sustaining more than one mild TBI on rehabilitation are unclear.

Reports of athletes sustaining repeated mild TBIs occurring over an extended period of time (i.e., months or years) have suggested that the effects are cumulative, as reflected by neurological and cognitive deficits (Guskiewicz et al. 2005; Iverson et al. 2004). It is unknown how often service members are exposed to these impacts, and blast injuries may be unreported or undetected. When reported, duration of unconsciousness is often unknown or unrecorded (Ross et al. 1994; Thatcher et al. 2001). However, studies based on self-report questionnaires and interview data obtained from service members and veterans of Iraq and Afghanistan have documented a subgroup with repeated exposure to blasts that caused alteration of consciousness (Terrio et al. 2009). Despite a dearth of prospective data, research has suggested that the effects of these repeated blast-related injuries may be cumulative (Guskiewicz et al. 2005; Laurer et al. 2001).

Age

Although age is fixed at time of injury, it is an important factor to consider when describing the heterogeneity of TBI. Age significantly impacts outcome from TBI and is one of the strongest predictors of mortality and functional outcome (Luukinen et al. 1999; Mosenthal et al. 2002; Murray et al. 2007). Self-reported symptoms in the months after mild, blast-related TBI have been worse in younger than older service members (Hoge et al. 2008; Terrio et al. 2009). However, older TBI patients are more likely to experience a delayed neurologic decline several months after injury, which can complicate prognosis and treatment management. After age 65, and in some studies as early as age 40, morbidity and mortality after TBI increased markedly (Mosenthal et al. 2004). This finding applies especially to severe TBI in adults, where mortality rises sharply in people 40 years or older. Furthermore, as people with TBI age, they are more likely to experience cognitive decline earlier or at faster rates than individuals without TBI. Prior TBI is associated with a significantly greater incidence of dementia or Alzheimer's disease, as established from large cohort studies from World War II, the Korean War, and the Vietnam War (Loane et al. 2009). However, the potential moderating effect of age on response to CRT is not currently known or documented.

Gender

The way gender contributes to heterogeneity of TBI varies depending upon the severity of the injury and the outcome of interest. Evidence concerning gender differences in outcome is mostly limited to sports-related concussion research, which shows that young females report more symptoms following injury (Cantu and Gean, 2010; Dikmen et al. 2010; Lovell et al. 2003). In the sports-related concussion literature, females are shown as possibly susceptible to increased risk of concussion in most sports (Colvin et al. 2009; Comstock et al. 2006; Gessel et al. 2007). In sports played by both men and women, females sustained a higher rate of mild TBI than males (Comstock et al. 2006; Gessel et al. 2007), and females were associated with worse physical and cognitive symptoms and delayed recovery following mild TBI (Broshek et al. 2005; Colvin et al. 2009; Covassin et al. 2007; Dikmen et al. 2010). Furthermore, in a large sample of junior high, high school, and collegiate soccer athletes, females had longer recovery time than males (Colvin et al. 2009). These results may be due in part to differences between genders in biomechanical forces of injury or symptom reporting. However, with increased severity of injury, evidence supports both a positive and negative effect of female gender on reducing risk of

mortality following TBI (Berry et al. 2009; Davis et al. 2006; Farace and Alves, 2000; Morrison et al. 2004; Ottochian et al. 2009).

Cognitive Reserve

Cognitive reserve is a construct that has been invoked to explain inter-individual variability in the response to brain injury. Higher preinjury cognitive reserve has been linked to a higher level of intellectual functioning on follow-up examinations. Operational definitions of cognitive reserve have generally used preinjury intellectual level, for which data has been available in the military. For civilians, an index based on demographic features including education history has been used; more than 11 years of education was associated with an improved outcome (Stulemeijer et al. 2008). This concept was initially proposed to explain individual differences in intellectual outcome of penetrating brain wounds sustained in combat by Korean War veterans (Weinstein and Teuber 1957). More recently, Grafman et al. (1988) extended the concept of cognitive reserve to describe long-term intellectual outcome after penetrating brain wounds in Vietnam War veterans. In both studies, higher preinjury intelligence was predictive of long-term intellectual outcome. Cognitive reserve may explain different responses to posttraumatic cognitive function, and may contribute significantly to posttraumatic outcomes and response to treatment. Higher cognitive reserve may be considered a form of resilience to neuropathological damage. A study by Jeon et al. (2008) explored premorbid demographic factors (e.g., age, sex, marriage status, educational status, occupation, residence, and premorbid intelligence) and concluded that higher levels of education, intelligence or higher IQ scores, and younger age were all prognostic indicators of recovery of memory function.

Genetic Variation

Another factor contributing to the heterogeneity of TBI is human genetic variation. At present, little is known about the role of genetic variation in brain injury or rehabilitation. However, as with many other disorders, genes are likely to emerge as an important focus in the near future and link to potential therapeutic interventions. Currently, many genetic components of the response to neurotrauma are under investigation for impact on functional outcomes. Research has shown that variation in the gene ApoE (Apolipoprotein E) can modulate the extent of brain injury (Teasdale et al. 1997). However, the nature of the effect has not been consistent (Crawford et al. 2002; Friedman et al. 1999; Millar et al. 2003). In addition, genetic polymorphisms in the p53 gene have been shown to affect TBI recovery course (Dumont et al. 2003).

Other Factors Affecting Recovery

Many chronic conditions—both clinical and premorbid demographic factors—affect outcome after TBI and therefore contribute to its heterogeneity (Jeon et al. 2008). Chapter 3 includes a more complete discussion of these other factors affecting TBI outcome, including pre- and comorbid conditions such as substance abuse or depression and posttraumatic stress disorder. In addition, the individual's social environment context, such as family or caregiver support systems, significantly influences the effectives of treatment. Social environmental context is also discussed in Chapter 3.

MEASURES OF OUTCOME

Choosing outcomes to measure or monitor postinjury change is critically important in making decisions about rehabilitation for patients as well as determining the efficacy of the rehabilitation program implemented. Furthermore, prediction of outcomes is also complicated by the uniqueness of the injury as discussed throughout the chapter. While many psychometric measures of outcome are used to evaluate and report on therapeutic interventions effects, more recent rehabilitation research has focused on functional outcome measures as more global indicators of patients coping or recovering from the disability.

The most frequent cognitive sequelae of TBI are impairment of episodic memory, slowed cognitive processing speed, and impaired executive functions (i.e., the ability to switch between tasks, plan, and set and monitor goals). These findings are generally transient and relatively subtle after a single, mild TBI without complications, whereas marked persistent deficits are common after more severe TBI. Although the pattern of cognitive deficits could differ in blast-related TBI, the evidence to date indicates that the long-term effects of these injuries are similar regardless of cause and related to injury severity (Belanger et al. 2009). Rehabilitation programs must address the complexity of the cognitive deficit affecting functional capacity to be effective.

Historically, the Glasgow Outcome Scale (de Guise et al. 2008) is a common measure, which uses a five-point scale to classify outcome as death, persistent vegetative state, severe disability, moderate disability, or good recovery (Jennett et al. 1976). This was one of the first scales developed to examine outcomes and has been used widely in TBI outcome research; however, because of its broad categories that are insensitive to change and difficulties with reliability, its research application is limited. From this scale the Extended Glasgow Outcome Scale (GOS-E) was developed to address the limitations of the original GOS, measuring global functioning as a combination of neurologic functioning and gross cognitive function (Wilson et al. 1998).

Other outcome scales that are more sensitive and specific measures of functional recovery than the GOS have been proposed, including the Disability Rating Scale (DRS), Rancho Los Amigos Levels of Cognitive Function Scale (LCFS), and Functional Independence Measure (FIM) (Zafonte et al. 1996). The FIM is a widely used 18-item ordinal scale, scored on the basis of how much assistance is required for the individual to carry out activities of daily living (ADLs) (i.e., feeding, bathing, grooming, and dressing), which therefore attempts to measure the level of a patient's disability and indicate the burden of caring for them. The FIM is often used with the Functional Assessment Measure (FAM), a 12-point scale that incorporates cognitive and psychosocial issues (Hall et al. 1993). In general these scales are more aptly suited for acute inpatient settings (Sohlberg and Mateer 2001). Many other psychometric tests are available to assess various cognitive functions (i.e., Attention Rating Scale [Ponsford and Kinsella 1991], Wechsler Memory Scale III [Wechler 1997], Wisconsin Card Sorting [Heton 1981]). However, often these measures are only indicators of what an individual can do at a particular time in a particular context (Sohlberg and Mateer 2001). Although patients may indicate improvement in by these outcome measures during or immediately posttreatment, they may fail to implement strategies learned in therapy, to home and work environments and therefore, true efficacy of therapy may not be fully captured.

Many patients, families and their caregivers are likely more interested in outcomes that generalize to real world patient functioning. These outcome measures may include those that capture patient-centered outcomes indicative of how treatment effects in the real world can be maintained or have meaning for patient (functional status and quality of life). These functional assessment measures, such as self-report or caregiver reporting of ADL functioning, can be a more useful gauge of the patient recovery trajectory. Other measures that may be more pertinent for personalized treatments involving cognitive rehabilitation therapy may include Goal Attainment Scaling (GAS) (Malec 1999, Malec et al. 1991), because it involves patients identifying general goals and articulating specific unique goals to their situation. Community participation measures including return to work, access to work, and community integration and participation measures are also important in assessing real-world functional outcomes. However, in its review of the evidence the committee focused not only on an immediate treatment benefit, but also on whether a benefit to everyday life and functional status via patient-centered outcomes, or maintenance of outcomes.

Selection of outcome measures for rehabilitation, specifically CRT, should be guided by the need to generalize treatment effects across situations and over time, while choosing measures that do not overlap with

the training tasks. Consequently, outcome measures should include cognitive function in everyday activities, and the overall study design should consider maintenance of posttreatment changes over time. Furthermore, many diagnostic tools are available to determine location of damage and lesions within the brain and to aid in determining treatment approach and options and to act as biomarkers in predicting and monitoring outcomes. These imaging techniques noninvasively monitor brain function, helping to provide information on the disease etiology and can aid in making decisions about patient recovery as well as monitor responsiveness to interventions. MRI (magnetic resonance imaging) technologies allow for the monitoring of blood flow in the brain and provide detailed images of brain anatomy to identify brain pathology. A modification of the original MRI, fMRI (functional MRI) is a relatively noninvasive monitoring and localizing of functional changes in the brain and changes in functioning following TBI. Other diagnostics include electroencephalography (EEG), which measures electrical activity from ion current within the neurons of the brain. It is generally a nonspecific indicator of general cerebral function. Positron emission tomography (PET) provides computer-generated images of blood flow, brain metabolism, and chemical processes generated from gamma rays emitted indirectly by a positron-emitting radionuclide tracer, which can be monitored while a patient is engaged in various activities. Transcranial magnetic stimulation (TMS) uses electromagnetic stimulation to activate specific or general parts of the brain with minimal discomfort, allowing study of the functioning and interconnections of the brain (Wagner et al. 2007).

These imaging technologies assist with the location of the injury and monitoring of brain function, but injury characteristic association with a performance on a functional task or with specific cognitive deficits has not been well established. However, recently, Diffusion Tensor Imaging (DTI), a method of assessing axonal integrity and white matter integrity, has shown promise as a predictor of some cognitive deficits (Kinnunen et al. 2011). White matter is one of the two components of the central nervous system and consists mostly of myelinated axons that connect regions of grey matter (the locations of nerve cell bodies) of the brain to each other, and carry nerve impulses between neurons, thus white matter acts as the tracts to connect brain functionality. Kinnunen and colleagues (2011) demonstrated the relationship between white matter abnormalities and cognitive function in two domains commonly affected by TBI, memory and executive function (Kinnunen et al. 2011). These imaging and biomarkers may have utility in determining responsiveness to behavioral/rehabilitative interventions and or medications and be useful in helping to define target populations.

CONCLUSION

In general, TBI is complex, and a multitude of factors may influence treatment approaches and course of recovery. The nature of TBI complicates the process of planning, delivering, and evaluating therapeutic interventions such as CRT. This chapter serves as background for the remainder of the report, including understanding what CRT is and the lack of definitive evidence regarding effective treatment for TBI.

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3

Factors Affecting Recovery

Multiple factors may affect recovery after traumatic brain injury (TBI), including the individual's severity of injury; access and response to treatment; age, preexisting environmental, genetic, or medical complications; or conditions co-occurring with the primary condition. It is important to note that recovery is not one dimensional. Practitioners and researchers measure outcomes in various ways, ranging from mortality to ability to return to preinjury employment status. However, TBI survivors themselves and their families are likely more interested in quality-of-life outcomes, such as reintegration into the community, successful return to work or school, and functional capacity in everyday life.

Previous chapters have addressed severity of TBI and other injury-related factors affecting outcome. This chapter describes the premorbid conditions (e.g., learning disabilities or psychiatric conditions), comorbidities (e.g., stress-related psychiatric disorders or somatic symptoms), and contextual factors (i.e., social environmental) affecting cognitive and functional recovery from TBI. The following sections are not intended to be an exhaustive review of all possible associated conditions; rather this synthesis of the literature focuses on those factors that the committee determined were most relevant for this report—those that may interfere with an individual's response to rehabilitation following TBI, including cognitive rehabilitation therapy (CRT). These issues are discussed within the context of both civilian and military populations. Figure 3-1 shows the environmental, personal, or medical factors that may affect recovery.

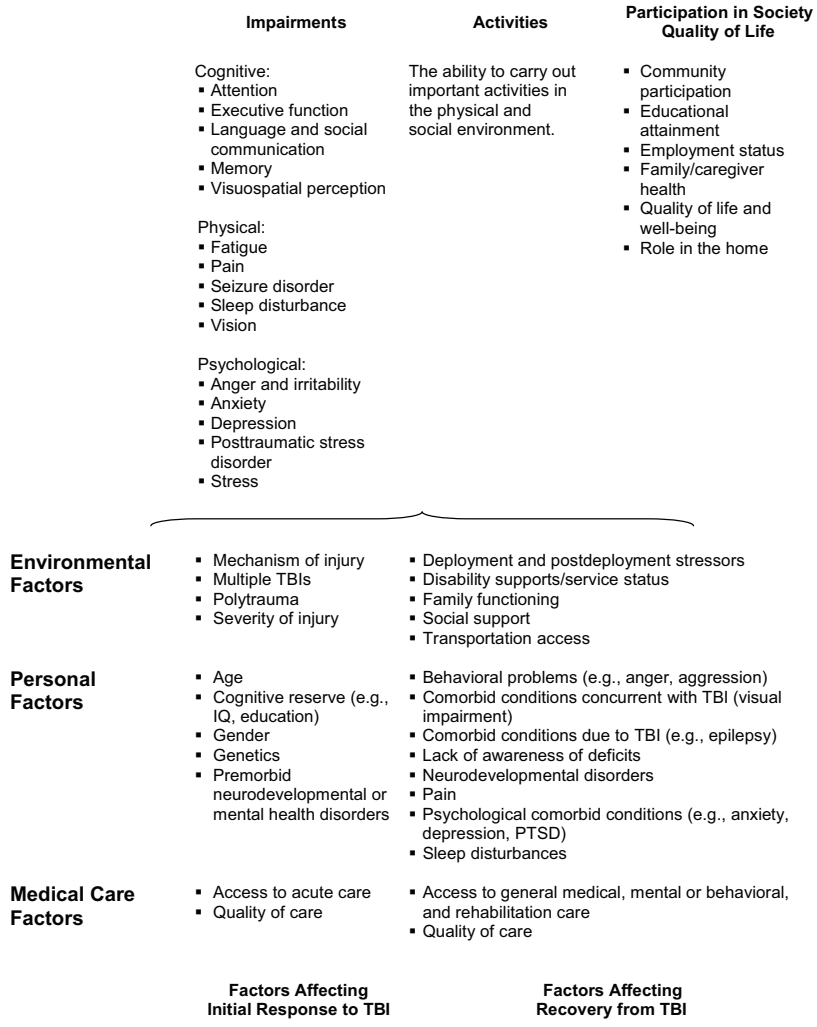

FIGURE 3-1 Factors affecting initial response to TBI and recovery from TBI.

PREINJURY CONDITIONS

Individuals who sustain TBI may have preexisting conditions, as well as diverse cognitive, medical, genetic, and environmental backgrounds that potentially moderate the effects of injury. Each of these elements (independently and collectively) along with the heterogeneity of TBI can affect an in-

dividual's initial response to trauma and subsequent response to treatment. Gaps in knowledge exist regarding the effects of preexisting conditions on outcome following TBI, and it is often difficult to differentiate the effects of preinjury factors from those related to the injury itself or the postinjury environment. Preinjury conditions, such as attention deficit hyperactivity disorder (ADHD), learning disabilities, or mild forms of syndromes on the autism spectrum (e.g., Asperger's), may also affect an individual's cognitive deficits after a TBI, as well an individual's ability to acknowledge an injury, seek screening or treatment, understand a diagnosis and subsequent treatment plans, and set appropriate goals for treatment success.

Preinjury depression may affect the manifestation of various TBI-related effects. In a study of TBI by Bombardier et al. (2010), a prior history of depression among patients correlated with higher post-TBI rates of major depressive disorder. Although screening attempts to prevent individuals with most major affective disorders from military service, instances of bipolar disorder, schizophrenia, or substance use disorder (SUD), among others, may go undiagnosed. Corrigan et al. (2003) demonstrate that about half of the civilian subjects in TBI Model Systems, a national data repository of information about the acute and postacute care of individuals with TBI, had preinjury SUD. Emotional disturbance and ongoing substance abuse can also affect a survivor's capacity to cognitively engage in and potentially benefit from even a well-designed cognitive rehabilitation program.

Other preexisting factors may contribute to poor outcomes following TBI, including a lack of social support systems and environmental factors. Socioeconomic status (SES) is an environmental factor that can affect cognitive, behavioral, and functional outcomes. Socioeconomic status is associated with low education status or low IQ. But the relationship between low SES and a worse outcome may be due to the limited resources available to the individual and the family, including access to high-quality rehabilitation and availability of family members to act as caregivers. If an individual from low SES suffers a TBI in the military, that person may be afforded the opportunity for continued treatment and care due to his service, which may otherwise be unavailable. However, due to work restrictions or other responsibilities, that person's family or other caregivers may not be able to provide the support system and care the person needs after hospitalization and during a structured rehabilitation program.

COMORBIDITIES

Comorbidities are conditions that occur in addition to the primary insult, injury, or disease. Comorbidities can occur by chance (i.e., two or more conditions occurring simultaneously, with one condition not the direct origin of the other), or by causal association (Valderas et al. 2009). Causal

conditions may be linked in one of two ways: by *direct causation*, where one disease or injury results in another disorder, e.g., when TBI leads to memory impairment or epilepsy, or by *associated risk factors*, where the environment or agents leading to one condition also may manifest in another, e.g., sustaining a TBI and broken femur in the same explosion (Valderas et al. 2009). Co-occurring conditions have also been explained by selection bias, meaning those who seek treatment may be more likely to have more than one disease or adverse health condition (Valderas et al. 2009).

Comorbidities of TBI may include behavioral, psychiatric, physical, or cognitive disorders. These are generally causal associations—either due to direct causation or associated risk factors. Just as cognitive and psychiatric disorders can occur as preexisting conditions, they are also the most common comorbidities following injury, particularly in the long term. For example, TBI has been shown to be associated with the premature onset of neurodegenerative diseases, including dementia (Kiraly and Kiraly 2007). Common comorbidities include depression, anxiety disorders (e.g., PTSD), and SUD, all discussed further in this chapter.

These comorbidities may also be differentially reflected in civilian and military populations due to the nature of deployment, prolonged battle, or other challenging war zone conditions experienced by members of the military. In severe TBI in civilian populations, behavioral disturbances including irritability, disinhibition, aggression, and lack of insight or awareness pose a burden to caregivers and a challenge for rehabilitation clinicians. Meanwhile, the most commonly reported comorbidities among military populations include depression and anxiety disorders. Of these, posttraumatic stress disorder (PTSD) has been reported in 43 percent of service members who sustained blast-related mild TBI associated with alteration of consciousness (Hoge et al. 2008). Mental health disorders can affect soldiers' and veterans' quality of life, ability to engage in social activities or employment, and capacity to resume satisfying lives within their families and communities (Sandberg et al. 2009). Additionally, mental health disorders may have direct effect on neuropsycological functioning. They also have the potential to interfere with recognition of the need for treatment or the ability to actively engage in therapies like CRT.

Depression

Depression is defined by symptoms including sadness, apathy, negative thoughts, low energy, cognitive distortions, inability to enjoy everyday activities, and suicidal ideation (APA 2000). Depression is a common and disabling mood disorder that can significantly diminish an individual's quality of life. Studies have found that the rate of depression post-TBI is nearly eight times higher than the general population's rate (53.1 versus

6.7 percent) (Bombardier et al. 2010). Furthermore, depression may also develop indirectly years after an injury as a result of the effects of TBI and maladaptive readjustment (Moldover et al. 2004).

Anxiety Disorders

According to a growing body of literature, anxiety disorders (e.g., Generalized Anxiety Disorder, PTSD, and others) can develop after mild, moderate, or severe TBI (Bryant et al. 2010; Zatzick and Grossman 2011). Furthermore, as anxiety disorders are a common preinjury condition, occurring in 29 percent of the general population (Kessler et al. 2005), it has been suggested that they continue to exacerbate issues postinjury (Moore et al. 2006). Anxiety disorders have been documented as co-occurring with TBI to varying degrees in many studies. Virtually all types of anxiety disorders have been documented individuals who have experienced mild TBI, including Generalized Anxiety Disorder at 3 to 28 percent, panic disorder at 4 to 17 percent, and obsessive-compulsive disorder at 2 to 15 percent (Moore et al. 2006).

Posttraumatic Stress Disorder

Individuals diagnosed with PTSD reexperience unwanted and disturbing memories associated with a trauma. To cope, these individuals avoid thinking about the event or experience psychic numbness, often vacillating between emotional numbing and distress in response to reexperiencing symptoms. PTSD is also characterized by increased arousal, which may manifest as hypervigilance, irritability, impaired concentration, exaggerated startle response, and sleep disturbance (Sayer et al. 2009). Sleep issues, cognitive problems, or emotional issues associated with PTSD may negatively impact one's ability to cope with effects of TBI (Lew et al. 2009). The prevalence of PTSD as a comorbid condition is higher in military TBI than in civilian TBI. Furthermore, a lack of research exists concerning how comorbid PTSD affects veterans and service members who have sustained mild, blast-related TBI.

A Rand report released in 2008 included survey results on previously deployed service members with TBI from Operation Enduring Freedom (OEF) in Afghanistan, and Operation Iraqi Freedom (OIF) in Iraq (Adamson et al. 2008). The report found that one-third of study participants "met criteria for probable PTSD" (Adamson et al. 2008). This strong association between TBI with PTSD was also reflected in a study of recently returned infantry soldiers, which shows that 43.9 percent of the infantry soldiers experienced PTSD symptoms after a loss of consciousness due to TBI, compared to 27.3 percent after an altered mental state, 16.2 percent

with other injuries, and 9.1 percent with no reported injuries (Hoge et al. 2008). Civilians may also experience PTSD associated with TBI, due to terrifying circumstances that may lead to an injury, such as a motor vehicle accident or assault. Studies have reported varying frequencies of connection between TBI and comorbid PTSD, ranging from 20 percent of individuals (Bryant and Harvey 1999) to 84 percent (Feinstein et al. 2000). While the relationship between PTSD and TBI severity has not yet been well studied, TBI severity appears to have a role in PTSD diagnosis. In civilians and military members, the prevalence of PTSD is higher in patients with milder injuries (Adamson et al. 2008; Hoge et al. 2008). Patients with more severe TBI show less risk of developing symptoms consistent with a PTSD diagnosis (Zatzick et al. 2010), possibly due to more prolonged periods of unconsciousness following the trauma.

Substance Use Disorders

Substance use disorders commonly occur among adults who have experienced a TBI. Substance abuse and dependence after TBI can complicate individuals' efforts to successfully recover from their injury, particularly in the areas of employment and social reintegration. A cross-sectional study of substance abuse program participants reported that 10 to 20 percent of individuals with TBI, with no preinjury substance abuse issues, were substance abusers after their injuries (Corrigan et al. 1995). Other studies reveal a different story, possibly due to differences in study design or patient populations. For example, several longitudinal studies of individuals with no preinjury history of substance abuse rarely develop alcohol or drug use problems after TBI (Bombardier et al. 2003; Kreutzer et al. 1996; Ponsford et al. 2007). These studies report that less than 10 percent of participants became substance abusers after TBI.

SUDs can be both a cause and effect of TBI. Alcohol and illicit drug use in civilian populations represents a risk factor for TBI, primarily through accidents or acts of violence. However, service members deployed in OEF and OIF have limited access to alcohol and illicit drugs; thus, use of these substances at the time of injury is uncommon (Warden 2006). However, substance use as a comorbid condition with TBI has been associated with military discharge. Compared with all those discharged from the military, people with mild TBI were more than two times as likely to be discharged for alcohol, drugs, or criminal convictions, and people with moderate TBI were about five times more likely to be discharged for alcohol or drug problems (Ommaya et al. 1996). Patients with more severe brain injuries who were substance abusers preinjury may have a period of abstinence in the immediate postinjury period, but many survivors return to preinjury use levels at 2 years from injury (Corrigan et al. 1995).

Other Comorbid Conditions

Other conditions associated with TBI that may adversely affect treatment success, especially when the injury is more severe, include lack of awareness, agitation, aggression, disinhibition, and apathy (Ciurli et al. 2011; Flashman and McAllister 2002; Kim 2002). Other comorbid conditions particularly relevant to service members are those commonly associated with blast injuries, which can include physical injuries to the musculoskeletal system (including amputation and fracture), soft tissue, oral/maxillofacial areas, auditory, and visual systems (Sayer et al. 2009). Fatigue, pain, and sleep disturbance are especially common conditions in service members or veterans who experience TBI, and these conditions are likely to affect an individual's participation in rehabilitation (DVBIC 2010).

Fatigue

Fatigue is a common complicating condition following TBI and is prevalent even months following injury (Belmont et al. 2006; Lundin et al. 2006a, 2006b; Ziino and Ponsford 2005). Fatigue is generally defined as a feeling of physical or mental exhaustion, tiredness, or weakness. It is highly interrelated with other conditions, such as sleep disturbance or depression, but these are often patient-specific correlations. Furthermore, after TBI, physical fatigue is more prevalent and severe than fatigue based on depression, pain, or sleep disturbance (Cantor et al. 2008). Fatigue may deter a person's active participation in rehabilitation activities, and therefore, may mediate response to CRT; however, these connections have not been studied extensively.

Pain

The co-occurrence of TBI and pain is common and may arise from cognitive and physical trauma often experienced with more severe injuries, or changes in brain functioning that affect sensory and motor functioning and, perhaps, perception of pain stimuli (Sherman et al. 2006). Following TBI, frequently reported locations of pain include the head, back, legs, and shoulders. Headaches alone are one of the most common symptoms after TBI, affecting more than 30 percent of the population and often continuing long after injury (Model Systems Knowledge Translation Center 2011). Pain, including headaches, may be referred to as chronic if it persists for an extended period of time (i.e., 3 to 6 months or more). Chronic pain is often associated with other problems, including functional disability, psychological distress, litigation/compensation issues, and family discord and vocational issues (Lew et al. 2009). A recent metaanalysis considering only

veteran populations with TBI found a 43.1 percent prevalence of reported pain (Nampiaparampil 2008). In addition, pain and PTSD are often intertwined, as a chronic pain flare-up may generate PTSD-related thoughts and PTSD symptoms such as hyperarousal may increase pain intensity (Lew et al. 2009).

Sleep Disturbance

Diagnosed sleep disorders following TBI include excessive daytime sleepiness, hypersomnia, insomnia, and parasomnia and circadian rhythm alterations, such as delayed sleep phase syndrome and irregular sleep–wake pattern (Ayalon et al. 2007; Baumann et al. 2007). Previous research has shown that among brain-injured adults, sleep disturbance causes daytime sleepiness, fatigue, poorer levels of overall functioning (Verma et al. 2007), and a lack of necessary quality sleep. For patients recovering from TBI, lack of quality sleep can exacerbate symptoms such as pain, irritability, and cognitive deficits (Ouellet and Morin 2007).

Insomnia is common following TBI and has been reported in frequencies from 3 to 84 percent of TBI patients (Zeitzer et al. 2009). The cause of insomnia following TBI can be *direct* (e.g., secondary to neural damage), *indirect* (e.g., secondary to depression), or *unrelated,* though still present. Population-based studies indicate that insomnia occurs in approximately 40 percent of individuals with TBI of any severity and is often the most prevalent somatic complaint (Schwab et al. 2007). Sleep apnea (i.e., sleep-disordered breathing), a prevalent disorder in the general population, has been reported to be present in about half of the U.S. Department of Veterans Affairs (VA) TBI patient population (Zeitzer et al. 2009).

Treatment Options for Pre- and Comorbid Conditions

Many treatment options are available for the preinjury conditions and comorbidities described in this chapter. Of particular concern is these factors' potential influence on or interference with CRT. In addressing the needs of the whole person for optimal outcome, the presence of pre- or comorbid conditions requires optimal coordination of treatments to address psychiatric or physical conditions in addition to cognitive impairments. Treatment coordination may include sequential versus concurrent treatment, or separate versus integrated approaches. For example, addressing PTSD symptoms first may enhance later response to CRT interventions for attention deficits, because the individual will be less distracted by psychological symptoms during rehabilitation. Likewise, one study showed improved cognitive function in patients treated for major depressive disorder (Herrera-Guzmán et al. 2010). Although the study did not include TBI

participants, the relationship between treatment for psychological disorders and cognitive function may warrant future study.

Medications are commonly prescribed to treat a range of physical or psychological symptoms. Medications that have a sedating effect or other adverse effect on cognition may affect the individual's attention and ability to participate in CRT. However, a lack of extensive data exists on this issue. In addition to pharmacologic treatment, cognitive behavioral therapy, a form of psychotherapy, is commonly used to treat psychological conditions such as depression or PTSD (Foa et al. 2009). A previous Institute of Medicine (IOM) report evaluating PTSD interventions found sufficient evidence to support the effectiveness of exposure-based interventions, of which cognitive behavioral therapy is one (IOM 2008). As described in Chapter 4, cognitive behavioral therapy is distinct from CRT in both the target of the intervention and the specific intervention components. Cognitive behavioral therapy for PTSD typically consists of four basic components: psychoeducation, imaginal or *in vivo* exposure to the trauma or feared stimuli, reappraisal of distorted beliefs and thoughts, and anxiety management training (Harvey et al. 2003). Cognitive behavioral therapy interventions are designated as a first-line strategy for mental health specialty treatment of PTSD within the VA/Department of Defense (DoD) Clinical Practice Guidelines for Management of Posttraumatic Stress (VA/DoD 2010) and by several other professional and scientific organizations.

CONTEXTUAL FACTORS

In addition to preexisting and comorbid conditions, relevant contextual factors (e.g., social environment) may influence the path to recovery from TBI. Social and family support can influence treatment outcome. In addition, compensation and disability status or application (e.g., through workman's compensation, disability insurance, or litigation) have been shown to create patterns of symptom reporting among TBI populations. Finally, contextual conditions such as deployment and subsequent return home are important for military populations.

Family and Social Support

Family members and significant others play a key role in the recovery of adults with TBI. A key social-environmental factor that can affect the recovery process and outcome is family functioning, as families are often partners in the rehabilitation process and can play a role in goal planning and generalization of skills and knowledge to the home setting (Levack et al. 2009). Successful rehabilitation requires family cooperation in a variety of areas such as transportation, finances, leisure, and emotional support

(Jacobs 1988). From a health care systems perspective, family members or caregivers provide a large portion of the care needed to help adults with TBI function on a daily basis. Family functioning has been associated with greater improvement in people with TBI, including improvement in overall disability, level of functioning, and employability. On the other hand, family stress and unhealthy family communication and roles can hinder the rehabilitation process (Sander et al. 2002). Holistic approaches to CRT often include some family interventions, which could include educational, skill-building, and psychological support components. The results of the few family-intervention studies, while mixed in their conclusions, have reported such benefits to families as a greater number of needs being met, a perception of fewer obstacles to receiving services posttreatment (Kreutzer et al. 2009), improvement in psychological distress (Brown et al. 1999; Sinnakraruppan and Williams 1991), reduced burden, improved satisfaction with caregiving, and increased perception of caregiving competency (Albert et al. 2002). However, use of effective problem solving and coping strategies by the family was related to lower levels of depression for the person with TBI (Leach et al. 1994).

Disability Status or Compensation-Seeking Behavior

Compensation-seeking behavior or litigation has been shown to impact recovery rates and symptom patterns. The majority of studies on this topic indicate that TBI survivors actively engaged in litigation report more postconcussional symptoms (versus nonlitigants). Compensation seekers or litigants experience longer-lasting symptoms, which may result in delayed work return and higher levels of psychological stress (possibly due to the injury, unresolved financial issues, or both) (Blanchard et al. 1998; Cook 1972; Feinstein et al. 2001; Miller 2001; Paniak et al. 2002; Wood and Rutterford 2006).

Deployment and Postdeployment Factors

In a war zone, individuals are exposed to a number of factors that can influence physical and emotional health. Among the most salient of these exposures are physical trauma and psychological stressors or trauma. Physical trauma can lead not only to TBI, but also to other bodily injuries. Psychological trauma can result in a broad array of adverse outcomes including, but not limited to, PTSD and depression. Moreover, physical trauma can be associated with adverse psychological consequences, and psychological trauma can have physical symptoms. War-zone stress exposures may be particularly potent, as they are not typically limited to a single trauma. The co-occurrence of trauma to multiple body systems is

often referred to as polytrauma (see Chapter 2 for more details on polytrauma). Furthermore, physically traumatic events are often embedded within a larger context, including exposure to psychological trauma, and service members are exposed to these types of recurring and relentless life-threatening events for extended periods of time (Vasterling et al. 2009).

In addition to direct combat exposure, stressors unique to military personnel within a war zone include episodes of extreme fear, exposure to the terrifying consequences of contemporary warfare, the lack of contemporary amenities and the comforts of daily life, and periods of boredom (King et al. 2008). Concerns about events at home may increase stress levels for deployed service members, and difficulties experienced during the transition from the war zone to home life may also increase the level of psychological distress (Vasterling et al. 2010). Combining TBI with repeated exposure to extreme stress and prolonged displacement from family, home, and community can cause interactive psychiatric and neurological disorders. Although most service members readjust successfully to their predeployment lives, an estimated 26 percent of troops develop postdeployment mental health conditions such as depression and anxiety disorders (Adamson et al. 2008). A 2006 survey assessed the health of more than 200,000 active duty service members and veterans from the Army and Marine Corps (Hoge et al. 2006). The study found that approximately 20 percent of active duty service members screened positive for one mental health condition, and 31 percent of veterans had at least one outpatient mental health care visit within the first year after returning home from Iraq or Afghanistan (Hoge et al. 2006). According to a recent report screening service members returning from combat, among those that screened positive for TBI, 33.8 percent screened positive for PTSD and 31.8 percent screened positive for depression (Adamson et al. 2008). Many of these deployment and postdeployment factors have the potential to influence the success of rehabilitation.

CONCLUSION

The factors described in this chapter may moderate an individual's response to CRT. Furthermore, preinjury conditions, comorbidities, or environmental features may differ between civilian and military populations with TBI. Preinjury depression and anxiety disorders may be present and contribute to persistent symptoms for anyone with TBI. However, more severe preinjury psychiatric disorders or substance abuse may be more common in civilians due to screening procedures used by the military. Depression is a common comorbid condition in both civilian and military TBI. In contrast, PTSD is far more prevalent after blast-related TBI, and service members are more frequently exposed to blasts than civilians. Although social support and other environmental factors should be considered in

both civilian and military situations, the stressors associated with combat and deployment are typically more adverse than what is experienced in civilian life.

Unfortunately, published literature evaluating how these factors may affect response to CRT is sparse. Clinical trials of CRT have not consistently reported the frequency of these conditions among study participants, nor have these studies consistently controlled for conditions that could ostensibly interfere with treatment response. Even with limitations in knowledge, rehabilitation professionals must consider these potential conditions when planning treatment programs for patients with TBI. Likewise, future research on the benefit of CRT interventions for TBI may plan for these issues, which may benefit continued development and understanding of CRT and its ability to treat whole-person functioning. Chapter 14 of this report includes specific directions regarding these issues.

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4

Defining Cognitive Rehabilitation Therapy

In the early part of the 20th century, improvements and advancements in medical care, protective gear, evacuation procedures, and early stabilization in the field began to contribute to the increased survival of brain injured soldiers, enabling even severely injured individuals to survive and attempt to recover from brain injuries. To enhance recovery of brain injury survivors, clinicians and researchers saw the need to provide cognitive as well as physical rehabilitation. They developed a range of therapies for patients with nontraumatic brain injuries, such as stroke, that causes language (aphasia) or visuospatial skill impairments. Likewise, for traumatic brain injury (TBI), clinicians and researchers developed a range of therapies for attention, memory, and executive function impairments; treatments for social and behavioral problems; and programs for adjusting to disability.

THE BREADTH OF REHABILITATION

In broad terms, rehabilitation principally focuses on the enhancement of human functioning and quality of life. In contrast, other branches of health care focus primarily on prevention and treatment of disease. Rehabilitation accepts the complex correspondence between disease and the ability to function: a disease may be eradicated while disability remains; disability can be reduced in the face of permanent injury or chronic disease. Rehabilitation is often considered in regard to improving physical disabilities. For a person with paralysis, rehabilitation might examine whether the individual's strength could be improved through exercise, whether the tendons of nonparalyzed muscles could be surgically transferred to a mechani-

cally useful site, whether braces or a wheelchair might allow the person to navigate the community despite the paralysis, and even whether architectural modifications, urban planning, or transportation services could help overcome barriers to mobility. The treatment interventions used in physical rehabilitation include traditional drug and surgical treatments, as well as physical exercise, technology (e.g., braces, wheelchairs), skill training (e.g., learning how to use a wheelchair), and social policies and services (e.g., accessible transportation).

However, rehabilitation is not limited to improving physical disability. Cognitive rehabilitation attempts to enhance functioning and independence in patients with cognitive impairments as a result of brain damage or disease, most commonly following TBI or stroke. As with physical rehabilitation, cognitive rehabilitation may include interventions that aim to *lessen impairments*, or interventions that aim to *lessen the disabling impact* of those impairments. Interventions are applied through technology and other compensatory strategies that may allow the individual with cognitive impairment to accomplish important life activities and more fully participate in society.

Cognitive *rehabilitation* therapy (CRT) may sometimes be confused with cognitive *behavioral* therapy. It is important to distinguish between the two. While not mutually exclusive and sometimes delivered conjointly, these two therapies are certainly separate and distinct, differing in both treatment goals and techniques. CRT is used to rehabilitate thinking skills (e.g., attention, memory) impaired by a brain injury. Cognitive behavioral therapy is commonly used for a variety of emotional and psychiatric disorders, including mood, anxiety, and psychotic disorders, as well as sleep disturbance and chronic pain. Cognitive behavioral therapy typically centers on modifying maladaptive thoughts and emotional behaviors and using psychoeducation regarding symptoms and expectations for recovery. The latter technique also may be a component of CRT. Cognitive behavioral therapy includes training in anxiety management and how to recognize and reappraise distorted negative thoughts, and, for some disorders, exposure to anxiety-provoking or distressing stimuli with the intent of forming new adaptive emotional associations with the feared stimuli. The 2008 Institute of Medicine (IOM) report, *Treatment of Posttraumatic Stress Disorder: An Assessment of the Evidence,* provides a more comprehensive description of cognitive behavioral therapy.

The breadth of treatments included in CRT mirrors that of the World Health Organization's International Classification of Functioning, Disability, and Health (WHO-ICF). As described in Chapter 1, the WHO-ICF framework recognizes impairments in *body structures and functions* (e.g., impaired memory) as a result of disease or injury, and limitations in *activities and participation*, i.e., the ability to carry out important daily activities

(e.g., remembering weekly appointments) and the ability to participate in society (e.g., employment, home, school, or community). Activity and participation limitations result when the person with the impairment(s) interacts with the physical and social environment. For example, an individual with TBI may have difficulty learning and remembering new information. With repeated training, the individual may be able learn some basic routines, such as writing appointments and other important information down in a daily planner and consulting it frequently. These routines enable the person to keep track of a schedule and other important tasks despite memory impairment. Several professional organizations endorse the use of the WHO-ICF for characterizing CRT, including the American Occupational Therapy Association, the American Physical Therapy Association, and the American Speech-Language-Hearing Association (American Occupational Therapy Association 2011; American Physical Therapy Association 2003; American Speech-Language-Hearing Association 2003b).

AN EVOLVING DEFINITION OF CRT

Specific cognitive and communication needs of patients with brain injury propelled the parallel development of CRT within multiple professional disciplines, including clinical psychology, neuropsychology, speech-language pathology, occupational therapy, physical therapy, and physiatry (i.e., rehabilitation medicine) (Prigatano 2005). Collaboration with academic colleagues in other disciplines such as cognitive psychology also occurred. The various disciplines share a common goal: each intends to help patients with cognitive impairments function more fully, either by focusing on the impairment itself or the activities affected by the impairment (as described by the WHO-ICF framework). Chapter 5 provides full descriptions of the disciplines and providers of CRT, and their approaches to treatment.

The heterogeneity of the possible interventions makes it challenging to narrowly define the concept of CRT, or how to effectively apply it. Current definitions of CRT focus on the *intention* to improve or accommodate one or more impaired cognitive functions, rather than on the *contents* or active ingredients of treatment. Intentional definitions can limit the interpretation of CRT evidence since treatment efficacy and effectiveness depend more on the contents and processes of treatment than the intention of the clinician providing it. Table 4-1 includes assembled definitions of CRT based on intent.

The most commonly referenced definition of CRT is interdisciplinary, endorsed by the Brain Injury Interdisciplinary Special Interest Group (BI-ISIG) of the American Congress of Rehabilitation Medicine (ACRM). This description allows for comprehensive, interdisciplinary rehabilitation programs with interventions to restore or reorganize function, compensate

TABLE 4-1 Definitions of Cognitive Rehabilitation Therapy by Organization

Organization	Definition
Brain Injury Association of America	"Cognitive rehabilitation is a systematically applied set of medical and therapeutic services designed to improve cognitive functioning and participation in activities that may be affected by difficulties in one or more cognitive domains. . . . Cognitive rehabilitation is often part of comprehensive interdisciplinary programs" (Katz et al. 2006).
Brain Injury Interdisciplinary Special Interest Group (BI-ISIG)	"Cognitive rehabilitation is 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 by (1) reinforcing, strengthening, or reestablishing previously learned patterns of behavior, or (2) establishing new patterns of cognitive activity or compensatory mechanisms for impaired neurological systems" (Harley et al. 1992).
U.S. Veterans Administration (VA)	"Cognitive rehabilitation is one component of a comprehensive brain injury rehabilitation program. It focuses not only on the specific cognitive deficits of the individual with brain injury, but also on their impact on social, communication, behavior, and academic/vocational performance. Some of the interventions used in cognitive rehabilitation include modeling, guided practice, distributed practice, errorless learning, direct instruction with feedback, paper-and-pencil tasks, communication skills, computer-assisted retraining programs, and use of memory aids. The interventions can be provided on a one-on-one basis or in a small group setting" (Benedict et al. 2010).

for impaired function through new cognitive patterns or external devices, and enable individuals to adapt to their new level of functioning. CRT may target specific cognitive domains (e.g., attention, reasoning, planning), and may be delivered in various contexts.

Differences across definitions of CRT are based on theoretical differences regarding the underlying cognitive mechanisms that result in behavioral changes. The Brain Injury Association of America, the largest U.S. advocacy organization for individuals with brain injury, summarizes this issue: "Theoretical models of cognitive rehabilitation vary along several different dimensions. Treatments may be process specific, focused on improving a particular cognitive domain such as attention, memory, language, or executive functions. Alternatively, treatments may be skill-based, aimed at improving performance of particular activities. The overall goal may be restoring function in a cognitive domain or set of domains or teaching compensatory strategies to overcome domain specific problems, improving

performance of a specific activity, or generalizing to multiple activities" (Katz et al. 2006).

CRT Attributes

This section includes descriptions of the key distinctions within CRT, which may be useful in clarifying the contents of treatment and analyzing efficacy for different types of patients. These dichotomies include modular versus comprehensive, restorative versus compensatory, and contextualized versus decontextualized treatments. These dichotomies are not mutually exclusive categories by which to classify CRT treatments; they serve as important distinctions at understanding underlying cognitive processes and ways providers have attempted to treat cognitive deficits. These approaches to CRT evolved somewhat differently, from different philosophical perspectives and for different purposes, such as treating focal versus diffuse injuries, although considerable overlap exists. Focal brain injuries, such as stroke or brain tumors, may result in one or a small number of cognitive impairments and largely spare other cognitive processes. In contrast, diffuse (i.e., multifocal) brain injuries resulting from trauma often result in multiple cognitive and behavioral impairments. Hence, an emphasis on interdisciplinary CRT for individuals with TBI is warranted.

Modular Versus Comprehensive Treatments

In modular models of CRT, treatments are generally aimed at a single cognitive impairment, such as memory ("memory remediation") or language ("aphasia therapy"). Such treatments, when delivered alone, might be expected to enhance activities and participation most effectively in patients with a single or predominant impairment (i.e., patients with a more focal impairment). In contrast, patients with multiple impairments (i.e., deficits in attention and memory, along with impulsivity and depression) may receive a comprehensive program also referred to as "holistic," "multi-modal," or "neuropsychological rehabilitation." Comprehensive programs typically contain a mix of modular treatments that target specific cognitive impairments, treatments that address self-awareness of the impact of cognitive deficits, and individual or group therapies that facilitate coping with residual deficits and their social consequences. For example, a comprehensive program for patients with moderate or severe TBI might begin with a comprehensive neuropsychological assessment, along with a patient and family interview of current difficulties in activities, social behavior, and mood. From this assessment, certain patient-specific modules might be selected. Consider a female patient who frequently becomes stalled in complex tasks and often forgets appointments and commitments. She might

receive specific individualized treatment focusing on task-related problem solving, along with training in the effective use of a daily planner. In addition, she might participate in daily group discussions with other patients about the ways in which their lives have changed; group members receive feedback and support for their attempts to cope with and adapt to those life changes. She might also receive individual psychotherapy to address depression, along with periodic joint sessions with her husband to help him understand the sources of her unreliability as well as address his own sense of the loss of his familiar partner. Specific adaptations of CRT for patients with TBI reflect the domains most commonly impaired, notably attention, memory, social communication, and executive function. Figures 4-1 and 4-2 illustrate the differences and overlap in these dichotomies.

Restorative Versus Compensatory Treatments

Restorative treatments are aimed directly at improving, strengthening, or normalizing specific impaired cognitive functions. Such treatments frequently have an "exercise-like" aspect in that they may involve intensive and repetitive use of a particular cognitive process while gradually increasing the level of difficulty or the processing demands. Patients with attention deficits may, for example, be provided with a series of computer tasks that require detection of targets on the screen at an increasing pace. Such tasks may increase in difficulty along a number of dimensions (e.g., pacing, to focus on speeded processing, or task duration, to focus on sustained attention), and the difficulty along each dimension increases as performance improves.

Compensatory treatments, in contrast, seek to provide alternative strategies for carrying out important activities of daily living despite residual cognitive impairment. The compensations may be internal, as when a person with memory impairment learns mental strategies for organizing material for better recall (e.g., learning to group items to be remembered in categories as an aide to retrieval), or external, as when such a person adopts the use of electronic reminder technology. Compensatory treatments are typically more tailored to specific needs of the individual, to the person's willingness to use the strategy, and to the demands of specific activities. For example, strategies for remembering a list of groceries are likely to differ from strategies for retaining class material at school. In both cases, writing may be used (a grocery list versus taking notes), but the form may differ. Paper and pencil may be sufficient for a grocery list, but taking notes may need to be supplemented by audio recordings of the lecture.

There is debate over whether true restoration ever occurs or whether the behavioral improvements simply become more like the norm and thus, less visible. Because there is no "window into the brain," it is difficult to

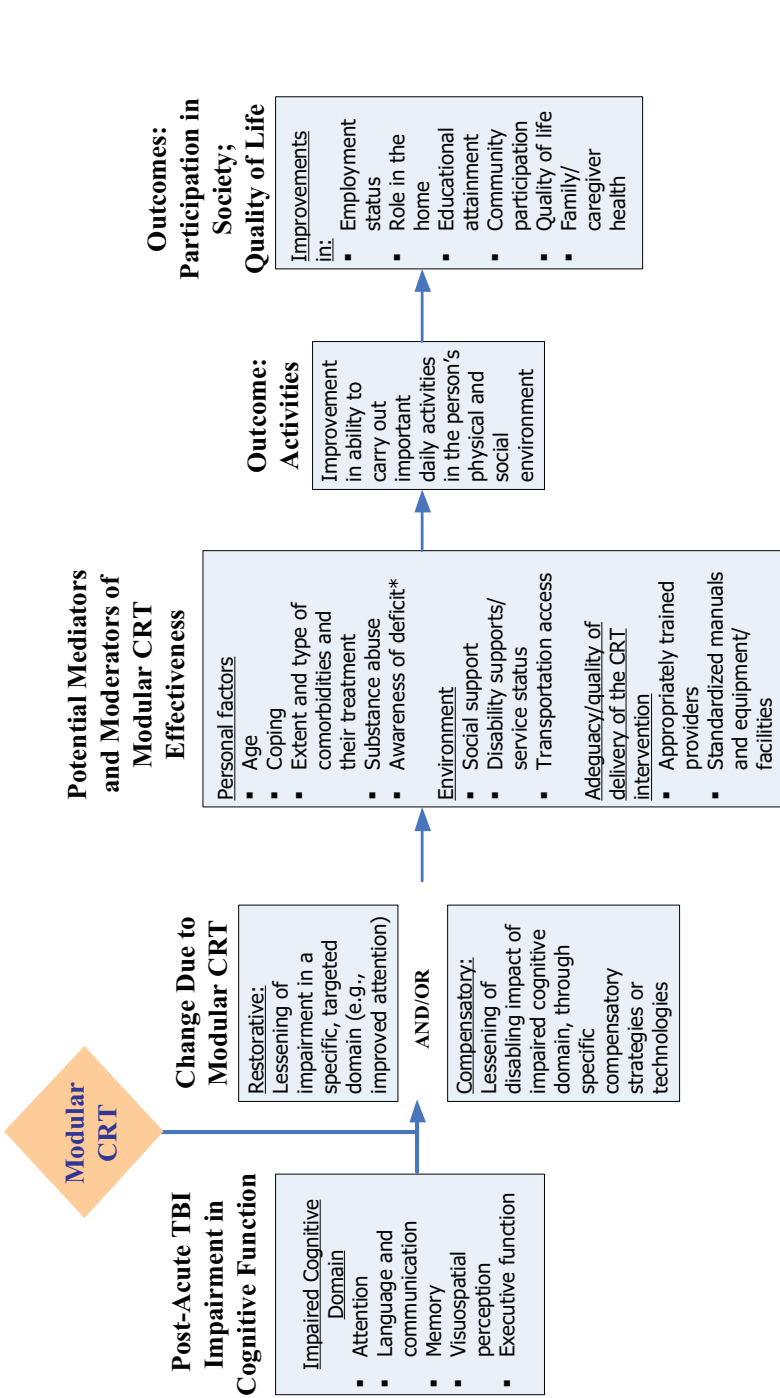

FIGURE 4-1 Model for modular CRT.
* For some domains, the CRT intervention may also *target* deficit awareness; for example, videotape of a social interaction followed by a critique will increase awareness of deficit in language and communication.

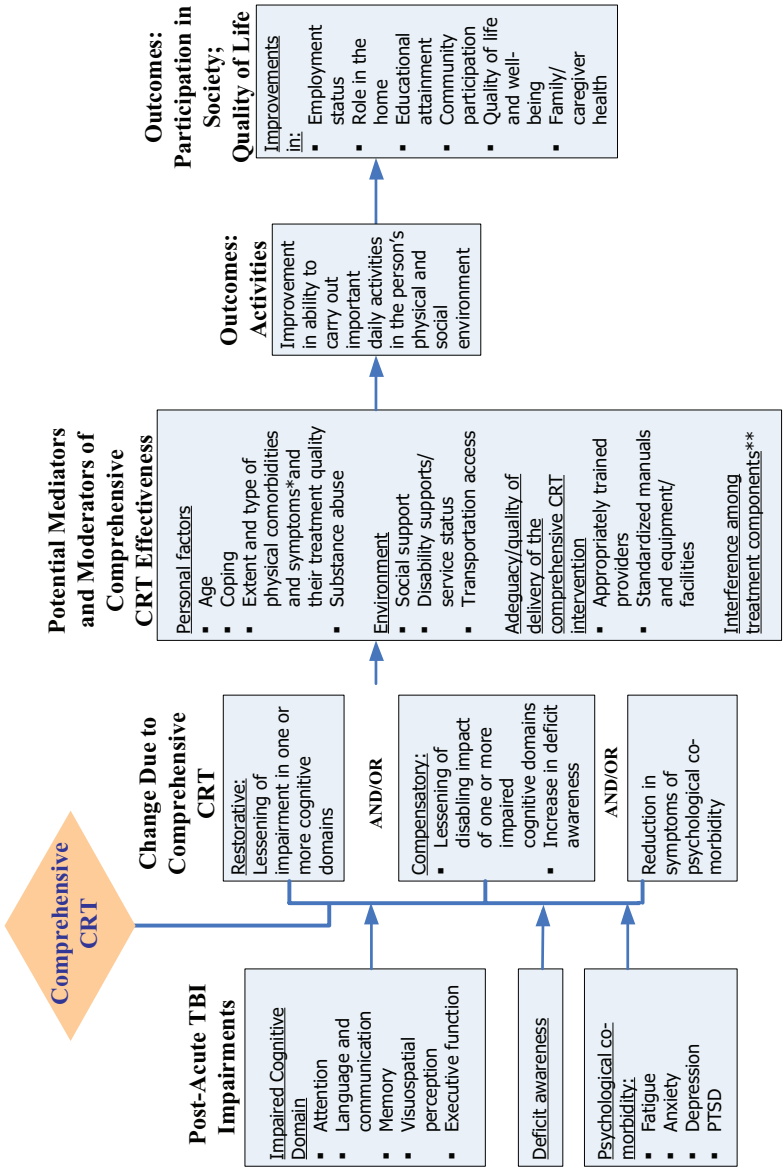

FIGURE 4-2 Model for multi-modal/comprehensive CRT.
* For example: visual impairment, headache, dizziness.
** For example: side effect of medication for depression interferes with attention.

determine if restoration of a cognitive process is possible. The ability to translate a treatment task to real-world applications is largely dependent on the circumstances of the individual with cognitive deficits. The lure of restorative approaches is that, if effective, they could impact a broad range of activities affected by the same impairment. For example, if attention capacity can truly be restored, then all of the activities suffering from inattention would likely improve. Compensatory strategies tend to be designed around important activities rather than around the impairment itself and, therefore, tend to be more local solutions. However, the impact of compensatory strategies may be more visible, since task accomplishment serves as direct evidence of the success of the strategy.

Contextualized Versus Decontextualized Treatments

CRT interventions also differ in the degree to which they take place in the real world or use materials and tasks from the patient's everyday life. Decontextualized assessment and treatment targets specific cognitive processes often using artificial treatment tasks, such as pressing a key when a computer presents a number but not a letter. This artificial task attempts to enhance attention. Another artificial task is repeating words in lists of increasing length in attempt to improve working memory span. Decontextualized approaches provide more opportunity for pure manipulation of a single dimension, on the assumption that specific cognitive processes can be isolated and treated somewhat independently from each other. However, attempting to train attention during a cooking task may reveal obstacles related to manual coordination in slicing and chopping, planning and sequencing of the cooking steps, and reading the instructions (Adamovich 1998; Sohlberg and Mateer 2001).

Contextualized therapy addresses cognitive impairments as they disrupt activities and skills in various milieus (American Speech-Language-Hearing Association 2003a; Hartley 1995; Ylvisaker and Feeney 1998). For example, a contextualized treatment may include a focus on driving to observe the occasions in which the patient appears to be distracted from the driving task, allowing for an opportunity to provide specific feedback about how to manage these difficulties (e.g., "When you approach an intersection, you should stop talking to your passenger."). It has been argued that contextualized treatments that occur within a familiar environment, or deal with personally important tasks, are likely to enhance motivation for treatment, improve self-awareness of strengths and weaknesses, and ensure that the strategies learned are applicable to the patient's personal situation. However, such treatments are more cumbersome to deliver than those based on standardized materials that can be delivered in a clinic or office.

Contextualized treatments also are more difficult to evaluate, standardize, and disseminate because doing so requires the therapist to have the skills necessary to design and execute them, and generally requires more availability/effort from the patient. A decontextualized attention training program can be a specific computer program with internal rules for task progression, which is disseminated in standard form. In contrast, contextualized attention training would be an approach to finding out what activities are most disrupted by inattention from the individual patient, how to simplify those activities during training, and how to assess progress.

Application of CRT Attributes

Attributes of CRT are not mutually exclusive options, and various attributes can be combined in a multitude of ways. Modular treatments, for example, can be aimed at either restoration or compensation. One treatment might consist of a hierarchical set of "attention exercises" designed to strengthen attentional capacities. Alternatively, one might provide compensations such as unpredictable auditory tones to alert an inattentive patient, training the patient to ask a speaker to repeat a point, or having the patient work in a quiet environment. Comprehensive programs may contain a mix of both restorative and compensatory treatment types. Modular treatments can also be either contextualized or decontextualized. As noted, modular treatments aimed at restoration, in particular, are likely to be decontextualized, in that they may seek to abstract the essence of a cognitive process from its natural context to more tightly focus the treatment. Compensatory modular treatments, however, such as training in memory strategies, are often applied to the real-world activities the patient faces.

Implications of CRT Attributes on Treatment and Research

Practitioners and researchers acknowledge that the ultimate goal of treatment should be functionally meaningful improvements in the patient (i.e., activities, participation, or quality of life), and there may be many approaches to reaching this goal (Sohlberg and Mateer 2001). A one-size-fits-all method of treatment may not be effective because of the heterogeneity of injuries, differences in premorbid personal, social, and environmental circumstances, and differences in the activities of importance to individual patients. Heterogeneity of TBI further complicates studies of CRT impact and may mask benefit in subgroups that the study cannot detect due to small sample size or other limitations in study design.

In general, CRT attributes may shape expectations about the types of possible treatment outcomes and the types of patients most likely to benefit, and therefore may be useful for clinical reasoning; however, rehabilitation

professionals often use a variety of therapy approaches, providing interventions that target activities and participation while systematically addressing the underlying cognitive impairment(s). For example, individuals may benefit from intensive practice of memory encoding strategies (modular, decontextualized, compensatory) to bolster remembering new information, while also practicing applying these strategies to various types of material and in various contexts (modular, contextualized, compensatory). Alternatively, a modular treatment may not have substantial impact on activities and participation in a patient with multiple impairments unless other coexisting cognitive and emotional factors are concurrently addressed, as in a comprehensive program. Likewise, a contextualized, compensatory treatment may not restore an underlying cognitive impairment or even impact behavior change in an environment beyond where the strategy was taught.

These treatment attributes also affect the feasibility and design of research that might advance the evidence regarding CRT. For patients with multifocal or diffuse injuries, evaluation of the effectiveness of CRT in terms of real clinical impact faces a particular challenge. Even highly efficacious modular treatments may have impact on specific measures of the targeted impairment, but may fail to show improvement in real-world activities, participation, or quality of life. For example, if attention can be substantially improved in a patient who still has memory deficits, difficulty solving problems, and inappropriate social behavior, this may have little impact on employment or the development of social relationships. Comprehensive treatment programs, by targeting multiple impairments as well as skills for coping with residual impairments, may have more substantial life impact, but they provide no insight into the necessary or sufficient ingredients for a successful treatment outcome.

These attributes also affect the experimental designs that are most applicable and feasible for advancing the science of CRT. Specifically, modular restorative treatments are relatively amenable to randomized controlled trials (RCTs). In an RCT, therapists can design similar appearing treatments that differ in the active ingredients and deliver one treatment or the other at random to research subjects. For example, to assess whether "continued attention deficits" is a critical attention challenge, a study may compare a program with static attention exercises with a progressive program that advances with patient improvement.

RCTs involving comprehensive treatments are more difficult to design and execute, because of the need to distill a multifaceted treatment, often individually tailored, into standard form. A study evaluating comprehensive treatment programs ideally will include a manual specifying the rules that link assessment to selection of specific treatment elements, and how those elements will be advanced or tailored to individual performance. It is difficult to deliver a control treatment in this case, since plausible but

inert treatments of a compensatory nature are modified to the person or environment and are more likely to be tailored to each patient's specific task priorities. Furthermore, such treatment programs are expensive to provide without clinical revenue, which would preclude intentionally designing an ineffective comparison treatment.

CONCLUSION

CRT is an umbrella term for a group of interventions that are used to support or ameliorate cognitive impairments, as well as the changes that occur in everyday functioning as a result of these impairments. Patients with TBI often have multiple identifiable cognitive impairments, coupled with mood or other behavioral disturbances, a reduced awareness of their own cognitive and behavioral limitations, and reductions in social competence. Although some patients with isolated impairments may achieve substantial treatment benefits in terms of activities and participation from treatment of a single deficit, others may require a combination of treatments aimed at multiple problems to achieve comparable outcomes. The heterogeneous array of treatments available, as well as the lack of a unified theoretical framework for defining and quantifying them, makes definitive evaluation of their effectiveness particularly challenging.

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5

State of Practice and Providers of Cognitive Rehabilitation Therapy

The multi-faceted nature of cognitive rehabilitation therapy (CRT) means there is no standardized nomenclature for clinical practice. Providers in various disciplines aim to improve their patients' cognitive functions to strengthen performance in daily activities, communication, or more complex activities at work or school. CRT is often described according to the intended outcome of treatment (e.g., improved memory or attention to tasks) or by the method or provider delivering the therapy. For practical purposes, CRT does not differ from occupational therapy, speech-language-pathology, and physical therapy when these treatments intend to reduce or compensate for an underlying cognitive disorder. Therefore, the committee concluded that these types of therapy sessions, when conducted to ameliorate deficits for patients with cognitive impairment, meet the definition of CRT.

STATE OF PRACTICE

Rehabilitation practice in the United States is affected by health care and related policies. Rehabilitation professionals regard therapy as a means to improve the lives of individuals with disabilities, and thus aid their return to active participation within family and social lives, communities, and work. Increased awareness of traumatic brain injury (TBI) and related cognitive deficits has promoted the rehabilitation needs of cognitively impaired individuals. At the same time, rising health care costs mean long-term rehabilitation programs are reduced, leading to shorter in-patient stays and condensed outpatient programs (Sohlberg and Mateer 2001). Providers adjust and modify programs to target outcomes as effectively and efficiently

as possible, while constrained by reduced health care funds and time with the patient.

The Role of Families

Family members, dedicated caretakers, or paraprofessionals provide an important support system to individuals with cognitive or behavioral deficits due to TBI, as discussed in Chapter 3. This support system also plays an important role in the rehabilitation process (Sohlberg and Mateer 2001). The changed cognitive or behavioral functioning caused by brain injury not only affects the injured individual, but also places enormous demands on families. Emotional stress, perceived burdens of caretaking, and disrupted family functioning as well as unmet needs of other members of the family may contribute to unhealthy family communication or functioning.

Because rising health care costs and the costly nature of neurorehabilitation have led to shorter inpatient stays, outpatient rehabilitation is an important component of therapy, one that relies on a support person for the injured individual (Harrison-Felix et al. 1996; Kreutzer et al. 2009; Sander et al. 2002). Successful rehabilitation requires cooperation, participation, and encouragement from the patient's support network for success; ongoing activities may include providing transportation, monitoring or maintaining finances, implementing leisure activities, providing emotional support, and reinforcing newly learned behaviors to compensate for brain injury-related deficits (Jacobs 1988). Long-term treatment efforts require collaboration among the providers, their clients, and the clients' families (Levack et al. 2009). Garnering family support throughout the treatment process captures a unique resource to maintain treatment effects, provide generalization from clinical applications to real-life situations, and facilitate ongoing recovery (Kreutzer et al. 2003; Malec et al. 1993). These partnerships can help ensure realistic treatment goals considering the expertise, needs, and concerns of client and family (Sohlberg and Mateer 2001).

Family stress and unhealthy family communication and roles can hinder the rehabilitation process; potential barriers arise to successful rehabilitation outcome when a family member does not align with treatment goals or objectives of the entire team (i.e., patient, clinician, and family) (Levack et al. 2009; Sander et al. 2002). Constructive family functioning has been associated with greater improvement in persons with TBI, lessening overall disability and increasing employability. Ideally, family members or caretakers act as facilitators to the brain-injured individual's care and recovery. Evaluations of CRT interventions sometimes include or require a family member or caregiver to participate in the study, because of the unique capability of caregivers to help translate clinical practices to real-world applications. For example, a provider may demonstrate use of a journal or

notebook to help an individual with a memory deficit stay on schedule; the provider also instructs the family member to provide prompts for use of the reminder notebook at home. Clinicians provide educational, skill-building, and psychological support components to the family as well as the patient. Results of a few studies have reported benefits to families such as

- A greater number of met needs and perception of fewer obstacles to receiving services post-treatment (Kreutzer et al. 2009),
- Improvement in psychological distress (Brown et al. 1999; Sinnakaruppan et al. 2005), and
- Reduced burden, improved satisfaction with caregiving and increased perception of caregiving competency (Albert et al. 2002).

Delivery of CRT

When, where, and how long CRT is provided are interrelated factors that vary depending on the patient's needs and means for participating in rehabilitation (e.g., willingness, affordability, family support). Currently, depending on the severity of injury and the patient's acute recovery, CRT typically includes a wide range of therapeutic ingredients and is practiced by professionals with specific expertise in different settings or environments. The current state of health care provision in the United States, with myriad payers for care, affects how patients receive care. Patients who would benefit from treatment, according to their physicians or ongoing research, may not receive prescribed treatments due to limitations in payer plans. Furthermore, when treatment is available, policies unique to individual payer plans may impact treatment type, timing and duration of delivery, the setting in which the treatment is provided, and the professional who provides it. As such, payment policy may affect how treatment is labeled. When delivered by a member of one of the disciplines described in this chapter, a treatment may be identified as "speech therapy," even though activities meet the definition of CRT. This may occur when health benefits provide coverage for speech therapy but not CRT.

Treatment approaches may include comprehensive inpatient or outpatient CRT programs, outpatient CRT delivered by a sole practitioner, or comprehensive CRT programs with multiple providers working together on a team. The individual treatment ingredients of comprehensive, interdisciplinary rehabilitation programs are not typically recorded. Therefore, ingredients delivered through these programs are harder to quantify for comparison purposes than modular CRT, which is more singularly focused, as described in the prior chapter. There is debate about when and where to deliver CRT. Some advocate for early intervention, while others call for intervention at more chronic recovery stages (Ben-Yishay and Diller 1993).

Most patients who receive CRT do so as inpatients when their medical status has stabilized. Few patients receive CRT more than 1 year after injury, even though spontaneous neurological recovery will have slowed by this time, and patients are more likely to have better awareness of their limitations and abilities. The timing of CRT is generally dictated by health payer policies, not by when the patient would benefit most from such rehabilitation. Unfortunately, unlike the injury itself, which may be a single discrete event, the effects of TBI may occur across time. Deficits associated with brain injury may require treatment throughout the patient's lifespan, which is in keeping with the World Health Organization's International Classification of Functioning and Disability (WHO-ICF) label of "chronic condition." As patients' conditions change (improve or decline) due to life transitions (e.g., new job, new home, new city), new cognitive rehabilitation treatments may be required. This type of care is similar to the ongoing care provided to patients with other chronic conditions, such as paralysis.

Inpatient Care

During acute, inpatient rehabilitation, professionals evaluate and treat patients' cognitive and communication abilities, functional daily activities, physical and mobility skills, and early psychosocial well-being. It is common for this early phase of CRT to aim to increase attention, learning, and basic communication skills, while at the same time reduce disorientation, confusion, and even agitation. Also during this phase, physiatry and rehabilitation nursing provide important medical care to patients, while social workers and psychologists provide support as families and friends plan for discharge to the patient's home or another facility.

Comprehensive, interdisciplinary inpatient CRT is provided to patients who have recovered from moderate or severe injuries sufficiently to participate (e.g., 3 hours of therapy a day). Based on their needs, patients receive a combination of restorative and compensatory CRT approaches from various professionals on the rehabilitation team. For example, patients who are highly confused and remain in posttraumatic amnesia (PTA) may receive reinforcement for using a simple calendar that logs their daily routine (compensating for poor memory) and work on decontextualized paper- and pencil-tasks aimed at improving their attention skills (restoring sustained attention).

Some comprehensive inpatient programs are specifically designed for patients who have severe cognitive impairments that cause serious psychological or behavioral problems, including aggressive and inappropriate behaviors, which are chronically disabling. These behaviors may cause family crises and render caregivers unable to supervise the patient without the risk of injury. While some patients may be transferred to these programs directly

from an inpatient multi-disciplinary CRT program, others are admitted after attempts by caregivers have failed at home.

Outpatient Care

Most individuals with TBI continue to need CRT long after inpatient rehabilitation ends because they have not yet learned the full impact of cognitive deficits on their ability to function at home, in the community, at work, or at school. While severity of injury predicts early and general recovery from TBI, the CRT services that patients receive later depend more on the amount of cognitive recovery, the projected goals and capacity of the patients to eventually reach those goals, and the nature of patients' cognitive strengths and weaknesses.

After acute inpatient rehabilitation, CRT approaches vary and become even more individualized as patient confusion subsides and attention and memory improve. Individuals who have a combination of cognitive, psychological, or behavioral issues after TBI may participate in a comprehensive, interdisciplinary outpatient program that "includes individual and group cognitive rehabilitation, psychotherapy, psycho-education, and family therapy" (Tsaousides and Gordon 2009). These patients typically are unable to reintegrate back into the community, find or keep a job, or succeed in college or other training programs. They also may engage in illegal activities and get in trouble with the law or cause family conflicts. Comprehensive outpatient or day programs are typically for patients who are able to live in less restrictive environments or who have family to care for daily needs. In these programs, providers not only help patients understand and accept limitations and deficits, but also provide strategies to compensate for cognitive or physical deficits (Rath et al. 2003; Wilson et al. 2008).

For example, patients may receive CRT through an occupational therapist (OT), speech-language pathologist (SLP), and vocational counselor, any one of whom may teach a patient how to manage a weekly schedule or develop organizational strategies needed to return to work. Other patients with severe cognitive impairments may have more limited goals that would allow them to be safe at home alone and perform daily activities without assistance. In this case, the OT and SLP may teach the patient to improve self-care activities, to use a cell phone, and to follow explicit instructions in an emergency.

Some patients may benefit from modular intervention aimed at strengthening specific skills. For example, patients who have trouble paying attention in noisy settings or have trouble switching their attention from one task to another may benefit from a combination of direct attention training, education about attention problems, and practical tools to manage attention problems at home, school, or work. And as patients return home or move to an alternative living environment, CRT can occur within the context in

which the skills will be used. For example, individuals who are returning to school may learn to use study strategies specifically tailored to their postinjury learning style. Providing CRT in context allows both the patient and clinician to focus explicitly on techniques and strategies immediately tested and tried (American Speech-Language-Hearing Association 2003; Ylvisaker et al. 2008). Contextualized therapy may also occur in comprehensive treatment. When contextualized therapy becomes possible, individuals typically become more aware of how their cognitive impairments may impact return to work, school, and community.

Delivery of CRT for Mild TBI

The delivery of CRT to patients with mild TBI may differ from the CRT provided to those with moderate or severe TBI, based on when the diagnosis is made and the specificity of symptoms expressed. In civilians with mild TBI, diagnosis can occur immediately after an athletic activity or other incident such as a motor vehicle accident. Not all mild TBIs are diagnosed immediately, however, due to the ubiquitous nature of the symptoms, which are not always recognized as being related to the incident. Likewise, mild TBI in military populations is frequently missed, and diagnosis occurs much later—sometimes not until the patient attempts to reintegrate into the home, community, work, and school. This fact is particularly true for those who have been injured by blasts, as discussed in Chapter 3 (Adamson et al. 2008). When this type of injury occurs, ideally the CRT provided would be individualized to the patient's needs, as would other treatments to address coexisting symptoms such as fatigue, headaches, vertigo, and visual deficits. For example, a male patient with mild TBI may have difficulty paying attention, and thus difficulty keeping track of a daily schedule. An OT or SLP would first educate him about the injury and symptoms; instruct him to use the calendar on an electronic device; have him log his activities and symptoms (e.g., fatigue or headaches) throughout the week so that an activity management plan could be put in place; and assist him in organizing the materials he needs to learn for work. *Clinical Practice Guidelines for Mild TBI*, from the U.S. Department of Veterans Affairs (VA)/U.S. Department of Defense (DoD), outlines management of concussion or mild TBI, including CRT for those who need it (VA/DoD 2009). Unfortunately, it is unclear how many service members and veterans with TBI receive this care.

PROVIDERS

Describing the roles of the professionals from the various disciplines that deliver CRT may help provide context for its definition and attributes

(as described in Chapter 4). The following sections provide descriptions of rehabilitation professionals and their role on the rehabilitation team. In general, an interdisciplinary team of rehabilitation professionals delivers CRT interventions to patients and provides education, training, and support to families or caregivers. These professions include medicine (physiatry, neurology), nursing, clinical or neuropsychology, speech-language pathology, occupational therapy, and physical therapy (Prigatano 2005). Other members of the rehabilitation team may include an audiologist, kinesiotherapist, neuro-ophthalmologist, or rehabilitation counselor. The shared intention among disciplines is to improve patients' cognitive impairments that interfere with the ability to function, or help patients learn to function more fully with persistent cognitive impairments, irrespective of strategy. In other words, rehabilitation aims either to restore functioning of an impaired cognitive system or compensate for the adverse effects of an impaired cognitive system by providing strategies and supportive aids or techniques.

Professional associations, such as the American Occupational Therapy Association, the American Physical Therapy Association, and the American Speech-Language-Hearing Association, determine the required education and training for providers to become credentialed. U.S. states regulate the licensing requirements for each profession, including education necessary to obtain a license. Requirements for licensing and credentialing of rehabilitation providers vary across states. Furthermore, general certification does not indicate all certified professionals are qualified to provide cognitive rehabilitation. Table 5-1 provides information for rehabilitation professionals services, education and training, licensing and credentialing, and the setting in which they work. Due to the diversity of requirements and certifications, the committee did not assess or compare U.S. state requirements for licensing and credentialing. However, the committee recognizes the authority of these licensing entities and the consideration of rigorous standards in establishing quality of care within respective disciplines.

Overall, rehabilitation professional organizations do not provide or promote continuing education credits in brain injury rehabilitation. However, a voluntary certification is available from the Academy of Certified Brain Injury Specialists (ACBIS). To become a Certified Brain Injury Specialist (CBIS), a professional must demonstrate 500 hours of supervised clinical practice as well as pass the national certification exam provided by ACBIS. No education level is required beyond a high school diploma or the equivalent. The certification exam includes topics such as brain anatomy, brain-behavior relationships, functional impact of brain injury, effective treatment approaches and medical management, as well as the role of families, and legal or ethical issues (ACBIS 2010). In 2010, ACBIS reported 4,207 individuals in the United States were CBISs. As previously

TABLE 5-1 CRT Providers: Services, Practice Requirements, and Professional Setting

Provider	Services	Education and Training	Licensing and Certification	Professional Settings
Clinical Psychologist, Neuro-psychologist 170,200 psychologists	• Assesses, diagnoses, treats, and prevents mental disorders • Uses a variety of approaches aimed at helping individuals through individual, family, or group therapy • Designs and implements behavior modification programs *Neuropsychology is a specialization within clinical psychology.*	• Doctor of Philosophy (Ph.D.) or Doctor of Psychology (Psy.D.) • Courses in quantitative experimental methods and research design, which include the use of computer-based analysis, are an integral part of graduate study and are necessary to complete the dissertation. • An approved internship • 1 to 2 years of post-doctoral, supervised professional experience	The American Psychological Association (APA) accredits doctoral training programs in clinical psychology. U.S. states' licensing boards determine requirements for clinical psychologists. Requirements vary by state, and generally include passing a standardized test and may include continuing education for license renewal.	• Community mental health centers • Crisis counseling or drug rehabilitation centers • Physical rehabilitation settings • Private offices • Hospitals • Universities and medical schools
Neurologist	• Examines patients with neurologic disorders (e.g., brain injury) or impaired function of the brain, spinal cord, peripheral nerves, muscles, autonomic nervous system, and related blood vessels • Generally sees patients referred by other physicians, but can serve as the primary physician for ongoing neurological disorders	• Doctor of medicine (M.D.) • 4 years of residency, specializing in neurology • Internship	The American Board of Psychiatry and Neurology oversees the competency examination to certify neurologists. Board certification ensures specialized skills and knowledge to diagnose and treat specific problems and to provide medical management for a range of problems.	• Hospitals • Outpatient clinics

	• Investigates, diagnoses, and treats neurological disorders. Diagnostic tests include: ▪ Computed axial tomography (CAT) ▪ Magnetic resonance imaging (MRI) ▪ Ultrasound ▪ Electroencephalography (EEG) ▪ Electromyography (EMG)		U.S. states regulate the licensing of physiatrists, and requirements vary by state. Licensing requires physicians pass the U.S. Medical Licensing Examination (USMLE).	
Registered Nurse > 10,000 rehabilitation nurses ~ 3,000 neuroscience nurses	• Assesses, plans, implements, and evaluates the care of a hospitalized patient • Promotes optimal functioning • Works with physicians (e.g., physiatrist or neurologist) to obtain detailed patient history and a comprehensive evaluation • Provides patient and family education, behavior management, and management of the patient environment	• Education levels vary among registered nurses (RNs) • Education includes courses in anatomy, physiology, microbiology, chemistry, nutrition, psychology, other behavioral sciences, and nursing. • Supervised clinical experience required	*Rehabilitation nurses* are credentialed as a Certified Rehabilitation Registered Nurse (CRRN). The Association for Rehabilitation Nurses oversees the certification of CRRNs. Requirements for CRRN certification include 2 years of recent practice in rehabilitation nursing, or a combination of one year of current practice as an RN and 1 year of graduate study. .	• Acute care • Assisted living facilities • Community re-integration programs • Hospitals • Outpatient clinics • Rehabilitation units or programs • Residential communities • Universities and medical schools

continued

TABLE 5-1 Continued

Provider	Services	Education and Training	Licensing and Certification	Professional Settings
			Neuroscience nurses are credentialed as a Certified Neuroscience Registered Nurse (CNRN). The American Association of Neuroscience Nurses oversees the certification of CNRNs. Requirements include 4,160 hours of recent experience in neuroscience nursing practice and passing a certification examination. U.S. states regulate the licensing for registered nurses (RNs), generally requiring graduation from an approved nursing program and passing the National Council Licensure Examination (NCLEX-RN).	

Physiatrist ~ 8,300 board certified physiatrists	• Trained in the physical medicine and rehabilitation (PM&R) specialty • Aims to restore maximum function lost through injury, illness, or disabling conditions, affecting any organ system • Provides assessment, diagnosis, and nonsurgical interventions • Develops treatment plans and leads a team of medical professionals • Facilitates education to patients and families about impairments	• Doctor of medicine (M.D.) • 4 years of residency, specializing in physical medicine and rehabilitation • Internship	The American Board of Physical Medicine and Rehabilitation (ABPMR) oversees the competency examination to certify physiatrists. Board certification ensures skills and knowledge to diagnose and treat specific problems and to provide medical management for a range of conditions. U.S. states regulate the licensing of physiatrists, and requirements vary by state. Licensing requires physicians pass the U.S. Medical Licensing Examination (USMLE).	• Hospitals • Outpatient clinics • Private offices • Rehabilitation centers

continued

TABLE 5-1 Continued

Provider	Services	Education and Training	Licensing and Certification	Professional Settings
Physical Therapist 185,500 physical therapists	• Evaluates and diagnose movement dysfunction and use interventions to treat patient/clients • May provide therapeutic exercise, functional training, manual therapy techniques, assistive and adaptive devices and equipment, and physical agents and electrotherapeutic modalities • Often consults and practices with a variety of other professionals, such as physicians, nurses, social workers, occupational therapists, and speech-language pathologists	• Education levels vary among PTs. • Education includes: • Science courses (biology, anatomy, physiology, cellular histology, exercise physiology, neuroscience, biomechanics, pharmacology, pathology, and radiology/imaging) • Behavioral science courses (evidence-based practice and clinical reasoning) • Clinically based courses (medical screening, examination tests and measures, diagnostic process, therapeutic interventions, outcomes assessment, and practice management) • Supervised clinical experience	The American Physical Therapy Association's accrediting body, Commission on Accreditation of Physical Therapy Education (CAPTE), accredits academic programs in physical therapy. U.S. states regulate the licensing and practice of physical therapy. Requirements vary by state, but typically include graduation from an accredited physical therapy education program; passing the National Physical Therapy Examination; and fulfilling other state requirements such as jurisprudence exams.	• Hospitals • Outpatient clinics • Private offices with specially equipped facilities

Speech-Language Pathologist 119,300 speech-language pathologists	• Assesses, diagnoses, and treats communication disorders associated with cognitive, language and speech impairments • Understands communication behavior and the underlying neurology, cognitive, sensory and motor processes that are required to communicate • Addresses the impact of cognitive and communication disorders in activities and participation in society	• Master's degree • Supervised clinical experience • 300 to 375 hours of supervised clinical experience • 9 months of postgraduate professional clinical experience	The Council on Academic Accreditation is an entity of the American Speech-Language-Hearing Association (ASHA) that accredits postsecondary academic programs in speech-language pathology. U.S. states regulate the licensing. Requirements vary by state, but generally include graduation from an ASHA-accredited program and passing a national exam, the Praxis Examination in Speech-Language Pathology.	• Assisted living facilities • Community re-integration programs • Hospitals, acute care • Rehabilitation units or programs • Residential communities • Schools and vocational programs
Occupational Therapist 104,500 occupational therapists	• Helps patients regain functioning within home, work or school, or community settings • Determines impact of impairments on everyday activities, incorporating knowledge of neurology and neuro-anatomy • Measures functional loss and design an intervention plan, from acute care to community reintegration	• Education criteria includes: • Master's degree or higher, and • Courses in biology, chemistry, physics, health, and the social sciences. • Supervised fieldwork	The Accreditation Council for Occupational Therapy Education (ACOTE) accredits educational programs. U.S. states regulate licensing criteria for OTs, and requirements vary by state. Licensing usually requires passing an exam approved by the National Board for Certification in Occupational Therapy (NBCOT).	• Ambulatory healthcare services • Community care facilities • Home healthcare services • Hospitals • Nursing care facilities • Outpatient care centers • Physicians' offices

mentioned, providers are not required to obtain certification, and many more professionals may be qualified via completed supervisory hours to provide cognitive rehabilitation services.

Physiatrist

Physiatrists are physical medicine and rehabilitation physicians with expertise in treating the impairments and disabilities resulting from a variety of conditions. Board-certified physiatrists in the United States are trained to diagnose, treat, and direct a rehabilitation plan to achieve optimal patient outcomes. The physiatrist provides leadership for an interdisciplinary rehabilitation team that may include occupational therapists, physical therapists, recreational therapists, rehabilitation nurses, psychologists, social workers, and speech-language pathologists. Based on a medical evaluation, the physiatrist designs and coordinates a treatment plan to address the whole person, considering physical, cognitive, emotional, and social needs. Treatment plans aim to maximize functional capacity and restore quality of life as much as possible. Physiatrists include the family or primary caregiver in an overall rehabilitation program and arrange family conferences as necessary (AAP 1999). Physiatrists earn a medical degree and complete a residency in physical medicine and rehabilitation; they receive certification from the American Board of Physical Medicine and Rehabilitation.

Physiatrists can prescribe pharmacological and behavioral interventions for the treatment of related disturbances occurring as a result of brain injury. The range of psychiatric disturbances that may follow brain injury is extensive (see Chapter 3). Preinjury conditions such as personality disorders, psychiatric disturbance, and genetic predisposition may also complicate recovery from brain injury. Physiatrists are trained to address these conditions or provide the most appropriate referral to another specialist on the team.

Neurologist and Neurosurgeon

A neurologist is a medical doctor specializing in diagnosing, treating, and managing disorders of the brain and nervous system. A neurologist assesses and treats neurological deficits resulting from TBI, with emphasis on physical impairments, such as movement disorders, seizures, and pain. Neurologists may also address neurobehavioral conditions, such as mood problems, or cognitive conditions, such as memory deficits. A neurologist can help distinguish between varied disorders (for example, mild TBI shares symptoms of other neurogenic disorders), and then design the most appropriate treatment plan for the patient, as treatment plans may not be identi-

cal for these different conditions. Neurologists earn a medical degree and complete a residency in neurology, which includes training in rehabilitation aspects of neurology as well as behavioral and cognitive neurology; they receive certification from the American Board on Psychiatry and Neurology. Neurologists can recommend surgical treatment, but they do not perform surgery. When treatment includes surgery, neurologists may monitor the patients and supervise their continuing treatment. Neurosurgeons are medical doctors who specialize in performing surgical treatments of the brain or nervous system; neurosurgeons are typically involved primarily in the acute phase. Neurosurgical evaluations diagnose or rule out the presence of conditions requiring neurosurgical attention (e.g., hematomas, skull fractures, elevated intracranial pressure), or deliver differential diagnoses that may require other, focused treatments.

Registered Nurse

The registered nurse (RN) is responsible for the assessment, planning, implementation, and evaluation of the care of a hospitalized patient with a brain injury. The RN's activities serve to promote optimal functioning. For example, the RN's role in cognitive rehabilitation includes working with physicians (e.g., physiatrist or neurologist) to obtain detailed patient history and a comprehensive neurological evaluation. In addition, nursing care includes patient and family education, behavior management, and management of the patient environment (U.S. Department of Labor 2011a).

Registered nurses must graduate from an accredited school of nursing and pass a state RN licensing examination called the National Council Licensure Examination for Registered Nurses (NCLEX-RN). A nurse providing rehabilitative care to patients with TBI may be either a Certified Rehabilitation Registered Nurse (CRRN) or a Certified Neuroscience Registered Nurse (CNRN). The Association for Rehabilitation Nurses comprises autonomous programs to oversee the certification of CRRNs. The American Board of Neuroscience Nurses oversees the certification of CNRNs. The American Board of Nursing Specialties accredits these speciality organizations. In 2011, the Association of Rehabilitation Nurses (ARN) and the American Association of Neuroscience Nurses (AANN) jointly published a clinical practice guideline for care of patients with mild TBI.

Occupational Therapist

An OT is the function expert who works with patients across the lifespan of the treatment to improve everyday function in daily routines. Common OT interventions include helping people who are recovering from brain injury to regain skills as they experience physical and cognitive

changes (e.g., visual deficits, cognitive and perceptual abilities to perform tasks in complex and multi-stimuli environments). The OT completes an individualized and comprehensive assessment of patients' skills and treatment goals, often with support from patients and their family or caregiver. The OT designs customized interventions to improve patients' ability to perform daily activities and reach their goals. Treatment goals are designed to enable patients to best manage their daily tasks, including self-care (feeding and dressing) and tasks in the community (shopping, driving, school, and work activities). Throughout treatment, OTs evaluate patient outcomes to ensure goals are being met and change the intervention plan as appropriate (American Occupational Therapy Association 2002, 2011).

To accomplish overall treatment goals, patients may need to use special techniques, modify their physical environment, or use equipment ranging from simple memory aids to more advanced computers and environmental controls. To help them with these tasks, OTs provide services such as a comprehensive evaluation of the patient's home and other environments (e.g., workplace, school), recommendations for adaptive equipment and training in its use, and guidance and education for family members and caregivers (American Occupational Therapy Association 2002, 2011).

Together with SLPs, OTs are among typical providers of CRT (Ashley and Persel 2003). The minimum requirement for entry into occupational therapy is a master's degree from an academic program accredited by the Accreditation Council for Occupational Therapy Education (ACOTE). For national accreditation and licensure, OTs must pass an exam provided by ACOTE. Those who pass the exam become an Occupational Therapist Registered (OTR). The American Occupational Therapy Association oversees the certification program by which OTs confirm their competencies. An OT may receive certification by board (e.g., physical rehabilitation or mental health) or specialty (e.g., driving and community mobility, feeding or swallowing). These certifications are renewed every 5 years, and qualified OTs must have completed a specific number of practice hours in order to be eligible (Golisz 2009).

Physical Therapist

Physical therapists provide assessment and treatment for balance disorders, dizziness, functional mobility, physical problems, and pain, all of which may result from or be related to TBI. Physical therapists can evaluate and address peripheral nerve and musculoskeletal injuries as well as weakness and balance issues related to brain trauma. Treatment goals include improving mobility, increasing strength, decreasing joint stiffness, improving static and dynamic balance, decreasing vertigo and dizziness, and

managing pain and discomfort. Physical therapists also evaluate a patient's need for equipment, such as canes or braces, to improve safety and endurance. Physical therapists practice in hospitals, outpatient clinics, and private offices that have specially equipped facilities (American Physical Therapy Association 2003).

Typical requirements for physical therapists include a graduate degree from an accredited physical therapy education program; passing the National Physical Therapy Examination; and fulfilling state requirements such as jurisprudence exams. A number of states require continuing education as a condition of maintaining licensure. The American Physical Therapy Association's accrediting body, the Commission on Accreditation of Physical Therapy Education (CAPTE), accredits graduate degree academic programs in physical therapy. These programs include foundational science courses such as biology, anatomy, physiology, cellular histology, exercise physiology, neuroscience, biomechanics, pharmacology, pathology, and radiology/imaging, as well as behavioral science courses such as evidence-based practice and clinical reasoning. Some of the clinically based courses include medical screening, examination tests and measures, diagnostic process, therapeutic interventions, outcomes assessment, and practice management. In addition to classroom and laboratory instruction, students receive supervised clinical experience (U.S. Department of Labor 2011b).

Speech-Language Pathologist

SLPs assist patients who have speech, language, and cognitive problems in gaining optimal communication skills. For patients with cognitive impairments from TBI, SLPs evaluate and provide intervention for the underlying cognitive deficits responsible for communication behavior in everyday life. Communication problems may include difficulty understanding complex and abstract written or verbal information, finding words and expressing coherent ideas, and using language in interpersonal relations. SLPs also address transitions to school and work. Underlying cognitive problems that may be caused by TBI, such as difficulty paying attention, learning and remembering information, organizing ideas, reasoning, and solving problems, all interfere with communication skills and the ability to broadly interact in the environment (school, work, home, or community). The American Speech-Language-Hearing Association (ASHA) endorses the use of the WHO-ICF to describe management of cognitive and communication disorders after TBI.

Together with OTs, SLPs are among the most typical providers of CRT (American Speech-Language-Hearing Association 2005; Ylvisaker et al. 2003). Typical licensing requirements are a master's degree from an accredited college or university; a passing score on the Praxis Examinations

in Audiology and Speech-Language Pathology, the national examination for certification in speech-language pathology, offered through the Praxis Series of the Educational Testing Service; 300 to 375 hours of supervised clinical experience; and 9 months of postgraduate professional clinical experience. Most states have continuing education requirements for licensure renewal. Medicaid, Medicare, and private health insurers generally require a practitioner to be licensed to qualify for reimbursement. The Council on Academic Accreditation, an entity of ASHA, accredits postsecondary academic programs in speech-language pathology. Furthermore, a graduate degree is required for ASHA credentialing. Speech-language pathology courses cover anatomy, physiology, and the development of the areas of the body involved in speech, language, and swallowing; the nature of disorders; principles of acoustics; and psychological aspects of communication. SLP graduate students may also learn to evaluate and treat speech, language, and swallowing disorders as part of a curriculum in supervised clinical practice (U.S. Department of Labor 2011c).

Neuropsychologist

A neuropsychologist (psychologist) is the key player in diagnosing cognitive impairments and emotional and behavioral sequelae of TBI. A neuropsychological assessment evaluates the areas of intellectual functioning: attention and concentration, problem solving and judgment, memory and learning, and flexibility of thought and speed of information processing. Evaluations in these areas help patients and families understand the nature and severity of deficits and assist other team members when planning patient treatment programs. Treatment services provided by neuropsychologists are designed to help patients achieve maximum benefit from the rehabilitation program and to help them manage adjustment problems. Counseling may be offered to patients and family members who wish to know more about brain injury and who may be having difficulty coping with family and/or work-related stress.

Clinical neuropsychologists are a subset of psychologists "dedicated to the understanding of brain–behavior relationships and applying this knowledge to human problems, in particular to persons with brain disorders" (CRSPPP 1996). The recommended education and training for licensure and accreditation includes a graduate degree in professional psychology, and relevant brain–behavior knowledge and clinical neuropsychology practice skills. Knowledge and skills are generally developed through a doctoral program and related internships (Boake 2008).

Recreational Therapist

Recreational therapists assist people with brain injury in resuming community life by helping them participate in play and leisure activities. Through leisure counseling, leisure education, leisure skills development, aquatic education, adaptive sports, resocialization programs, and community readjustment outings, people with brain injury learn how to participate in community life. Recreational therapists assess individuals through observations; medical records; standardized assessments; and consultations with medical members of the rehabilitation team, with patients themselves, and with their families. Recreational therapists use this information for developing and implementing therapeutic interventions consistent with clients' goals. For example, a recreational therapist may encourage a client who is isolated from others or who has limited social skills to play games with others. Therapists may teach right-handed people with right-side paralysis how to use their unaffected left side to throw a ball or swing a racket. Recreational therapists may teach patients relaxation techniques to reduce stress and tension, stretching and limbering exercises, proper body mechanics for participation in recreational activities, pacing and energy conservation techniques, and team activities (U.S. Department of Labor 2011d).

In acute settings such as hospitals and rehabilitation centers, recreational therapists treat individuals with specific health conditions, usually in conjunction or collaboration with physicians, nurses, psychologists, social workers, and physical and occupational therapists. In long-term and residential care facilities, recreational therapists use leisure activities—specially structured group programs—to improve and maintain patients' general health and quality of life. Community-based recreational therapists may work in park and recreation departments; special education programs within school districts; or assisted living, adult day care, and substance abuse rehabilitation centers. In these facilities, they work on specific skills with patients and provide opportunities for exercise, mental stimulation, creativity, and fun (U.S. Department of Labor 2011d).

Most entry-level recreational therapists need a bachelor's degree in therapeutic recreation. A few may qualify with some combination of education, training, and work experience that would be equivalent to competency in the field. Therapeutic recreation education programs include courses in assessment, treatment and program planning, intervention design, and evaluation. Education also includes the study of human anatomy, physiology, abnormal psychology, medical and psychiatric terminology, characteristics of illnesses and disabilities, professional ethics, and the use of assistive devices and technology. Work in clinical settings often requires certification by the National Council for Therapeutic Recreation Certification. The

Council offers the Certified Therapeutic Recreation Specialist credential to candidates who pass a written certification examination and complete a supervised internship of at least 480 hours. Therapists must meet additional requirements to maintain certification (U.S. Department of Labor 2011d).

Social Worker

Social workers help patients and their families respond to social, emotional, or financial problems resulting from physical disability or chronic illness. Treatment modalities include individual and group psychotherapy, crisis intervention, family counseling, and family support groups. Social workers explore community resources and entitlement programs available to the patient and family. They may arrange for at-home services, such as meals-on-wheels or home care. Some social workers help people who face a disability, life-threatening disease, substance abuse, or social problem, such as inadequate housing or unemployment. Social workers also assist families who have serious domestic conflicts, sometimes involving child or spousal abuse. Some work on interdisciplinary teams that evaluate and treat certain kinds of patients, such as geriatric or organ transplant patients. Many social workers specialize in serving a particular population or working in a specific setting, such as a hospital, nursing and personal care facility, individual and family services agency, or local government (U.S. Department of Labor 2011d). In all settings, these professionals may be called Licensed Clinical Social Workers (LCSWs) if they hold the appropriate license. Additionally, social workers may conduct research, advocate for improved services, or become involved in planning or policy development.

A bachelor's degree in social work is the most common minimum requirement to become a social worker; however, majors in psychology, sociology, and related fields may qualify for some entry-level jobs, especially in small community agencies. Although a bachelor's degree is sufficient for entry into the field, an advanced degree is required for some positions. A Master of Social Work (MSW) is required for clinical work and typically required for positions in other health or school settings. U.S. states maintain the licensing, certification, or registration requirements regarding social work practice. Most states require 2 years or 3,000 hours of supervised clinical experience for licensure of clinical social workers (U.S. Department of Labor 2011e).

Other Members of the Rehabilitation Team

Audiologist

Audiologists evaluate hearing deficits and determine the type of hearing loss. Hearing changes after TBI may include tinnitus or loss of acuity, especially in noisy environments. Hearing aids may or may not be prescribed,

depending upon the nature and severity of the problem. Audiologists may also be involved in diagnosing vestibular deficits (i.e., vertigo) that may lead to balance problems. A doctoral degree from an accredited institution is required to practice as an audiologist. The Council on Academic Accreditation (CAA)—an entity of the ASHA—accredits education programs in audiology. U.S. states regulate licensing.

Kinesiotherapist

A kinesiotherapist can recommend a cardiovascular conditioning program that promotes wellness and reduces the risk of injury or further disability, generally to improve extended periods of physical exertion. The American Kinesiotherapy Association defines kinesiotherapy as "the application of scientifically based exercise principles adapted to enhance the strength, endurance, and mobility of individuals with functional limitations or those requiring extended physical conditioning" (American Kinesiotherapy Association 2011). Because fitness can enhance a person's mental and physical stamina, reduce pain, and elevate feelings of well being, the goals of kinesiotherapy align well with CRT. The physical conditioning program should be initiated in the health care facility and gradually transferred to a community gym as the person becomes more independent. Kinesiotherapists work with physicians or nurses on the rehabilitation team who prescribe and direct services for patients, which then is delivered by kinesiotherapists. Kinesiotherapy is commonly provided to soldiers due to the extended physical exertion often required by military profession.

Neuro-Ophthalmologist

Neuro-ophthalmology is a subspecialty of both neurology and ophthalmology. Neuro-opthalmologists may address double vision, blurry vision, or other visual deficits following brain injury. Deficits in the visual system are often overlooked in mild TBI. A common visual deficit after mild TBI is convergence insufficiency, which is often described by the person as "blurry" vision. The neuro-ophthalmology evaluation should rule out potential eye damage involving the cornea, retina, vitreous fluids, occipital lobe (visual cortex), and optic nerve functioning. Therapeutic intervention may involve prism glasses and/or eye exercises. Training and education follows the guidelines for physicians pursuing a subspecialty, with the accompanying residencies and certifications.

Rehabilitation Counselor

Rehabilitation counselors deal with the key issues regarding work reentry. They consult, and may provide a vocational evaluation covering

vocational interest, work values, academic testing, etc., to complement the neuropsychological evaluation in setting work-relevant goals. Rehabilitation counselors may act as a treatment coordinator for patients who have difficulty returning to work after brain injury. Some rehabilitation counselors set up community-based functional vocational evaluations or may do active job placement and retention. In addition, rehabilitation counselors may help develop collaborative relationships between clients and their employer or coworkers. Licensed rehabilitation counselors often must have a master's degree. U.S. states regulate licensing for counselors. Voluntary certification is available through the Commission on Rehabilitation Counselor Certification.

CONCLUSION

The overall goal of rehabilitation is to improve functioning and quality of life of the patient with chronic disease or disability. Factors such as who provides CRT and for how long is it provided are interrelated factors that vary depending on the patient's needs and ability for participating in rehabilitation. Providers work in multi-disciplinary teams to design and implement treatments plans that meet the goals of patients and their families. Because U.S. states regulate the licensure requirements for each profession, and a variety of professional organizations determine accrediting standards, a unified brain injury rehabilitation specialty or related requirements do not exist for most professions.

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PART II:
REVIEW OF THE EVIDENCE

6

Methods

This chapter describes the methods by which the committee evaluated the evidence regarding the efficacy and effectiveness of cognitive rehabilitation therapy (CRT) for traumatic brain injury (TBI), including the means by which the committee searched for and organized the literature. The chapter also includes an assessment of the quality of study design and its related impact on how the studies were evaluated. The committee searched for and reviewed evidence of CRT interventions by either specific cognitive domain (i.e., memory, attention, executive function, visuospatial perception, and communication and language) or multi-modal/comprehensive CRT.

The committee iteratively developed a protocol to address the following questions:

- *Do cognitive rehabilitation interventions improve function and reduce cognitive deficits in adults with mild or moderate-severe TBI?*
- *Are any cognitive rehabilitation interventions associated with risk for adverse events or harm?*
- *Are cognitive rehabilitation interventions delivered through telehealth technology safe and efficacious?*

LITERATURE REVIEW

The committee reviewed published systematic reviews (Cicerone et al. 2000, 2005, 2011; ECRI 2009; Kennedy et al. 2008) and worked with a research librarian to develop search strategies to identify pertinent evidence. The strategy included searches in the following electronic bibliographic

databases: Medline, EMBase, PsycInfo, Education Resources Information Center (ERIC), and Cochrane (e.g., Cochrane DB of Systematic Reviews, Database of Reviews of Effects [DARE] and Cochrane Central Register of Controlled Trials). Key terms and Medical Subject Headings (keywords for Medline) focused on subject areas related to brain injury and CRT. Strategy parameters limited searches to human subjects, the English language, and results published between January 1991 and April 2011. The time period was chosen to include articles prior to Operation Desert Storm, which began in 1991. Setting time parameters allowed for the evaluation of the most recent research of relevance, acknowledging that more recent studies build on the evidence base created by older literature. Furthermore, because TBI has occurred more frequently among service members in recent conflicts, beginning with Operation Desert Storm, research in the field of TBI and CRT has greatly expanded since that time. To ensure it captured all relevant studies, the committee conducted a secondary search to identify articles not found during the electronic search. This practice is common when conducting a literature review. To complete the secondary search, the committee extensively examined the bibliographies of previously published systematic reviews on cognitive rehabilitation therapy for TBI, reading all full-text articles contained in those reference lists that had not been identified in the primary search. The committee determined it would include studies from these reference lists that met inclusion criteria (as described in Box 6-1), regardless of publishing date. The committee reviewed many excellent studies during this process; however, not all studies met inclusion criteria. The secondary search identified 12 additional articles, 2 of which were published prior to 1991. No other study published prior to 1991, that the committee reviewed, met inclusion criteria.

The committee focused on studies that used one or several forms of CRT to ameliorate the effects of traumatic brain injury. Per its charge, the committee considered CRT for TBI across all severities of injury (mild and moderate-severe) and across all stages of recovery (acute, subacute, and chronic). For the purposes of this review, the committee defined the time periods for acute, subacute, and chronic phases of recovery following TBI (see Table 6-1). The searches limited the scope of terms to traumatic brain injury, and did not consider other forms of acquired brain injury, such as those due to stroke, ischemia, infection, or malignancy. Similarly, the committee did not review literature on the effects of CRT for non-TBI cognitive conditions, such as schizophrenia, dementia, or learning disabilities.

The initial electronic search identified 856 studies. Upon review of titles and abstracts, 121 studies were selected for more detailed review. At least two committee members reviewed each full text article to determine relevancy, based on the committee's inclusion and exclusion criteria, shown in Box 6-1. Upon full-text review, 43 studies were excluded. An additional

BOX 6-1
Inclusion and Exclusion Criteria

1.0 Participants

1.1 Sample is composed of individuals with TBI (open or closed, with or without secondary hypoxic/ischemic injury), as evidenced by

a. Initial loss/alteration of consciousness on clinical assessment (abnormal GCS or posttraumatic amnesia); OR
b. Findings on neuro-imaging consistent with TBI; OR
c. Focal impairment on neurologic exam consistent with TBI; OR
d. Documentation of injury for patients with mild TBI (plausible history is sufficient for patients with moderate-severe TBI);

OR

1.2 Sample is mixed between TBI and non-TBI but results are reported separately for TBI subjects (who meet the above definition); OR
1.3 Sample is mixed but contains a majority of TBI participants; AND
1.4 Sample is composed of individuals age 18 or older.

2.0 Treatment

2.1 The intervention is sufficiently described for classification/categorization as CRT; AND
2.2 Studies that primarily evaluated drug efficacy are excluded.

3.0 Outcome Measures

3.1 Outcome measure(s) could be either objective or subjective measures; AND
3.2 Studies where the only outcome measures are performance of tasks that were directly practiced in the treatment protocol are excluded.

4.0 Study Design

4.1 Uncontrolled case reports or case series are excluded.
4.2 Single subject experimental designs (i.e., designs focusing on outcome within a subject, while incorporating experimental controls) are included.
4.3 For pre-post studies conducted during a postinjury period and over a duration in which substantial change might be expected in the primary outcome(s), studies with no comparison group (since measured improvement may be "spontaneous") (e.g., if mild TBI occurred over 6 months or fewer, and moderate-severe TBI occurred over 12 months or fewer) are excluded.
4.4 For studies conducted in a postacute period, pre-post studies with no comparison group and only subjective self-report outcomes (which may be strongly affected by expectation) are excluded.

5.0 Other

5.1 Only studies available in the English language are included.

TABLE 6-1 Definitions of Acute, Subacute, and Chronic Phases of Recovery Post-TBI

	Mild TBI	Moderate-Severe TBI
Acute	< 3 months	Acute hospital care
Subacute	> 3 months < 6 months	Inpatient rehabilitation
Chronic	> 6 months < 12 months	Outpatient rehabilitation

12 studies were added through the secondary search (i.e., culling reference lists), for a total of 90 studies upon which the committee based its conclusions.

The committee designed forms for extracting and summarizing data from each study, including information about study design and methods, patient characteristics, treatment interventions and outcomes (i.e., World Health Organization International Classification of Functioning, Disability and Health [WHO-ICF] framework), and funding source. The Institute of Medicine (IOM) contracted two individuals with knowledge and expertise in CRT to extract data from selected studies; these individuals (i.e., coders) were neither IOM staff nor members of the committee. At least two committee members read each of the original articles and compared information from the studies to the evidence tables completed by the independent coders. The committee assessed methodologic limitations of studies, described each study, and synthesized the evidence in a narrative form.

The committee conceptually categorized CRT interventions as either (1) modular strategies aimed at attention, memory, executive function, language or social communication, or visuospatial deficits or (2) multimodal, comprehensive strategies. The intent of the therapy was categorized as restorative or compensatory and the goals and setting of therapy as decontextualized or contextualized. Compensatory strategies for cognitive impairment (e.g., memory aids) that involved changes to the environment were categorized as external; strategies that did not involve environmental changes were categorized as internal. The committee recognizes that conceptual categorizations may not translate to real-world application; these categories were useful for organizing and evaluating of the evidence. The separation between modular and multi-modal/comprehensive strategies was specific to the committee's charge.

EVALUATION OF THE EVIDENCE

The committee found 90 studies that met selection criteria. Of these, 37 were randomized controlled trials (RCTs) (2 of the 37 addressed both memory and attention deficits); 15 were nonrandomized, parallel group

controlled trials; 19 were pre-post single group studies; and 15 were reports of one or more single subject, multiple baseline experiments. Of the studies, 21 addressed multi-modal or comprehensive cognitive rehabilitation, including RCTs, crossover group, nonrandomized controlled parallel group, and pre-post single group designs. Table 6-2 provides information about the number of studies, by design, were identified in each cognitive domain or multi-modal/comprehensive CRT.

The committee did not identify any CRT studies in the acute phase of recovery following TBI. Several studies of multimodal/comprehensive treatment programs were conducted in the subacute phase, but most of the modular treatment studies were conducted in the chronic phase. Few studies included in this review specifically enrolled individuals with mild TBI, or reported results separately for those with mild injuries who were enrolled in mixed studies. Where evidence exists with respect to treatment of participants in the subacute phase, or those with mild injuries, the committee highlighted these studies and relevant findings.

As charged, the committee reviewed evidence across intervention types to determine if there was evidence regarding efficacy or effectiveness in individual cognitive domains and multi-modal/comprehensive CRT. Studies were assessed for improvements in objective measures of benefit, or short- and long-term treatment effects. Studies were also assessed for subjective self-reports by patients or family members of treatment benefit, or patient-centered outcomes. These distinctions are useful because achievements on objective measures of benefit may not translate into improvement in real-world functioning. It is important to note that standards for other aspects of medical practice and research, such as pharmacologic agents, do not require patient-centered outcomes, such as return to work or improved quality of life, to show any treatment benefit or to receive regulatory ap-

TABLE 6-2 Study Design by Treatment Domain or Strategy

Study Design by Treatment Domain or Strategy	Attention	Executive Function	Language and Social Communication	Memory	Multimodal/ Comprehensive CRT
RCTs	6	10	4	13	6
Nonrandomized, Parallel Group	0	4	1	2	8
Pre-Post Single Group	2	4	0	6	7
Single Subject Multiple Baseline	1	8	0	6	0
TOTAL	**9**	**26**	**5**	**27**	**21**

proval or coverage by insurers. Therefore, the absence of patient-centered outcomes did not necessarily detract from a study's evidence base. However, the committee acknowledges that these are important outcomes to report, especially in goal-oriented and interactive rehabilitation. The committee also reviewed studies where use of telehealth technology was employed, to determine the safety and efficacy of CRT applied through these technologies, compared to interventions applied in clinical settings. The potential for adverse effects or harm was also evaluated among the included studies.

Also per its charge, the committee separately evaluated studies by the type of comparator arm, including inert or no treatment, a non-CRT treatment, or another form of CRT. Varying comparators were not considered more or less useful, only that they answer different questions about the value of CRT for TBI. To determine efficacy, the committee relied on studies that compared the primary CRT treatment to either no treatment or a non-CRT treatment. To determine effectiveness, the committee evaluated studies comparing CRT treatment to another form of CRT. Comparative effectiveness studies may be premature without preceding efficacy trials of the interventions applied in each arm. Furthermore, cognitive processes are complex and intertwined. Likewise, treatment activities generally employ multifaceted tasks. Therefore, attempts to predict a highly specific effect of one CRT intervention (e.g., attention process training) on an isolated cognitive process (e.g., attention) is difficult without considering the effect another CRT treatment (e.g., notebook training for a memory deficit) may have on the original cognitive function of interest (e.g., attention). For these reasons, interventions comparing one form of CRT to another were less helpful in determining the impact of a specific intervention to improve a specific cognitive function.

The committee discussed at length the need to establish relevant criteria for interpreting the studies under review to address the study questions asked by the Department of Defense. The committee reached consensus on the grading system shown in Box 6-2.

In an interactive and collaborative process, the committee graded the overall body of evidence for each CRT category (by domain, TBI severity, and recovery phase [for example, CRT interventions for attention in moderate-severe TBI patients in the chronic phase of recovery]). To draw conclusions about treatment efficacy or effectiveness, the committee qualitatively assessed the strength of individual studies, as well as the consistency of treatment effect among studies. The strength of each study was based on an iterative quality assessment, considering study design, size of the sample, reported characteristics of the sample (e.g., injury severity) and treatment (e.g., dosage, frequency, and timing), control for potentially confounding factors, magnitude of the treatment effect, statistical significance of the findings, and the length of follow-up.

BOX 6-2
Evidence Grades

- **None or Not informative (0):** No evidence because the intervention has not been studied or uninformative evidence because of null results from flawed or otherwise limited studies
- **Limited (+):** Interpretable result from a single study or mixed results from two or more studies
- **Modest (++):** Two or more studies reporting interpretable, informative, and largely similar results
- **Strong (+++):** Reproducible, consistent, and decisive findings from two or more independent studies characterized by the following: (1) replication, reflected by the number of studies (multiple, at least two) in the same direction (2) statistical power and scope of studies (N size of the study and single or multi-site); and (3) quality of the study design to measure appropriate endpoints (to evaluate efficacy and safety) and minimize bias and confounding

The committee gave more weight to controlled designs than uncontrolled (e.g., results of RCTs were given more weight than results from pre-post single group designs). Conclusions were not based solely on findings from uncontrolled studies; however, the committee included pre-post single group designs and single subject, multiple baseline experiments in the review because uncontrolled studies may include useful information about nascent interventions or lend support to a controlled design with similar results. Where evidence was informative, the committee specifically identifies the treatment mode and cites the one or more studies that led to its conclusion.

QUALITY OF STUDY DESIGNS

In making its conclusions, the committee found most informative those studies that failed the fewest criteria. Evidence ruled "limited" does not mean an intervention was inadequate; it may simply mean there were methodological flaws in the study design. As is commonly seen among studies evaluating rehabilitation strategies, the overall limitations of the evidence were due to a number of identified issues in study designs. Some of these issues involved the heterogeneity and lack of operational definitions of different forms of CRT; small sample sizes; the variety of premorbid, comorbid, and environmental factors that may moderate the value of a given form of CRT across patients; and the range of outcomes that may be targeted.

None of the included studies were absent of limitations in study design. About one-third of the RCTs were small studies involving fewer than 20 participants, and about 20 percent were larger studies involving more than 50 participants. The severity of TBI was described as moderate or severe in 22 trials and as mild to moderate or mild to moderate-severe in 5 trials, and was unclearly specified in 10 trials. Most trials included participants who were many months postinjury (i.e., chronic TBI). Settings for 7 of the larger trials included a suburban rehabilitation hospital in the northeastern United States (Cicerone et al. 2008), a rehabilitation center in Colorado (Dahlberg et al. 2007), three brain injury units in Sydney, Australia (McDonald et al. 2008), a neuropsychological rehabilitation program at a metropolitan medical center in New York (Rath et al. 2003), a U.S. military medical referral center (Salazar et al. 2000),[1] four U.S. Department of Veterans Affairs' acute inpatient rehabilitation programs (Vanderploeg et al. 2008), and an academic neurosurgical unit in Hong Kong (Zhu et al. 2007). About 20 percent of the trials described adequate methods to generate random allocation sequences and assure allocation concealment. A few trials used quasi-experimental designs that matched patient characteristics such as age and severity of injury before or after randomization. Few reports detailed a priori sample size calculations. Some trial reports provided consort figures or detailed descriptions of follow-up including number of participants randomized to groups, completeness of follow-up, and amount of missing data by group; most trials did not report all of this information. Few trial reports detailed analytic methods that were used to handle missing data or specified numbers of people included in analyses of each outcome measure that was reported. Trials generally evaluated a heterogeneous group of interventions including focused interventions targeted at specific and sometimes narrow deficits and more complex interventions targeted toward multiple deficits. Trials also had heterogeneous comparison groups. Whether participants received co-interventions or ancillary treatments such as antidepressants or pain medications that might augment or interfere with cognitive rehabilitation effects was rarely described. In only a few trials were attempts made to blind personnel administering objective outcome measures to group assignments of trial participants. The limitations of the evidence do not rule out meaningful benefit. The committee did not identify methodological issues in this report to hold CRT research to a higher standard than rehabilitation research at large; it serves merely as an overt discussion of the issues that cloud determination of efficacy and effectiveness.

[1] The committee reviewed Salazar et al. 2000, with Braverman et al. 1999, and Warden et al. 2000.

ORGANIZATION OF THE EVIDENCE CHAPTERS

In the chapters that follow, the committee applies the methods and background knowledge described in the present and previous chapters to assess the available evidence on CRT treatments for TBI-related deficits in attention, executive function, language and social communication, memory, and multi-modal/comprehensive CRT (Chapters 7 through 11, respectively). The committee did not identify any relevant literature for treatment of visuospatial perception deficits, which are more common after stroke than TBI. These five chapters include evidence tables with key information about included studies. Chapter 12 summarizes studies that applied telehealth technology, and Chapter 13 describes possible adverse events or harm from CRT. Conclusions are made within each chapter. Conclusions about the evidence were not compared to the findings of other systematic reviews, which the committee deemed beyond its charge.

Each chapter begins with an overview describing the presentation of studies. As various domains required differential distinctions for proper analysis, the chapters do not follow a consistent format. The evidence is organized by the conceptual categories that provided the most use in drawing overall conclusions, dictated by the available body of evidence. The committee did not interpret the evidence differently within these categories. For example, memory strategies were divided by internal, external, or restorative within mild or moderate-severe TBI. Whereas attention strategies were divided by those found in the subacute or chronic phase of recovery in patients with moderate-severe TBI (as no studies were identified of patients with mild TBI with attentional deficits). When the committee found evidence showing treatment benefit, the conclusions explicitly identify the specific intervention and cite the study in which it was described.

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7

Attention

OVERVIEW

Deficits in attention are more commonly found among individuals with more severe traumatic brain injuries (TBI), and may encompass delayed reaction time, reduced speed of information processing, or challenges with concentration, forgetfulness, or doing more than one thing at a time (e.g., walking and talking). This chapter presents cognitive rehabilitation therapy (CRT) interventions aimed to restore attentional capacity, divided by phase of recovery following moderate-severe TBI (i.e., subacute and chronic). Controlled studies are described in detail within these sections, divided by treatment comparator arm, followed by descriptions of the noncontrolled studies. The committee's conclusions are presented at the end of the chapter.

The committee reviewed six randomized controlled trials (RCTs), including two crossover studies, of treatments intended to improve attention. All six involved modular treatment directed at one or more attentional processes. All used decontextualized treatment materials, and all were categorized as restorative. The trials involved a total of 264 study participants; treatment group sizes in individual trials ranged from 7 to 43 patients. Nearly all of the patients suffered moderate-severe injuries 6 weeks to many months prior to study enrollment. Study participants were generally in their late 20s to early 30s.

The committee did not identify any nonrandomized, controlled parallel group designs of treatments for attention deficits, however it did review two pre-post single group studies and one single-subject, multiple baseline experiment. These studies also employed primarily modular restorative

treatments, and all were delivered to patients in the chronic phase with moderate-severe injuries. The committee did not identify any studies assessing CRT interventions for attention in patients with mild TBI. Table 7-1 presents a summary of all included studies in this review.

MODERATE-SEVERE TBI

Subacute Phase of Recovery

Comparator Group: Non-CRT Content

Gray et al. (1992) compared approximately 17 hours of computer administered modules stressing various dimensions of attention to about 12 hours of recreational computing that excluded externally paced tasks or tasks that required rapid processing and responding. This study found a positive effect of training on psychometric measures of attention, particularly the type that require numerical manipulation in working memory. These effects grew in significance in follow-up compared to the immediate posttreatment measures. This pattern is of some concern, since the median time postinjury was 20 weeks, a point at which natural recovery may be ongoing; therefore, imbalance in the acuity of injury between groups might produce such a result. However, time postinjury was statistically controlled for, and measures of functions unrelated to attention did not show greater improvement in the treatment group, lending some specificity to the findings. In this study nearly half of the subjects had nontraumatic injuries, but the authors report no interaction between diagnosis and treatment benefit. The credibility of this study is compromised due to its nonreporting of sample sizes for analysis posttreatment, especially at the 6-month follow-up. Furthermore, standard deviations of the outcomes were not provided.

Comparator Group: Other CRT Content

Novack et al. (1996) studied participants who were 3 to 6 months postinjury. This study was conducted in an acute inpatient rehabilitation population approximately 3 to 6 weeks postinjury, a time when many of the patients were confused and highly impaired. One group received a structured program of attention training. The other group received a variety of other rehabilitation interventions that involved cognitive rehabilitation components that did not specifically focus on attention. Outcomes were assessed with respect to several psychometric measures of attention as well as the Functional Independence Measure (FIM). Both groups improved significantly from pre- to posttreatment, but to a comparable degree.

TABLE 7-1 Evidence Table: Attention

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
RCT						
Gray et al. 1992	31	Mild, moderate, severe	Patients with attentional deficits randomized to two groups. The treatment group received computerized attention training including: • Reaction time training • Rapid number comparison • Digit symbol transfer • Alternating Stroop program • Divided attention tasks	Y Non-CRT Content: Recreational computing	• Psychometric measures: ▪ Paced Auditory Serial Addition Test (PASAT) ▪ Wechsler Adult Intelligence Scale-Revised (WAIS-R) • Frontal functions: ▪ Wisconsin Card Sorting Test (WCST) ▪ Finger tapping ▪ Word fluency • Other attentional functions: ▪ Letter cancellation ▪ Picture completion ▪ Time estimation	Significant differences between groups on psychometric measures of attention at immediate and six-month follow-up.
McMillan et al. 2002	145	Moderate	Sessions of supervised mindfulness practice using an audiotape obtained from Jon Kabat-Zinn. Participants were asked to practice daily with this tape in the intervening periods.	Y No or Non-CRT Content: • Group with therapist contact and physical exercise (PE) • Group with no treatment	• Test of Everyday Attention • Adult Memory and Information Processing Battery • PASAT • Trail Making Test • Self-reported: ▪ Sunderland Memory Questionnaire ▪ Cognitive Failures Questionnaire ▪ Hospital Anxiety and Depression Questionnaire	Between-group comparison not significant for any measure.

continued

TABLE 7-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
					▪ General Health ▪ Rivermead Post-Concussional Symptoms Questionnaire	
Niemann et al. 1990	26	Moderate-Severe	Computerized attention training with visual, auditory, and divided (i.e., both) training components, further subdivided into focused and alternating attention tasks Training accompanied by feedback and strategy teaching	Y Other CRT Content: Memory training of equivalent duration and intensity	• Attention ▪ Test d2 ▪ PASAT-R ▪ Divided Attention Test ▪ Trail Making Test, Part B • Memory ▪ Rey Auditory Verbal Learning Test-Modified (RAVLT-M) ▪ Block Span Learning Test	Authors report attention group improved significantly more than control on the three measures of attention; memory group improved more than attention group on one measure.
Novack et al. 1996	44	Severe	Hierarchical training of attention skills for lowest level of functioning involved focused and sustained attention, more challenging tasks requiring selective attention, alternating attention, and divided attention. Each level of the hierarchy included multiple tasks.	Y Other CRT Content: Unstructured stimulation program	• Wechsler Memory Scale-Revised (WMS-R) • Single reaction time • Choice reaction time • Functional Independence Measure (FIM)—Activities of Daily Living • FIM—Cognition • Neuropsychological tests: ▪ Logical Memory I and II ▪ Sentence Repetition Test	Between-group comparison not significant for any measure.

					▪ Judgment of Line Orientation ▪ Trail Making Test ▪ Wide-Range Achievement Test-Revised (WRAT-R), arithmetic subtest ▪ Visual imperception	
Ruff et al. 1994	15	Severe	Two groups received two treatments (attention and memory training) delivered via THINKable, a computer-based, multimedia program.	Y Other CRT Content: Group A received attention training, then memory training. Group B received memory training, then attention training.	• Attention ▪ Ruff 2 & 7 Selective Attention test ▪ WAIS-R Digit Symbol ▪ Continuous Performance Test • Memory ▪ Rey Auditory Verbal Learning Test ▪ Corsi Block Learning Test • Behavioral assessments	Attention measures at posttreatment did not show significant between-group comparison.

continued

TABLE 7-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Sohlberg et al. 2000	14	Moderate-Severe	Compares Attention Process Training (APT) to education, delivered to two groups in a crossover design. APT aims to improve memory, learning, and some aspects of executive control.	Y No or Non-CRT Content: Placebo—Brain Injury Education and Supportive Listening	• Neuropsychological attention tests: ▪ Trail Making Test ▪ PASAT ▪ Gordon Diagnostic ▪ Controlled Oral Word Association Task (COWAT) ▪ Covert Orienting ▪ Continuous Performance Task ▪ Stroop task ▪ Sternberg tasks • Self-report: ▪ Attention Questionnaire ▪ Brock Adaptive Functioning Questionnaire (BAFQ) ▪ Dysexecutive Questionnaire (DEX)	Training showed improvement on PASAT, Stroop, and Trail Making Test. Patients reported a significant difference in attention and memory in the treatment group versus education. Subjects with greater changes had improved score on PASAT. Significant more reports of improvement to daily life (via questionnaires) were given by participants after APT.
Pre-Post Single Group						
Park et al. 1999	23	Moderate-Severe	Examined the use of the Attention Process Training (APT) to determine if APT improves cognitive function versus learning specific skills.	N	• PASAT • Consonant trigrams (Brown-Peterson task) • Beck Depression Inventory (BDI)	Post-testing showed significant improvement on PASAT and Consonant trigrams. No significant improvement on BDI. Results are mediated by lack of control group.

Stathopoulou and Lubar 2004	5	Severe	Included a "Captain's Log" computer training program for attention skills with tasks for vigilance, inattention, prudence, impulsivity, focus, variability, and speed. Participants selected, discriminated, or matched visual pictures or sounds.	N	• Electroencephalogram (EEG) variables • WAIS-R • PASAT • Self-report measure of severity (of deficit) for memory and attention symptoms	Sustained attention, alternating attention, and divided attention improved in three of five subjects. Selective attention improved in all subjects. Focused attention improved in two of five subjects. Results are mediated by lack of control group.
Single Subject, Multiple Baseline Experimental Design						
Gansler and McCaffrey 1991	4	Severe	Hierarchically organized attention training program based on Posner's four component model of attention.	N	• Neuropsychological tests: ▪ WMS-R ▪ Trail Making Test ▪ Minute Estimation Test ▪ Thurstone Word Fluency Test ▪ Grooved Pegboard Test ▪ WAIS-R • Psychological variables for depression, anxiety, and anger • Self-report of ADLs	Posttreatment test results proved not significant for all participants. Participants reported increase in ADLs.

Chronic Phase of Recovery

Studies of chronic, moderate-severe TBI included four RCTs (McMillan et al. 2002; Niemann et al. 1990; Ruff et al. 1994; Sohlberg et al. 2000) comparing five treatment arms with patients in the chronic phase. Interventions in three (Niemann et al. 1990; Ruff et al. 1994; Sohlberg et al. 2000) of these RCTs consisted of some form of attention training exercises, similar to those employed by Gray et al. (1992) (see above), and most were delivered via computer. Training ranged from 10 to 24 hours and typically involved several different attention-demanding tasks that progressed in difficulty with patient improvement. Some treatments included therapist-delivered goal setting, feedback, and review of performance, including one study of Attention Process Training (APT), a manualized treatment approach that specifies therapist feedback more systematically. The fourth RCT (McMillan et al. 2002), also the largest trial, used mindfulness training. Unlike the other attention treatments, mindfulness training did not involve practice with attention-demanding tasks but rather separate sessions focused on breathing. Therapist-led training in this study was fewer than 4 hours for both mindfulness training and the active comparison condition, but with home practice assigned.

Comparator Group: No or Non-CRT Content

McMillan et al. (2002) compared the effects of instruction in mindfulness training to comparable instruction in physical exercise (non-CRT content) and a no-treatment control where participants received no therapist contact but were assessed at the same intervals. Thus, this was the only study that had a comparator arm of no treatment. Outcomes were assessed in terms of neuropsychological measures of attention as well as several self-report measures of mental health status and lapses of attention in everyday life. The mindfulness intervention outcomes on attention were no different than those of physical exercise or no intervention.

Sohlberg et al. (2000) compared 24 hours of manualized APT delivered over 10 weeks to 10 hours of brain injury education—a non-CRT intervention—delivered over the same time period, in an RCT with outcomes assessed at the point of crossover and again at trial completion. Outcome measures included standardized neuropsychological measures of attention, laboratory measures of information processing intended to assess the functioning of specific neural networks subserving separable attentional domains, and coded qualitative interviews regarding real-world changes resulting from treatment. This trial found positive effects of attention training on the Paced Auditory Serial Addition Test (PASAT), a measure of working

memory and speeded mental addition, and on the Memory for Location task, a measure of location working memory. On the Stroop task and the Trail Making Test, members of the APT group were characterized by "low vigilance" at baseline. The trial did not find such effects on verbal working memory, verbal fluency, or on the laboratory tasks designed to isolate the functions of specific neural networks. Although the patients were not blinded to the content of their treatment, there were significantly more reports of attention improvements in daily life after the APT treatment than after brain injury education. Lending some support to the validity of these reports, reports of everyday attention benefits correlated with improvement in PASAT scores. This was a small study, with 14 participants, all with moderate-severe injuries. Two subjects were not included in the structured interview to assess improvement because they did not recall their participation in the treatment. This situation is problematic, as it reduces the sample size to 12 and raises concerns about generalization to patients with substantial memory impairment. In addition, there were several statistical tests, with no adjustment for multiple testing.

Comparator Group: Other CRT Content

Two trials (Neimann et al. 1990; Ruff et al. 1994) studied the impact of an attention training program, compared to a memory training program, on measures of attention; thus memory training served as the control treatment.

Neimann et al. (1990) provided approximately 36 hours of training on three different aspects of attention, or a comparable amount of training on internal and external memory strategies. Neuropsychological measures of attention and memory were assessed. Based on a significant result from a MANOVA test for the four attention measures, the authors reported "partial support" for the treatment prediction that attention training would provide more robust impact on attention measures than the comparison memory training. However, in *post hoc* testing, only one of the attention measures differed significantly between groups. Inspection of the pattern of improvement suggests that three attention measures improved more in the group that received attention training, and one improved more in the group that received memory training.

Ruff et al. (1994) conducted a similar study in which the two treatment groups received both attention training and memory training, but in counterbalanced order. However, the authors did not conduct statistical testing at the midpoint of treatment (when a parallel group comparison would have been possible) because of the small sample size. They report benefit in both domains at the end of combined treatment, but inspection of

the pattern of scores at the midpoint suggests that some attention measures improved more in one group and some in the other.

Pre-Post Designs

Park et al. (1999) studied the effects of 40 hours of APT training in 23 individuals with chronic, moderate-severe TBI using the PASAT and Consonant Trigrams tests as outcome measures, along with the Beck Depression inventory. Stathopoulou and Lubar (2004) studied five people with severe brain injury between 1.5 and 23 years postinjury. The patients received 18 hours of attention training using "Captain's Log," a commercial computerized product that administers tasks involving various challenges to verbal and visual attention and memory. Participants were tested only once pre and once post, using digit span and digit symbol subtests of the Wechsler Adult Intelligence Scale (WAIS), the PASAT, a continuous performance test, a self-report measure of severity of a number of attention and memory symptoms rated on a five-point scale from "no problem" to "severe problem," and electroencephalogram (EEG) spectral measures. These studies—all of which were conducted at a time when rapid natural recovery would be unexpected—showed improvement in some of the outcome measures relevant to treatment. However, none of these studies had an adequate control for practice on the outcome assessments themselves, which were assessed twice, so none provides strong support for a treatment effect.

Single-Subject, Multiple Baseline Experiment

Gansler and McCaffrey (1991) conducted four single-subject experiments in which individuals with severe TBI—4 to 27 years postinjury—received repeated testing on a set of information processing measures modeled on Posner's attention components. The measures were administered weekly, beginning 4 weeks prior to training, during the 8 weeks of training, and at 1 month after training. Training consisted of 8 weeks of hierarchically organized modules of attention totaling about 64 hours. Other psychological measures were also administered weekly and neuropsychological measures at baseline, after training, and at follow-up; participants also completed a self-assessment of ADL performance and their satisfaction with it. Improvement on attention measures and psychological measures was negligible for all participants, though there were larger effects on self-appraisal of ADL performance. This result could suggest that the treatment imparted compensatory skills for managing attention deficits that were evident in real-world ADL tasks but not on controlled attention processing tasks.

However, the result is also consistent with biasing of self-reported benefit because of expectation.

CONCLUSIONS: ATTENTION

The committee found limited evidence from one RCT (Sohlberg et al. 2000) to support conclusions about the impact on patient-centered outcomes (quality of life, functional status) in moderate-severe TBI.

The committee found limited evidence from one RCT (Gray et al. 1992) on long-term impact of treatment (6 months) in the subacute phase as assessed with psychometric measures, particularly the type requiring numerical manipulation in working memory.

Considering subacute and chronic studies together, the committee found limited evidence from two studies (Grey et al. 1992; Sohlberg et al. 2000), that intensive practice of hierarchical attention-demanding tasks had a positive impact on psycho-metric measures of attention in the immediate posttreatment period and/or at follow-up.

The review did not include any RCTs or other study designs on CRT for attention in mild TBI. Two studies (Gray et al. 1992; Novack et al. 1996) provided limited evidence to conclude that CRT improves attention in subacute, moderate-severe TBI patients. In studies of moderate-severe TBI patients in the chronic phase of recovery, a few, relatively small RCTs with several methodologic limitations provided mixed support for treatment benefit. These trials tested intensive practice of hierarchical attention-demanding tasks on some psychometric measures of attention, with positive immediate outcomes. However, none studied the durability of benefits, and only one study assessed treatment impact with respect to patient-centered outcomes (i.e., Sohlberg et al. [2000] found a preliminary association of improved psychometric measures of attention with real-world benefits). Data from pre-post designs, although consistent with some treatment benefit, provide weak support because of the possible confounding effect of practice on the outcome measures.

Several of the RCTs with equivocal results (Niemann et al. 1990; Ruff et al. 1994) used intensive memory training as a control condition. Since all tasks requiring effort place demands on attention, it is possible that the overlap in treatment outcomes between treatment groups in such studies reflects the overlap in mental demands of treatment content, potentially attenuating or accounting for the lack of finding of differences in attention outcomes. Of note, the two studies that provided the strongest support for

the efficacy of hierarchical attention training employed non-CRT comparator conditions.

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8

Executive Function

OVERVIEW

Executive function is generally described as a set of integrated cognitive processes necessary to perform or accomplish everyday life activities. These cognitive processes allow individuals to plan or develop goals, initiate behavior, solve problems, anticipate consequences of actions, monitor progress toward goals, reason, strategize, direct attention to goal-relevant information, and manage time and space (Cicerone et al. 2000; Kennedy et al. 2008). Deficits in executive functions may include an inability to perform these cognitive processes or a lack of awareness that these or other cognitive and physical deficits exist and impede everyday life (Kennedy et al. 2008; Stuss 1991). Therefore, this chapter reviews the evidence for treatment of executive function in two main sections: awareness (i.e., deficits in self-awareness) and non-awareness (e.g., deficits in problem solving, planning, initiating behavior). Because executive function incorporates a number of subprocesses, and there is no consensus on precisely how to subdivide this complex domain, treatment development has typically focused on addressing individual subcomponents rather than the entire domain of executive function. Multiple approaches to the larger executive domain are sometimes included in comprehensive treatment programs. The committee's conclusions are provided at the end of each section, in awareness and non-awareness.

AWARENESS

The committee could not find any randomized controlled trials (RCTs) of mild traumatic brain injury (TBI) and awareness, perhaps reflecting the

fact that awareness deficits are more typically associated with more severe injuries. The committee reviewed four studies of participants with moderate-severe injuries who were in the chronic stage of recovery—two RCTs (Cheng and Man 2006; Goverover et al. 2007) and two single-subject, multiple baseline experiments of treatments intended to improve awareness of deficits (Sohlberg et al. 1998; Toglia et al. 2010). The committee did not find any nonrandomized, parallel group studies or pre-post designs on awareness. Table 8-1 presents a summary of all included studies in this review.

Chronic Phase of Recovery, Moderate-Severe TBI

Randomized Controlled Trials

Goverover et al. (2007) examined the effects of an awareness training protocol embedded within the practice of instrumental activities of daily living (IADLs) as compared to IADL training without any self-awareness training. The 20 participants had moderate-severe injuries that occurred an average of about 10 months prior to trial entry; participants' phase of recovery ranged between the subacute and chronic stages. Participants were randomly assigned to either group, and treatments were provided in six, 45-minute sessions, two or three times per week, across 3 weeks. Tasks were identical in the treatment and control groups; however, the treatment group participants were asked to predict their own performance on the IADL tasks and to self-evaluate performance immediately after tasks. They received immediate feedback from therapists, as well as instruction to write about their experiences in a journal. Improvement in task-specific self-awareness (AAD scores) was not significantly different between the groups. Improvement in a self-regulation skill inventory was significantly greater in the treatment group, after adjusting for baseline scores. Functional performance as reflected by Assessment of Motor and Process Skills (AMPS) scores also improved significantly more for the treated group than for the control group. Distal outcomes (e.g., secondary measures) were not significantly different between the groups, including an Awareness Questionnaire.

Cheng and Man (2006) investigated a newly developed Awareness Intervention Program (AIP) compared to a conventional rehabilitation program. The AIP focused on improving awareness of the patient's disease and related deficits such as physical or cognitive function. The AIP included educational sessions based on the types of deficits manifested by the patients and functional training sessions, in which patients practiced setting performance goals and then evaluating their own performance against those goals. The conventional rehabilitation program included physical, functional, and cognitive aspects of occupational therapy. The 21 subjects participating in the study were in the subacute phase of recovery from

TABLE 8-1 Evidence Table: Executive Function

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
AWARENESS						
RCT						
Cheng and Man 2006	21	Moderate-Severe	Comparison of a systematic intervention, Awareness Intervention Program (AIP), versus conventional rehabilitation, to improve self-awareness.	Y Other CRT Content: Conventional rehabilitation	• Self-Awareness of Deficits Interview (SADI) • FIM • Lawton Instrumental Activities of Daily Living (IADL) scale	Analysis showed the AIP training group improved significantly over conventional rehabilitation group.
Goverover et al. 2007	10	Moderate-Severe	Examined a self-awareness retraining program using practice of IADLs to improve task-specific self-awareness and self-regulation.	Y Other CRT Content: IADL training	• Awareness Questionnaire • Assessment of Awareness of Disability • Self-Regulation Skills Inventory (SRSI) • Assessment of Motor and Process Skills (AMPS)	Improvements in self-regulation skill and functional performance were significant in intervention group.
Single Subject, Multiple Baseline Experiment						
Sohlberg et al. 1998	3	Moderate-Severe	Examined three categories of awareness to determine optimal outcome measures in awareness interventions for future research (a pilot study).	N	• Caregiver rating of subject awareness • Self/Other Rating Form ▪ Caregiver rating ▪ Subject rating • Photograph (portion of the "Picture This!") rating • Behavioral measure	Qualitative analysis suggested improved awareness after treatment via behavioral measure; no change in awareness via Self/Other measures.

continued

TABLE 8-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Toglia et al. 2010	4	Not reported	Identified multifaceted task training approach to assess use of and skill in cognitive strategies to accomplish tasks and assess changes in general awareness (a pilot study).	N	• Proximal outcomes: ▪ Executive Function Performance Test subtask ▪ Multiple Errands Test ▪ SRSI • Distal outcomes: ▪ Awareness Questionnaire ▪ Behavior Rating Inventory of Executive Function	Participants improved in self-regulatory skills and strategy use across tasks; general awareness deficits were unchanged.
NON-AWARENESS						
RCT						
Constantinidou at al. 2008	35	Moderate-Severe	Evaluating the Categorization Program (CP) to determine if it improves cognitive abilities. • Part A included object categorization, teaching perceptual features to describe objects or living things, and higher levels of cognitive function including analyses, synthesis, linguistic flexibility, and abstract reasoning;	Y Other CRT Content: Typical treatment regimen of the rehabilitation site	• California Verbal Learning Test II • Community Integration Questionnaire (CIQ) • Control Oral Word Association • Mayo-Portland Adaptability Inventory III • Rey Complex Figure Test • Scales of Cognitive Ability for TBI • Symbol Digits Modalities Test • The Booklet Category Test • Trail Making Tests • Wechsler Abbreviated Scale of Intelligence	Both groups improved on a number of neuropsychological measures, and functional improvement was comparable between groups; the experimental group showed significant improvement on more measures, with better maintenance. A group comparison for change in neuropsychological measures was not performed.

			• Part B included new category learning, focusing on learning rules for categorization, with use of errorless learning principles and cueing hierarchies.		• Wechsler Memory Scale III • Wisconsin Card Sorting Test • Woodcock-Johnson III	
Couillet et al. 2010	12	Severe	Research on a rehabilitation program for divided attention, i.e., the ability to complete dual tasks simultaneously (e.g., walking and talking). Subjects randomized in a crossover design.	Y Other CRT Content: Nonspecific cognitive training	• Divided Attention Tests: ▪ Test for Attention Performance (TAP), subtest for divided attention ▪ Go–no go, and digit span • Executive and working memory tests: ▪ Brown-Peterson Paradigm ▪ Stroop ▪ TAP, subtest for flexibility ▪ Trail Making Test • Rating Scale of Attentional Behaviour	Significant treatment effect shown for dual task on the TAP (divided attention subtest), go–no go, and digit span.

continued

TABLE 8-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Evans et al. 2009	19	NR	Evaluated the efficacy of a cognitive–motor dual-tasking training program to improve performance with dual-tasking difficulties.	Y No Content: Placebo (no training) control	• Spot the Word Test or National Adult Reading Test • Divided Attention and Dual-Tasking Battery: ▪ Walking ▪ Clicking ▪ Speed of Comprehension Task, adapted ▪ Tone counting	Improved performance among treatment group shown for sentences and walking dual-task. Treatment group showed a reduction in self-reported difficulties (authors suggest caution in interpretation).
Fasotti et al. 2000	22	Severe	Evaluates attention deficit rehabilitation program, Time Pressure Management (TPM). In brief, videotaped stories, a compensatory cognitive strategy is outlined with four objectives: • Recognize time pressure in the task at hand; • Prevent as much time pressure as possible; • Deal with time pressure as quickly and effectively as possible; and • Urge the patient to monitor himself while using TPM.	Y Other CRT Content: Concentration training from an existing memory training program	• Auditory Concentration Test • Dutch version, Rey's 15 Words Test • PASAT • Rivermead Behavioural Memory Test (RBMT) • Visual Choice Reaction Time • Visual Simple Reaction Time	No significant difference between groups on use of anticipatory strategies or actual task performance. Treatment group showed some improvement on neuropsychological measures; authors do not identify how strategies could be evaluated by standardized tests.

Hewitt et al. 2006	30	Severe	Examines a method to aid individuals with "dysexuctive syndrome," or problems with planning and problem solving, with overcoming related challenges.	Y No Content: Control received no treatment	• Brixton Test • Hayling Test • RBMT screening score • Speed and Capacity of Language Processing Test • The Modified Six Elements Test	Group by time interaction significantly improved for the treatment group, but no effect for group or time separately.
Levine et al. 2000	30	Moderate-Severe	Assessed the effects of Goal Management Training to improve disorganized, or maintenance of goal-directed, behavior.	Y Non-CRT Content: Motor skills training	• Paper-and-pencil tasks • Proofreading • Grouping • Room layout • Neuropsychological tests: ▪ Stoop ▪ Trail Making Test ▪ WAIS-R, digit symbol subtest	Treatment group improved significantly from pre- to post-test compared to control. Treatment group reported to take more time to complete tasks—authors determined as evidence of care and double-checking.

continued

TABLE 8-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Rath et al. 2003	60	Mild, Moderate-Severe	Group treatment focusing on emotional self-regulation strategies for problem orientation as well as problem-solving skills; including weekly "consolidation sessions" to review materials and notes from each group.	Y Other CRT Content: Conventional treatment	• Problem solving tests: ▪ Perseverative Response score ▪ Problem Solving Inventory (PSI) ▪ Wisconsin Card Sorting Test (WCST) • Psychosocial functioning tests: ▪ Brief Symptom Inventory ▪ Community Integration Questionnaire ▪ Problem Checklist ▪ Recreation + Social Interaction composite score ▪ Rosenberg Self-Esteem Scale ▪ Sickness Impact Profile • Cognitive Skills tests: ▪ FAS-COWAT ▪ Stroop Color-Word Task ▪ WAIS-III ▪ Watson-Glaser Critical Thinking Appraisal ▪ Wechsler Memory Scale-III ▪ Weinberg Visual Cancellation Test ▪ Will-Temperament Scale	Nearly 25 percent of participants overall (both groups) dropped out prior to post-test measures. Both groups improved on a wide range of measures generally subject to practice effects or expectation of improvement.

Webb and Glueckauf 1994	16	NR	Goal setting training involving orientation, goal setting, goal monitoring with use of worksheet and follow-up form.	Y Other CRT Content: Less intensive goal-setting activities	Goal Attainment Scaling (GAS)	Both groups improved to comparable degree. Treatment group maintained effect at 1-month follow-up.
Nonrandomized, Parallel Controlled Group						
Cicerone 2002	8	Mild	Evaluating the efficacy of a treatment, based on conceptualization of deficits related to working memory, to address deficits of attention.	Y No Content: Control group did not receive treatment	• 2 and 7 Test • Attention Rating and Monitoring Scale (ARMS) self-report scale • Continuous Performance Test of Attention • PASAT • Trail Making Test ▪ Automatic Detection Speed ▪ Controlled Processing Speed	Difference between groups was significant, with treatment group demonstrating clinically meaningful improvement on majority of initially impaired measures. Treatment group demonstrated significantly greater reduction in the experience of attentional difficulties.
Fong et al. 2009	33	Moderate	Examined the effectiveness of a problem-solving skills training program, delivered to the treatment group, when provided with conventional cognitive training, which all participants received.	Y Other CRT Content: Conventional cognitive training	• Key Search test • Means-Ends Problem-Solving Measure (MEPSM) • Metacomponential Interview (MI) • Modified Six Elements test • Raven's Progressive Matrices (RPM) • Social Problem-Solving Video Measure (SPSVM)	Significant improvement was reported in the treatment group by the MI. No significant difference in change scores between groups for most outcomes.

continued

TABLE 8-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Man et al. 2006	50	NR	Evaluated the efficacy of a pictorial-based analogical problem-solving skills training program to help patients better learn problem-solving skills through systematic, theoretically driven strategies.	Y No Content: Placebo (no treatment)	• Halstead Reitan Test Battery (HRTB), Category Test • Lawton IADL scale, Hong Kong-Chinese version	Treatment group demonstrated some improvement in functional and overall problem-solving skills, immediately posttreatment and maintained at 4 weeks.
Manly et al. 2002	10	Mild, Moderate, Severe	Examines treatment for dysexecutive syndrome, or challenges in planning and problem solving for everyday life activities, using a brief auditory stimuli to interrupt activity and cue patients to consider the overall goal.	Y Other CRT Content: Controls were tested on task without use of auditory cues	• Hotel Task ▪ Compiling individual bills ▪ Sorting the charity collection ▪ Looking up telephone numbers ▪ Sorting conference labels ▪ Proofreading ▪ Opening and closing garage door • Version B *same tests, different timing*	Treatment group did not perform significantly different than control.

Pre-Post Single Group

Constantinidou et al. 2005	23	Moderate-Severe	Explores the effects of the Categorization Program (CP), a systematic treatment program, to improve categorization performance.	N	• Categorization tests ▪ Object categorization ▪ New category learning tasks • Community Integration Questionnaire (CIQ) • Mayo-Portland Adaptability Inventory-3 (MPAI-3) • Probe Tasks	All participants showed improvement following CP training at and second posttests. Probe Tasks elicited much lower responses from TBI participants than at the first probe, and their performance improved systematically in a linear fashion as they received more training on the CP. The overall multivariate probe effect was also significant, reflecting the improvement on the three probes demonstrated by participants with TBI.
Fish et al. 2007	20	Severe	Examined use of an alerting strategy with a content-free cue to determine utility for a prospective memory task, comparing cued and non-cued days for completion of telephone calls.	N	• Cambridge Prospective Memory Test • Cattell Culture Fair Test • Hotel test • National Adult Reading Test (NART) • RBMT, story recall • Rey Auditory Verbal Learning Test • Sustained Attention to Response Test (SART) • Trail Making Test	Significant difference reported after cued calls versus non-cued days.

continued

TABLE 8-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Marshall et al. 2004	20	Mild, Moderate, Severe	Examined the effects of behavioural intervention, an interactive strategy modeling training (ISMT), on challenges with problem solving. Participants asked to use a question-and-answer game to identify a picture.	N	• Raven Colored Progressive Matrices • Boston Naming Test • Rapid Assessment of Problem Solving test (RAPS) ▪ Number of questions ▪ Percent of constraint-seeking (CS) questions ▪ Question-asking efficiency scores	Significant difference on pre- and posttest scores for number of questions and percent of CS questions. No differences between post training and follow-up on all measures.
Serino et al. 2007	9	Mild, Moderate, Severe	Investigated the efficacy of a rehabilitative program—Working Memory Training (WMT)—to improve working memory and other, dependent cognitive functions by targeting the central executive system.	N	• General stimulation training (GST) • PASAT • Patient Competency Rating Scale • Rivermead Head Injury Follow-Up Questionnaire	Significant performance improvement reported from intermediate to final for WMT, as noted by tests for working memory, divided attention, executive function, but not in speed processing and sustained attention. No differences seen between screening and intermediate testing sessions (for GST).

Single Subject, Multiple Baseline Experimental Design

Dawson et al. 2009	3	Mild, Severe	The study trained three adults to use a meta-cognitive strategy (Goal-Plan-Do-Check) to solve everyday performance problems.	N	Canadian Occupational Performance Measure	Changes according to self- and significant other ratings showed performance improvement (on seven of nine trained goals, four of seven untrained goals) as well as satisfaction with treatment results.
Delazer et al. 1998	3	Severe	Studies three patients with severe cognitive impairment leading to difficulty solving problems	N	• Number of correct steps • Number of correct answers • Number of encoding errors • Number of execution errors • Time for completion • Neuropsychological measures: ▪ Munchner Gedachtnis Test ▪ Rey Osterrieth Complex Figure ▪ Digit span forward ▪ Digit span backward ▪ WCST ▪ Tower of London ▪ Trail Making Test ▪ Raven SPM ▪ Graded Difficulty Arithmetic Test	Number of correct steps increased for all three participants from baseline to session two. No notable changes were recorded on neuropsychological measures.

continued

TABLE 8-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Ehlhardt et al. 2005	4	Severe	Evaluating the TEACH-M program to assess ability to learn multistep procedures utilizing specific cognitive rehabilitation principles.	N	• Number of correct e-mail steps completed in sequence • Number of correct e-mail steps completed, regardless of sequence • Number of training sessions required to reach criterion for mastery	All increased number of steps learned in sequence and overall number of correct steps; the number of sessions required to reach goal varied. All reported the program helpful. Maintenance of treatment effects observed with three of four participants. Some generalization to novel email task observed for all participants for probes within three days of treatment.
Nott et al. 2008	8	Mild, Moderate, Severe	Occupational therapy alternated with a rehabilitation program, Perceive, Recall, Plan, and Perform (PRPP), to track information processing capacity during tasks.	N	PRPP system of task analysis	Difference in performance across phases was statistically sig for seven of eight participants. Post hoc testing different between baseline and intervention.

Vallat-Azouvi et al. 2009	2	Severe	Assess effectiveness of rehabilitation program to address working memory in two individuals with central executive deficits.	N	• Central executive tasks: ▪ Brown-Peterson paradigm ▪ N-back • Digit and visuo-spatial span • Ecological questionnaire • Non-target tasks ▪ Go-no go ▪ Trail Making Test • Working memory tasks: ▪ Arithmetic problem solving ▪ Dual task	Improvements noted in working memory and central executive tasks, as well as the ecological questionnaire. Non-target measures were unchanged. Authors suggested that improvements were maintained in one subject.
Zencius et al. 1998	2	NR	Orientation questions presented to two individuals with executive deficits. Varied formats included individual sessions of flashcards with oral questioning, or group sessions with peer questions, written response, and verbal repetition.	N	Frequency of correct answers to questions	Improvement noted for both individuals from baseline to post-treatment, providing support for increasing orientation to person, place, and time using questions as well as for fading the prompting used during the training procedure.

what was likely moderate-severe TBI. The AIP treatment program consisted of two individual sessions a day, 5 days per week, for 4 weeks. The AIP group demonstrated significantly improved awareness as compared to the conventional rehabilitation group. Functional outcomes did not differ between the groups.

Single-Subject, Multiple Baseline Experiments

Sohlberg et al. (1998) conducted a pilot study to assess three categories of awareness measures administered to three individuals with moderate-severe brain injury and their caregivers. Individuals were 7 to 21 years postinjury. This pilot study intended to determine which set of outcome measures would be more useful for further research in awareness interventions. Two groups of outcome measures were used to determine improved awareness in participants: behavioral indicators (e.g., increased independence, decreased interruptive behavior) and perceptions (self and others' [e.g., caregivers']) regarding awareness abilities (e.g., caregiver ratings and self-ratings of competency, self-judgments about likely cognitive breakdowns depicted photographically, or global ratings by a significant other). The treatment consisted of showing patients pictures of activities they were likely or unlikely to experience as cognitive failures (e.g., forgetting peoples' names, forgetting to move the wet laundry from the washing machine to the dryer). To judge self-awareness, the examiner asked each subject whether the photographs represent problems they were likely or unlikely to experience. Qualitative analysis suggested dissociation between behavioral and perceptual indicators of awareness. Behavioral measures showed improved awareness after treatment; others'/self-perception measures showed no change in awareness.

Toglia et al. (2010) conducted a single-subject design trial with four subjects, using a multi-context approach to promote strategy use across situations and increase self-regulation, awareness, and functional performance. Treatment included nine 75-minute treatment sessions, provided twice a week for approximately 5 weeks. Sessions were divided into three phases: error-discovery, strategy training and mediation, and reinforcement of strategy. Each session included different multi-step (i.e., 10–15 steps) tasks, approached in various settings such as a kitchen or office. In qualitative analysis, participants demonstrated improvement in self-regulatory skills and strategy use. General awareness of deficits remained unchanged in these subjects.

CONCLUSIONS: AWARENESS

The committee found no evidence from two RCTs (Cheng and Man 2006; Goverover et al. 2007) that self-awareness training produced

an overall increase in self-awareness beyond the types of tasks and activities that were the subject of self-appraisal (i.e., patient-centered outcomes).

The committee found no evidence from two RCTs (Cheng and Man 2006; Goverover et al. 2007) that measured posttreatment follow-up to show whether awareness treatment effects were maintained.

The committee found limited evidence from two RCTs (Cheng and Man 2006; Goverover et al. 2007) that showed an immediate increase in accuracy of self-assessment and self-regulation from treatments that involved practice in prediction and evaluation of task performance, for individuals with chronic stage, moderate-severe TBI.

The committee found no studies of cognitive rehabilitation therapy (CRT) for awareness deficits in mild TBI or subacute, moderate-severe TBI. The committee reviewed two RCTs and two single-subject, multiple baseline studies to address awareness deficits in patients with moderate-severe TBI in the chronic phase of recovery. The evidence provides no support for long-term treatment effect. Treatment effects show benefit for immediate/short-term outcomes, such as improvement in self-regulatory skills.

NON-AWARENESS

The committee reviewed eight RCTs of treatments intended to improve cognitive aspects of executive function (i.e., aspects other than self-awareness). These studies speak primarily to treatments for individuals in the chronic phase with at least moderate injuries. Seven of them were conducted in the chronic phase, with one (Couillet et al. 2010) enrolling patients in both subacute and chronic phases. Seven of the studies enrolled only participants with traumatic injuries, while one (Evans et al. 2009) included a mixture of individuals with TBI and stroke, although a majority had TBI. Most studies included only patients with moderate or severe injuries, while two RCTs (Levine et al. 2000; Rath et al. 2003) included individuals with mild injuries; however, the results in these two studies were not separated by subgroup for analysis. One study (Evans et al. 2009) defined severity with respect to the executive impairment of interest, rather than injury severity. The ages of those treated ranged from the late 20s to early 40s. The studies enrolled a total of 218 participants, with sample sizes in each treatment arm ranging from 5 to 30. Two of these studies compared the experimental intervention to no treatment (Hewitt et al. 2006, used an unfilled waiting interval; Evans et al. [2009], used "usual care"), one to a physical skill training intervention (Levine et al. 2000), and five

to other forms of cognitive treatment. Five of the treatments studied were compensatory in nature, two (Couillet et al. 2010; Evans et al. 2009) were restorative, and one (Constantinidou et al. 2008) was less clearly classifiable between restorative and compensatory. The committee also identified four nonrandomized, parallel group designs, four pre-post single group designs, and six single-subject, multiple baseline experiments.

Chronic Phase of Recovery, Moderate-Severe TBI

Comparator Group: No or Minimal Content

Evans et al. (2009) evaluated the effectiveness of a 5-week cognitive–motor dual-tasking training program developed to improve the performance of a group of people with divided attention difficulties arising from brain injury and thought to place demands on executive function. A treatment group of 10 people was compared with a control group of 9; the control group received no training. The intervention involved twice-daily exercises involving walking in combination with tasks of increasing cognitive demand over the course of the intervention. The primary outcome measure was a task requiring participants to walk and carry out a spoken sentence verification task simultaneously. Secondary outcome measures were measures of dual-tasking involving either two motor tasks or two cognitive tasks. A questionnaire measure relating to daily activities requiring divided attention was also completed. Compliance with the training program was good. Results showed evidence of improvement in performance on the primary outcome measure, but little evidence of generalization to other measures. Some evidence showed that participants believed their dual-tasking performance in everyday life improved after the intervention. The study was limited in terms of sample size, was not blinded, and did not control fully for therapist contact time, but it has produced valuable data relating to effect sizes associated with this form of intervention.

Hewitt et al. (2006) assessed participants' ability to develop a plan to accomplish a minimally familiar task such as planning a trip. Participants were asked to list the steps required to accomplish a simulated task prior to treatment. They were randomized to then have a 30-minute break or 30 minutes of instruction in an approach to task planning that asked them to recall an example of a similar activity that they had planned in the past and consider that task in planning a new one. The outcome measures were number of steps listed and effectiveness of the new plan, and they were assessed immediately after the break/strategy training by raters blinded to the group assignment. Both groups improved on these measures, with the strategy training group improving more from pre- to posttest. This study suggests that such a strategy is useful in improving the planning of complex

activities, but does not answer the question of whether the strategy can be trained in such a way that it is retained and used in daily life.

Comparator Group: Non-CRT Content

Levine et al. (2000) assessed a strategy entitled Goal Management Training (GMT), in which an overt sequence of steps leading from a goal, to a set of actions to accomplish the goal, to a checking process that assesses progress toward that goal, is taught as a way to enhance the completion of goal-directed activities. Participants attempted to perform a set of laboratory-based simulations of real-world tasks, which were scored for time and errors. The participants were then randomized to receive either a motor skills training group or a GMT group for a single, 4- to 6-hour training session. In the GMT group, the training session involved didactic teaching of the GMT concept and practice applying it to a set of simulated activities similar to those used at baseline. Subsequently, both groups were reassessed on a similar set of simulated activities. The degree of improvement in errors from pre- to posttesting was significantly larger for the GMT group than the motor skills group, and GMT group members performed some activities more slowly, interpreted as evidence of care and "checking." Although two of the trained activities were used in the assessment, another task that was not part of the GMT also showed differential improvement suggestive of short-term generalization of the strategy. This study suggests that GMT can be helpful when used, but does not answer the question of how to achieve regular spontaneous use of the strategy in daily life.

Comparator Group: Other CRT Content

Constantinidou et al. (2008) examined whether intensive training in categorization results in improvement in two untrained categorization tasks, a battery of neuropsychological tests, and a functional assessment scale. The comparison group received "usual care" including a range of cognitive rehabilitation activities, but without an intense focus on categorization training. Both groups received approximately 60 hours of training over about 13 weeks. The experimental group performed significantly better on both categorization tasks after treatment than the comparison group, whereas the two groups did not differ significantly prior to treatment. Also, the ability to categorize appeared better maintained across follow-up probes in the experimental group. Both groups improved on a number of the neuropsychological measures, and the experimental group improved significantly on more of them. However, a comparison of change in neuropsychological measures was not conducted. Functional improvement was comparable between the two groups. These conclusions are tempered by the

small group size, the fact that direct tests that group by time comparison were not statistically significant, and the lack of direct comparison of the neuropsychological outcomes.

Couillet et al. (2010) conducted a randomized crossover design addressing divided attention difficulties. The study included 12 patients at a subacute or chronic stage of recovery after severe TBI. Treatment consisted of training to perform two concurrent tasks using a hierarchical order of difficulty that progressively increased task difficulty following each patient's individual improvement. A variety of task combinations were used during training. The control group practiced a range of computerized and paper and pencil tasks that did not require divided attention. Training lasted 6 weeks, with four, 1-hour sessions per week. Outcome measures included specific divided attention measures, other executive and working memory tasks, nontarget cognitive tasks to assess the specificity of treatment, and the Rating Scale of Attentional Behaviour addressing attentional problems in everyday life. The authors reported a significant treatment effect for divided attention measures and on the divided attention item of the Rating Scale of Attentional Behaviour. Less consistent effects were seen on other executive and working memory measures, and no significant effect was seen on nontarget measures.

Fasotti et al. (2000) studied a strategy training intervention entitled Time Pressure Management (TPM), which is based on the premise that slowed information processing leads to task failures and that strategies such as avoiding interruptions, taking the necessary time, taking pauses, etc., may lead to improved task performance. The experimental group was taught this strategy and practiced it for about 7 hours over 2 to 3 weeks. The comparison group was given didactic instruction in "how to concentrate." Both were then assessed on two simulated tasks in which they had to recall directions provided via videotape or perform a computer task when given recorded directions. Performance on these tasks was coded with respect to specific TPM strategies that were performed in anticipation of task problems and in response to task problems, as well as quality of actual task performance. Both groups were also assessed on a range of neuropsychological and psycho-social measures. After treatment, the two groups did not differ on the use of anticipatory strategies; the TPM group using TPM strategies in response to task problems. Actual task performance did not differ between the groups. Interestingly, performance on the neuro-psychological test battery, but not the psychosocial measures, improved more in the TPM group, despite the fact that it is not obvious how the strategies taught can be applied during standardized testing.

Rath et al. (2003) compared two multi-component group treatment programs for problem solving deficits. Both groups received 2 to 3 hours of treatment per week over 24 weeks, although the experimental group

received treatment in a single, longer weekly block while the comparison group had shorter sessions across the week. The experimental group followed a structured lesson plan that started with problem orientation (i.e., identification of problems, attitudes toward problem solving, attribution of problem sources) and then focused on applying specific problem solving strategies to real-world problems. The comparison group's treatment focused on several different cognitive domains as well as psychosocial adjustment, but without the specific focus on a problem solving framework. Multiple outcome measures focusing on attention, memory, problem solving, emotional adjustment, and physical symptoms, as well as caregiver reports, were assessed. Unfortunately, 5 of 32 participants assigned to the experimental group and 9 of 28 participants assigned to the comparison group dropped out prior to outcome assessment (nearly 25 percent overall). Moreover, the degree of improvement seen in the two groups was not directly compared statistically. Relative improvement between the two groups was impossible to assess because the outcome measures that improved significantly within each group (10 measures in the experimental group, 8 in the comparison group) were reported with effect sizes. However, no effect sizes were reported for those measures that did not improve significantly, nor were confidence intervals around the effect sizes reported. Both groups appeared to show significant improvement in a wide range of measures, but some of the measures are subject to practice effects and/or expectation of improvement.

Webb and Glueckauf (1994) assessed whether participant involvement in setting and reviewing treatment goals affected progress toward those goals or retention of improvement. Two groups participated in the identification of a priority behavioral goal, as well as a goal attainment scaling (GAS) exercise to anchor potential outcomes with respect to that goal into a five-point scale. One group was involved in more intensive discussion of the goal and more intensive review and reflection on the goal and progress toward it at weekly follow-up sessions. Both groups made progress on the GAS scale from pre- to posttreatment. The intensive goal group maintained this improvement at 2-month follow-up, whereas the other group regressed by the follow-up assessment. Each group lost participants; two dropped from the intensive training, and three dropped out from the other. Moreover, the degree of GAS improvement or maintenance was not statistically assessed head to head.

Nonrandomized, Parallel Group Designs

Fong and Howie (2009) studied a program of explicit problem solving training. Experimental and control groups were formed from pairs of participants matched on demographic and injury severity measures. All

participants received conventional cognitive training composed of functional skills training. The experimental intervention consisted of additional explicit training in problem solving skills with an emphasis on metacomponential strategies, delivered in 22 75-minute sessions over 15 weeks. The treatment was oriented toward the primary metacomponents of problem solving: defining the problem, representing the problem, planning problem solving strategies, monitoring selected strategies, and evaluating outcomes. Patients from the treatment group improved significantly on tests that assessed metacognitive ability. The significance level of this result would not have survived corrections for multiple comparison, and it was not clear which of the 22 outcome measures would have been considered sufficiently relevant to require correction.

This and the other nonrandomized, parallel group studies (Cicerone 2002; Man et al. 2006; Manly et al. 2002), single group pre-post studies (Constantinidou et al. 2005; Fish et al. 2007; Marshall et al. 2004; Serino et al. 2007), and single-subject, experimental designs (Dawson et al. 2009; Delazer et al. 1998; Ehlhardt et al. 2005; Nott et al. 2008; Vallat-Azouvi et al. 2009; Zencius et al. 1998) provided modest support for the conclusions of the RCTs. In general, the methodology of these studies was weaker, not only due to the nonrandomized nature of treatment assignment or single group design, but also due to very small sample sizes and inappropriate use of statistics in some cases. Like several of the RCTs, many were pilot studies or proof-of-principle trials that aimed to test the potential for a new intervention to be utilized in larger studies with more substantial statistical power.

In addition, the generalizability of some of the studies was limited due to extensive methodological overlap between the intervention and the primary outcome measures (e.g., Constantinidou et al. 2005; Ehlhardt et al. 2005; Marshall et al. 2004). However, supportive evidence was provided for interventions that demonstrated early promise, some of them with implications for the functional consquences of the interventions. Externally originated alertness enhancement (random beeps during a reasoning task) facilitated attention and reasoning performance during a time-allocation task (Manly et al. 2002). The notion that metacognitive interventions such as context-free reminders could be successfully applied to facilitate memory for real-world tasks was also supported (Fish et al. 2007).

CONCLUSIONS: NON-AWARENESS

Not Informative

- **The committee found studies of goal management training, intensive goal setting, familiar tasks as a planning template, and TPM**

(Constantinidou et al. 2008; Fasotti et al. 2000; Hewitt et al. 2006; Levine et al. 2000) not informative for conclusions about the impact on patient-centered outcomes (quality of life, functional status).

- **The committee found studies of goal management training, intensive goal setting, familiar tasks as a planning template, TPM, or training in divided attention (Constantinidou et al. 2008; Couillet et al. 2010; Evans et al. 2009; Fasotti et al. 2000; Hewitt et al. 2006; Levine et al. 2000) not informative regarding measures of posttreatment follow-up to show whether goal management training treatment effects were maintained.**
- **The committee found studies of goal management training, intensive goal setting, familiar tasks as a planning template, and TPM (Constantinidou et al. 2008; Fasotti et al. 2000; Hewitt et al. 2006; Levine et al. 2000) not informative to show benefit from goal management training beyond the training session for individuals with chronic, moderate-severe TBI.**

Limited Evidence

- **The committee found limited evidence for conclusions about the impact (efficacy) of training in divided attention on patient-centered outcomes (Couillet et al. 2010; Evans et al. 2009).**
- **The committee found limited evidence that training in divided attention led to immediate enhancement of divided attention performance beyond the combination of tasks trained (Couillet et al. 2010; Evans et al. 2009).**

In summary, the committee evaluated a wide range of strategies, primarily compensatory, in patients with executive deficits related to moderate-severe TBI. There is evidence that GMT, using prior planned tasks as guides to planning new tasks, intensive involvement in goal setting, and delivery of content-free alerting stimuli during performance of complex tasks, may enhance task accomplishment. However, these studies did not establish the spontaneous use of these strategies after longer-term treatment or the breadth of tasks for which such strategies might be beneficial. The evidence for TPM is weaker since the use of the trained strategies did not result in clear improvements in performance, and, again, longer-term treatment with intent to generalize to daily life was not studied. The benefits of categorization training are less clear from research to date. Two of the trials (Hewitt et al. 2006; Levine et al. 2000) were essentially proof of principle studies, which assessed the immediate benefit of a single session of strategy training, as opposed to the longer-term benefit of a course of treatment.

Studies of divided attention training provided somewhat conflicting results. Both studies suggest improvement in performance of combinations of tasks that were performed together in training (Couillet et al. 2010; Evans et al. 2009), but only one (Couillet et al. 2010) suggested generalization to other task combinations. Because many combinations of tasks were used in training and their similarity to the outcome tasks is unclear, the degree of generalization implied by the outcome task performance improvement is unclear.

Other intensive executive treatments, such as those studied by Rath et al. (2003), are difficult to assess because of the lack of direct comparison to an alternative treatment (i.e., comparator included other CRT-like components). Because of the preliminary nature of most of the executive treatments studied, patient-centered outcomes were rarely included in the outcome measures. Thus, although several compensatory strategy training approaches show enhanced executive management of complex tasks on a short-term basis, there is limited evidence from two RCTs to document longer-term change to demonstrate the impact of such treatments on real-world performance (Couillet et al. 2010; Evans et al. 2009).

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9

Language and Social Communication

OVERVIEW

Traumatic brain injury (TBI) may cause deficits in language and social communication, sometimes experienced by delayed word recall or a diminished ability to detect emotion while communicating with others. Such impairments may lead to frustrating or embarrassing experiences and affect an individual's family dynamic, social life, and employment status. Cognitive rehabilitation therapy (CRT) interventions for language and social communication impairments may target social or emotion perception, social skills, or communication skills. Aphasia is another possible language impairment following acquired brain injury, although more common after stroke than TBI. The committee did not identify literature describing CRT interventions for aphasia after TBI. The following chapter describes controlled studies in language and social communication, followed by the committee's conclusions.

The committee identified and reviewed four randomized controlled trials (RCTs) of language and social communication cognitive rehabilitation (Bornhofen and McDonald 2008a, 2008b; Dahlberg et al. 2007; McDonald et al. 2008). The committee found no studies of CRT for the domain of language and social communication for mild TBI, or for moderate-severe TBI in the subacute phase. All four trials were in the outpatient setting and enrolled moderate-severe TBI patients in the chronic phase of recovery. Two of the four RCTs focused solely on CRT for emotion perception deficits, one RCT focused on social communication skills training, and one RCT incorporated a combination of both social skills training and social/

emotion perception training. To be included, participants generally had to have sufficient language and cognitive capability to participate in a group, and have impairment in social communication skills either based on a questionnaire or a referring clinician's assessment. One of the four RCTs had some form of CRT in both trial arms but also included comparison to a waitlist arm. The committee also identified one nonrandomized, parallel group controlled design (Hashimoto et al. 2006). This study was in the chronic phase of recovery for patients with moderate-severe TBI. Subjects were instructed on social skills training; no treatment was provided to the comparator arm (Hashimoto et al. 2006). Table 9-1 presents a summary of all included studies in this review.

CHRONIC, MODERATE-SEVERE TBI

Randomized Controlled Trials

Two trials focusing on treatment of emotion perception deficits were reported by Bornhofen and McDonald (2008a, 2008b). Emotion perception was defined as "accurate decoding and interpretation of visual and aural stimuli that signal 1 of 6 emotional states." The CRT program reported by Bornhofen and McDonald (2008a) included group activities, and a notebook and home practice to teach increasingly complex skills on emotion perception. Sessions were held twice weekly, for 1.5 hours each over 8 weeks; 25 hours total. One therapist (background not described) was assigned to every two or three participants. The 12 participants were receiving outpatient services for TBI and were recruited and allocated at random to treatment or to a waitlist group; there was one dropout. Study outcomes were measures of facial expression (naming and matching), The Awareness of Social Inference Test (TASIT), and psychosocial reintegration. Immediately posttreatment, the intervention yielded significantly better TASIT scores relative to the waitlist group. While the intervention group scored better posttreatment on one form of the facial expression measure (matching), the groups scored the same on the alternate form of the facial expression measure (naming), and psychosocial reintegration. One month follow-up scores in the treatment arm were significantly higher than scores prior to treatment on all measures.

The other trial reported by Bornhofen and McDonald (2008b) had the goal of teasing apart the effective components of the intervention in the trial described above, by separating and comparing an errorless learning strategy with self-instruction training (which were combined in the 2008a study intervention), with a waitlist control group; both interventions also aimed to remediate emotion perception deficits. The interventions comprised a total of 25 hours of treatment across 10 weeks, divided into weekly, 2.5-hour

TABLE 9-1 Evidence Table: Language and Social Communication

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
RCT						
Bornhofen and McDonald 2008a	12	Severe	This study investigated whether social perception deficits could be remediated through cognitive rehabilitation, using a treatment program that incorporated techniques previously known to be effective with the TBI population.	Y No Content: Waitlist control group	• Facial Expression Matching Task • Facial Expression Naming Task • The Awareness of Social Inference Test (TASIT), Parts 1, 2, and 3 • The Sydney Psychosocial Reintegration Scale (SPRS), Current Status – Self Ratings	At immediate post-treatment, the intervention yielded significantly better social inference (TASIT) scores relative to the waitlist group. While the intervention group performed better posttreatment on scores of one form of the matching measure, there was no difference between groups on the alternate form of the matching measure, naming facial expression, or psychosocial reintegration. One month follow-up scores in the treatment arm were significantly higher than prior to treatment on all measures.

continued

TABLE 9-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Bornhofen and McDonald 2008b	18	Severe	The objective of this study was to compare the efficacy of two strategies, errorless learning (EL) and self-instruction training (SIT), for improving deficits in emotion perception.	Y No Content: Waitlist control group	• Primary outcome measures: ▪ Audiovisual emotional displays: TASIT, Part 1 (Forms A and B) and social inferences based on emotional demeanor ▪ Higher order social inference making: TASIT, Parts 2 and 3 (Forms A and B) ▪ Identification of static emotion: Facial Expression Same/Different, Naming, and Matching Tasks • Generalization measures: ▪ Current Status–Relative Ratings (SPRS–Relative) ▪ Depression Anxiety Stress Scales (DASS) ▪ Katz Adjustment Scale–Relative Report Form (KAS–R) ▪ Relative Ratings (SPSS-Positive and SPSS-Negative) ▪ Social Performance Survey Schedule ▪ SPRS and SPRS-Self	Both treatment groups improved modestly in emotion perception; there is limited evidence to suggest that SIT may be a favorable approach for this type of remediation.

Dahlberg et al. 2007	52	Moderate-Severe	The study evaluates the efficacy of a group treatment program that targets the broader definition of social skills, uses a group process approach, emphasizes self-assessment and individual goal setting, and encourages generalization through homework and family or friend involvement.	Y No Content: Waitlist control group	• Community Integration Questionnaire social integration and productivity subscales (CIQ) • Craig Handicap Assessment and Reporting Technique Short Form social integration and occupation subscales (CHART-SF) • Goal Attainment Scaling (GAS) • Profile of Functional Impairment in Communication (PFIC) • Satisfaction with Life Scale (SWLS) • Social Communication Skills Questionnaire–Adapted (SCSQ–A)	PFIC subscales showed more improvement for treatment versus control; SCSQ–A self-report ratings showed more improvement for treatment versus control. Scales showed immediate improvement, with some preserved improvement at 3- and 6-month follow-up.
McDonald et al. 2008	39	Severe	The aim of this study was to determine whether remediation would be effective in improving social skills deficits, such as unskilled, inappropriate behavior; social perception; and mood disturbances (e.g., depression and anxiety).	Y No Content and Non-CRT Content: Waitlist control group; Social activity group	• Primary outcomes: ▪ Emotional adjustment: DASS ▪ Social behavior: BRISS-R, PDBS, and PCSS ▪ Social perception: TASIT • Secondary outcomes: ▪ Katz Adjustment Scale–RI ▪ La Trobe Communication Questionnaire ▪ Social Performance Survey Schedule ▪ Sydney Psychosocial Reintegration Scale	Relative to the waitlist control, social activity alone did not lead to improved performance on any outcome variable. The skills training group did improve differentially on the PDBS of the BRISS-R, while no treatment effects were found for the other primary outcomes or any of the secondary outcomes.

continued

TABLE 9-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Nonrandomized, Parallel Controlled Group						
Hashimoto et al. 2006	37	Moderate-Severe	This study assessed the efficacy of a comprehensive day treatment program.	Y No Content: Patients who did not join the day treatment program	• Activities of daily living: ▪ FIM version 3.0 ▪ FAM • Societal participation: ▪ Community Integration Questionnaire (CIQ)	The enrolled subjects displayed significant improvements in speech intelligibility, problem solving, memory, attention, and social integration scores in the FIM/FAM and scores in social integration and productive activity in the CIQ.

sessions; in each session, a therapist worked with a group of two or three patients. The 18 participants were randomized to one of the three study arms; of these, there were five dropouts. Outcome measures included facial expression recognition, facial expression naming and matching, psychosocial reintegration, and depression and anxiety, as well as relative ratings of adjustment, social performance, and psychosocial reintegration. There were few statistically significant differences across these very small (four or five patients per arm) arms on study outcome measures.

Dahlberg et al. (2007) used a randomized trial to evaluate an outpatient group treatment program aimed at improving social communication skills after TBI. They employed a treatment workbook (*Social Skills and TBI: A Workbook for Group Treatment*) and limited each group's size to eight participants. Each group met weekly for 1.5 hours for 12 weeks (18 hours) and was co-led by professionals from social work and speech pathology. Early sessions focused on self-assessment and goal setting, middle sessions focused on learning strategies for those goals, and later sessions focused on generalization; homework was assigned between sessions. Family members were involved outside the group setting. The 60 adults with TBI were randomized to either immediate participation in the social communication program or delayed treatment 3 months later; 52 people completed the study. The early treatment arm was followed for 36 weeks following completion of the program, and the delayed treatment arm was followed for 24 weeks. Primary outcomes were an objective measure of social communication skills (based on blinded raters' assessments of videotaped interactions of the participant with research assistants, who were blinded to group assignment); a subjective assessment of social communication; and a Goal Attainment Scaling measure. Secondary outcomes were two assessments of community integration and one measure of life satisfaction. The researchers found that 12 weeks after the treatment sessions had ended, the intervention versus the control group had better scores on 7 of 10 scales of the primary outcome measure, which was the objective measure of social communication skills, as well as on the subjective assessment of social communication. There were no differences on the secondary outcome measures. Score improvements were maintained in both groups through 6-month follow-up.

McDonald et al. (2008) conducted a randomized trial of social behavior and social/emotional perception training compared to one control group receiving the same amount of time in grouped social activities; a second control group was waitlisted. The CRT intervention was 12 weeks at 4 hours per week, or 48 hours total, at an outpatient or community facility. It included group sessions each week focusing on social behavior training (2 hours) and social perception training to help decode expressions of emotion and social inferences (1 hour). The fourth hour each week was an individual session with a clinical psychologist who employed cognitive be-

havioral therapy (CBT) techniques to address emotional adjustment. Across the three trial arms, 51 subjects were enrolled and randomized. Due to scheduling conflicts, nine subjects were reassigned to other arms after randomization and to balance numbers across arms. Outcomes measured included social behavior (based on blinded raters' assessments of videotaped encounters of participants with an actor), measured by the Partner Directed Behavior Scale and the Personal Conversational Style Scale; both scales are part of the Behaviorally Referenced Rating System of Intermediary Social Skills (Revised). Other primary outcomes were the TASIT to assess social perception, and self-reported depression and anxiety. Secondary outcomes included a relative's rating of social behavior on the Katz Adjustment Scale, a social performance survey, a communication questionnaire, and both self- and relative ratings on a psychosocial reintegration scale. Findings showed that the social skills treatment arm performed significantly better on the Partner Directed Behavior Scale compared to the social activity or waitlist trial arms ($p = 0.004$; effect size 0.70). There were no other differences across arms on any other primary or secondary outcome measures. Study limitations included insufficient power due to both attrition and to smaller effect sizes than anticipated, as well as the reassignment of participants from their initial randomization arms.

Nonrandomized, Parallel Group Studies

Hashimoto et al. (2006) evaluated an outpatient, day treatment program in Japan targeting social skills training. The treatment ranged from of a minimum of therapy for 2 hours per day, twice each week over 3 months (52 hours), to 4 hours per day, twice per week for 6 months (208 hours). The rationale for the variation in volume of day treatment program sessions was not provided. CRT content included social skills training by a clinical psychologist/speech therapist based on an approach of teaching improved behaviors by "redesigning the subjects' environment." CRT interventions also included occupational therapy, family conferences, sports, vocational rehab, and cooking. Services were delivered by a rehabilitation team, including the following: doctor/nurse, social worker, clinical psychologist/speech therapist, vocational rehabilitation counselor, physical therapist, rehabilitation gymnastic trainer, occupational therapist, and others. The sample was 25 adults (22 with TBI) ages 19 to 56. A control group consisted of 12 outpatients with TBI from the same medical center who met eligibility criteria but did not participate in the program. The study does not explain how participants were selected or why some selected participants did not participate in the program. Functional Independence Measure (FIM) and Functional Assessment Measure (FAM) scores and the Community Integration Questionnaire (CIQ) were collected before and after

participants completed the program (although it is not clear when the data were obtained for controls). CRT recipients were compared with controls on mean improvement in scores on these measures. While the groups did not differ on total social cognition, communication, or FIM motor score improvement, the participants improved more than controls on 5 of 12 FIM/FAM scales including social integration, attention, memory, problem solving, and speech intelligibility. On the CIQ, program participants improved significantly more on the total score and on subscale scores of social integration and productive activity than did controls; there was no difference in improvement on home integration.

CONCLUSIONS: LANGUAGE AND SOCIAL COMMUNICATION

The committee found the evidence of language and social communication CRT not informative about impact (efficacy) on patient-centered outcomes (quality of life, functional status). The evidence does not rule out a potentially meaningful effect of social communication skills or emotional perception skills training on psychosocial outcomes of community reintegration in adults with chronic, moderate-severe TBI (Hashimoto et al. 2006).

The committee found limited evidence for sustained effect of language and social communication CRT among chronic, moderate-severe TBI patients from the two RCTs that assessed sustained treatment effects. These studies found that beneficial effects on social communication skills or emotion perception were maintained through 1 month (Dahlberg et al. 2007) and 6 months (Bornhofen and McDonald 2008a).

The committee found modest evidence from a synthesis of findings across four RCTs and one nonrandomized trial for benefit of CRT on social communication skills among chronic, moderate-severe TBI patients. Efficacious interventions were small group, outpatient programs, meeting once to twice weekly for approximately 3 months. These interventions also employ a standardized protocol for social communication skills training, with or without emotion/social perception deficit training or CBT. In general, appropriate candidates for these programs were individuals with demonstrated language and social communication deficits, and who had sufficient language and cognitive capacity to participate in a group program (Bornhofen and McDonald 2008a, 2008b; Dahlberg et al. 2007; Hashimoto et al. 2006; McDonald et al. 2008).

In summary, the committee identified and reviewed four RCTs of language and social communication cognitive rehabilitation (Bornhofen and

McDonald 2008a, 2008b; Dahlberg et al. 2007; McDonald et al. 2008), all with chronic phase, moderate-severe TBI patients. Two studies focused solely on CRT for emotion perception deficits, one focused on social communication skills training, and one incorporated a combination of both social skills training and social/emotion perception training. Participant eligibility included having sufficient language and cognitive capability to participate in a group, and impairment in social communication skills either based on a questionnaire or a referring clinician's assessment. The committee also identified a nonrandomized, parallel group controlled design study of social skills training versus a "no treatment" comparator arm (Hashimoto et al. 2006), for a total of five studies reviewed. There were no studies on CRT for language and social communication deficits among patients in the subacute phase of TBI or patients with chronic, mild TBI. One noteworthy aspect of these five CRT interventions was their relative feasibility in terms of service delivery. These CRT interventions ranged in time from 18 to 52 hours of services over 3 months; they all included delivery with small groups of patients; one employed an available workbook/manual; and most involved no more than two therapists (either social work, clinical psychology, or speech pathology, where specified). The types of intervention in these trials were either social communication skills training, emotion perception deficit training, or both; one trial also included 12 sessions with a clinical psychologist to deliver CBT.

Despite the fact that none of the five trials had more than 30 subjects in a given treatment arm, four of the trials yielded positive findings of the CRT intervention relative to controls on primary study outcomes of either improved social inference, where emotion perception deficits was a target (Bornhofen and McDonald 2008a), or social communication skills (Dahlberg et al. 2007; Hashimoto et al. 2006; McDonald et al. 2008); the exception to these findings was one very small trial (Bornhofen and McDonald 2008b). Only two studies examined outcomes after the immediate follow-up after the CRT program ended. One RCT (Dahlberg et al. 2007) found persistence of improvements in social communication skills through 6 months after the program ended, and another (Bornhofen and McDonald 2008a) found persistence of improvements in awareness of social inference through 1 month after the program ended. Only the nonrandomized, parallel group study (Hashimoto et al. 2006) showed improvements on more "distal" outcomes of social integration and productive activity. While not powered to detect smaller but potentially meaningful effects, Dahlberg et al. (2007) and McDonald et al. (2008) found that scores across treatment and waitlist groups on psychosocial outcome measures did not trend toward a difference in magnitude.

There is evidence to support benefit of small group outpatient programs, meeting once to twice weekly for approximately 3 months, and

employing a standardized protocol for social communication skills training. Applied in the community setting, such a program may or may not include concurrent emotion/social perception deficit training and CBT. Evidence shows these programs have beneficial impact on social communication skills among adults with moderate-severe TBI in the chronic phase of recovery. Patients with demonstrated language and social communication deficits should have sufficient language and cognitive capacity to participate in a group program. Evidence does not show if any subgroups are more likely to benefit than others.

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10

Memory

OVERVIEW

Memory impairments are common cognitive problems associated with TBI. As such, myriad cognitive rehabilitation therapy (CRT) interventions aim to restore or compensate for memory deficits. This chapter presents descriptions for studies by method of memory strategy (e.g., internal, external, or combined). Within these sections, the controlled studies (e.g., RCTs and nonrandomized, parallel group) are divided by treatment comparator arm (e.g., no treatment, non-CRT treatment, other CRT treatment); following controlled studies, the noncontrolled studies (e.g., pre-post or single-subject, multiple baseline experiments) are described. The chapter closes with the committee's conclusions for all memory studies reviewed, drawing out notable findings for mild or moderate-severe traumatic brain injury (TBI), as possible.

The committee reviewed 13 randomized controlled trials (RCTs) of treatments intended to improve or compensate for memory deficits. These trials varied in their intent to restore memory, show improvements in learning, or train individuals to use external or internal aids to compensate for poor memory. These trials enrolled a total of 315 study participants, with the size of the treatment group ranging from 8 to 39. The average age of participants ranged from early 20s to late 50s. Of the 13 trials, 12 enrolled participants in the chronic phase of recovery, averaging 4 to 7 years postinjury. One RCT enrolled participants who were in the subacute recovery phase, at 6 to 9 months postinjury (Watanabe et al. 1998).

The committee reviewed two nonrandomized, parallel group controlled studies of treatments intended to compensate for poor memory by train-

ing the use of internal strategies. Goldstein et al. (1996) enrolled 20 participants and O'Neil-Pirozzi et al. (2010) enrolled 94 participants. In both studies participants were considered chronic, averaging 1 to more than 11 years postinjury; the average participant age ranged from the 20s to the 40s. The committee reviewed six pre-post single group design studies and six single-subject, multiple baseline (SS/MB) designs. Table 10-1 (at the end of the chapter) presents a summary of all included studies in this review.

INTERNAL MEMORY STRATEGIES

Internal memory strategies may include the use of visual imagery or other repetitive, drilled practices. The committee reviewed seven RCTs and two nonrandomized, parallel group studies that used internal memory strategies; comparator arms included no treatment (n = 3), non-CRT treatment (n = 1), and other CRT treatment (n = 5). The committee also reviewed one pre-post single group design and five single-subject multiple, baseline experiments. Table 10-2 presents all internal memory strategy studies by design, strategy and treatment comparator.

Controlled Studies

Comparator Arm: No Treatment

Tam and Man (2004) conducted a small RCT in which 26 participants were randomly assigned to four computerized learning conditions: self-paced practice, stimuli/multi-sensory feedback, personalized training contents, and visually enhanced presentation. Treatment dosage ranged between 3 and 5 hours. Performance on drilled content improved significantly for all treatment groups compared to no treatment, with the feedback group showing the most gain. On a self-efficacy scale however, the feedback group demonstrated significant change after treatment, whereas others' self-efficacy did not change. None of the groups improved significantly on the Rivermead Behavioural Test. The group that received stimuli/multi-sensory feedback appeared to improve memory for drilled content, which also may be related to their changes in self-efficacy for memory ability. It is unclear if improvement was related to the treatment, spontaneous neurological recovery, or other treatment participants were receiving at the time. With six and seven participants per group, interpretation and generalizability are limited. Also, specific time since injury was not reported, though individuals fewer than 3 months from injury were excluded.

Thickpenny-Davis and Barker-Collo (2007) conducted a small RCT that included moderately and severely injured participants who were more than 1 year postinjury. The 14 participants were randomly assigned either

TABLE 10-2 Internal Memory Strategies

		Strategy		Treatment Comparator		
Study	Design	Multiple	Visual Imagery	No Treatment	Non-CRT	Other CRT
Bourgeois et al. 2007	RCT	X				X
Dirette et al. 1999	RCT	X				X
Dou et al. 2006	RCT	X				X
Ruff et al. 1994	RCT	X				X
Ryan and Ruff 1988	RCT	X			X	
Tam and Man 2004	RCT	X		X		
Thickpenny-Davis and Barker-Collo 2007	RCT	X		X		
O'Neil-Pirozzi et al. 2010	Parallel	X		X		
Goldstein et al. 1996	Parallel	X				X
Milders et al. 1998	Pre-Post	X				
Benedict and Wechsler 1992	SS/MB		X			
Ehlhardt et al. 2005	SS/MB	X				
Hux et al. 2000	SS/MB	X				
Manasse et al. 2005	SS/MB	X				

to receive a structured memory program or to join a waitlist. The memory intervention consisted of educating participants about memory (four parts of memory: attention, encoding, storage, and retrieval), assisting participants in understanding their own memory impairment and its effects, introducing and practicing strategies to aid memory and learning, and assisting participants in identifying the most appropriate and useful strategies for them. Strategies included didactic teaching, small group activities, discussions, problem solving and practice implementing memory strategies, errorless learning, and repetition. Postintervention, the experimental group as compared to the control group improved in many neuropsychological measures of memory (California Verbal Learning Test [CVLT]) long delayed free recall, Wechsler Memory Scale (WMS) logical memory delayed recall, and response time on the attention test (Continuous Performance Test [CPT]). The experimental group also showed increased knowledge of memory/memory strategies, increased use of memory aids/strategies, and decreased behaviors indicative of memory impairment. Results were maintained at follow-up with the exception of response time on the attention test

and immediate recall of narratives on the WMS. In addition to the initially small sample sizes, four of the seven participants in the waitlist control drop dropped out before providing posttreatment and follow-up measures.

O'Neil-Pirozzi et al. (2010), a large nonrandomized, parallel group study, examined the effects of memory training on individuals with mild, moderate, and severe injuries. Of the 94 enrolled participants, 54 received memory intervention and 40 received no specific intervention. Memory intervention, called I-MEMS focused on memory education and teaching individuals to use internal memory strategies, particularly "semantic association (i.e., categorization and clustering); semantic elaboration/chaining and imagery were emphasized secondarily" (O'Neil-Pirozzi et al. 2010). The memory intervention included 12 group sessions, 90 minutes each, held twice each week for 6 weeks, totaling 18 hours. Primary outcome measures were memory performance on the Hopkins Verbal Learning Test–Revised and the Rivermead Behavioural Memory Test II. Additional standardized tests of memory and executive functions were included. The treatment group demonstrated significant improvement on T-tests after treatment. Over time, these improvements went beyond changes in the control group. Regressions were used to determine if performance could be predicted after treatment (or second testing of control group). Consistent with the hypothesis, treatment predicted performance on both primary outcome measures at the second testing. Participants who received memory intervention improved more than those who did not. Furthermore, mild and moderately injured participants improved beyond those severely injured, even though the severely injured participants still improved beyond severely injured participants who received no treatment. At 1 month posttreatment, no significant changes were seen in memory performance. Aside from the limitation of not being completely randomized, the pre-post study design provides some evidence that the instruction of internal memory strategies has positive treatments effects when compared to no treatment, even for individuals who are at least 1 year postinjury.

Comparator Arm: Non-CRT Treatment

Ryan and Ruff (1988), a small RCT, enrolled 20 mildly to moderately injured participants who averaged 5 to 6 years postinjury. Participants were randomly assigned to the memory strategies arm or to the control arm. The memory strategies arm included training to use internal memory strategies such as associational tasks, chaining, rehearsal, visual imagery, and ritualized recall. The control group received psychosocial support and played cognitive games. Each group received 48 hours of treatment over 6 weeks. On neuropsychological measures of memory, both groups improved after treatment; however. those who were mildly injured and received strategy

training improved significantly more than moderately injured participants in both groups, as well as mildly injured participants in the psychosocial support group. Participants were not available for follow-up and no patient-centered measures were included. This study's limitations include its small number of participants and data analysis by severity *post hoc*, even though it makes sense scientifically to examine treatment effects by injury severity. It should be noted however, that this was one of the earliest studies in memory intervention to find a severity effect.

Comparator Arm: Other CRT Treatment

Bourgeois et al. (2007), another modest-sized RCT, involved adults (average age 42) with persisting memory problems several years after a documented closed head injury. Participants also needed a family member willing to participate. Participant-caregiver pairs were assigned to either spaced retrieval training or a didactic control therapy that consisted of strategy education. Assignments were made using stratified pairing based on race and sex (quasi-experimental). Both interventions were delivered via telephone by clinician trainers. After initial face-to-face assessments of cognitive difficulties and social participation (Community Integration Questionnaire), the trainer discussed treatment goals with the patient and caregiver, and the group selected three specific goals. The trainer then provided memory logs and asked patients and caregivers to record the frequency with which each problem occurred over the next week. The trainer called the participant the following day to make sure instructions and data collection methods were understood. The trainer then called participants four to five times weekly for 30-minute sessions. Participants in the spaced retrieval group received an instructional technique focused on selected goals. During sessions, the therapist modeled correct responses to questions related to the goals and instructed the participants not to struggle to retrieve responses, but to respond immediately. Participants in the control arm received the same total amount of therapy time in sessions that included discussion about memory strategies such as association, verbal rehearsal, imagery, and written reminders. Outcomes included goals mastered, generalization, the frequency of reported memory problems, cognitive difficulties scale, and community integration. Immediately and at 1 month posttraining, the space retrieval group (and their caregivers) reported more treatment goal mastery and use than the didactic instruction group (and their caregivers). Both groups reported some generalization to other nontargeted behaviors, but the difference between these improvements among groups was not statistically significant. There were no reported important or statistically significant improvements in quality of life between or within groups on these measures. One limitation was that data about "objective, observable

behaviors" related to selected goals was obtained from memory logs, and these data were sometimes incomplete or not turned in. Of the 51 pairs that agreed to participate, only 38 completed the study: 22 spaced retrieval training pairs and 16 didactic control pairs.

Dirette et al. (1999), a small RCT, included 30 participants, the vast majority of whom had mild, moderate, or severe TBI. Injury severity was distributed equally across two treatment arms: one in which internal compensatory strategies (verbalization, chunking, pacing) were taught and one in which remedial computer work involving visual processing was provided. Both treatments were delivered via a computer for a total of 3 hours, in four 45-minute sessions, once per week for 4 weeks. The compensatory strategies came from a program called "IQ Builder," which included "memory for numbers" and "memory for letters." Outcomes included weekly measurement of working memory using the PASAT and two pre-post measures of computer-based visual processing for data entry and reading. Following treatment, both groups improved significantly on weekly and posttreatment measures, although performance did not differ by group, i.e., there was no treatment effect for learning internal compensatory strategies. Demographic variables, including injury severity and time since injury, did not account for participants' performance either. *Post hoc* analyses of self-report and observations of strategy use indicated that about 80 percent of all participants, regardless of which treatment they participated in, used compensatory strategies. Unfortunately, treatment dosage was very low; there was no description of the instruction of the strategies. Furthermore, only F statistics and p-values were presented, which limits the applicability of these results to inform future research and interpretation.

Ruff et al. (1994) conducted a small RCT that involved 15 participants with severe TBI. Participants were randomized into two groups, in which the order of receiving restorative attention therapy and compensatory memory therapy was counterbalanced; i.e., both groups received both kinds of therapy in a crossover design. Participants received 20 hours of therapy via a computer program called "THINKable." Outcomes were computer scores, neuropsychological tests of attention and memory, and behavioral assessments. After intervention, the computer scores showed significant improvement in attention but no significant improvement in memory. Results of the neuropsychological measures were mixed: immediate memory improved while delayed memory did not; only one attention measure improved. Self and other behavioral assessments of memory-based behavior did change after intervention, but only observer rating of attention-related behavior showed significant change after intervention. Thus, this study provides nonspecific, limited evidence on the efficacy of internal compensatory memory training (versus attention training) in that although subjective

ratings showed improved memory, improvement on computerized memory scores and neuropsychological test scores was inconsistent.

Dou et al. (2006), a small RCT, involved 30 participants with TBI who were several months post neurosurgery. Exclusion criteria include a history of psychiatric problems or computer phobia. Participants were randomly assigned to three groups: computer assisted memory training, therapist assisted memory training, and a control group that did not receive any specific memory training. In the computer assisted training, participants were asked to identify or define the information to be learned with computerized assistance. This decontextualized training consisted of instruction in internal, compensatory memory strategies aimed at memory and management of typical daily activities. The computer then provided the necessary information for the participants to generate correct decisions through an errorless approach. Participants were not encouraged to engage in guesswork, to avoid mistakes, and were told to consider alternatives to and consequences of an intended action. The therapist assisted training covered the same content but converted the instruction into a picture album; therapists gave directions face to face. The 15 hours of training were delivered in 20 sessions occurring 6 days a week, with each session lasting about 45 minutes. Immediately after treatment, both groups improved on multiple standardized measures of memory (Neurobehavioural Cognitive Status Examination, Rivermead Behavioural Memory Test) compared to the no-treatment group, although not on every measure. The treatment groups performed similarly in comparison to each other. Performance was the same at 1 month posttreatment. Thus, there appears to be some benefit to those at a chronic recovery stage to learning to use to internal, compensatory memory strategies; the delivery (therapist versus computer) does not appear to matter. Estimates and effect sizes were not provided, so the results cannot be used to inform the design of future studies.

Goldstein et al. (1996), a small nonrandomized, parallel group study, enrolled 20 participants with TBI and persistent amnesia who were provided with computerized instructions on how to create stories from word lists ("The Ridiculously Imaged Story" technique). Of the 20 participants, 10 received the computerized presentation on how to make associations between names and faces, as well as additional initial coaching and instruction about the cues the computer would provide for the list-story task. The other participants were instructed to make these associations using the original therapist delivery mode (Goldstein et al. 1988). Both groups were trained in these imagery techniques using roughly equivalent procedures. Data from 10 participants in a previous study that used therapist delivery were included as a comparison group. The number of words recalled from lists appeared to improve during generalization trials, though

no individual trials were significantly different between computerized and the noncomputerized comparison group (from original data in Goldstein et al. 1988). After treatment, both groups recalled significantly more from examiner-provided lists when compared to pretraining, and the computerized group appeared to improve slightly more. On participant-provided lists, pretreatment to posttreatment recall improved significantly, though the computerized group lost its advantage. On the name-face learning task, the computerized group had a clear advantage over the original method group, both in learning trials and pre- and posttreatment comparisons; in fact, the therapist delivery group did not recall significantly more names after treatment. Authors stated that the decontextualized methods did not provide evidence of long-term use of learned strategies to improve memory, though there was no long-term follow-up.

Other Study Designs

Benedict and Wechsler (1992), a single-subject, multiple baseline study, examines the effects of teaching the method of loci (MOL, for word list learning) and Preview, Question, Repeat, State, and Test (PQRST, for paragraph learning). Two individuals participated in the study—one with moderate TBI and moderate memory impairment and the other with severe TBI and severe memory impairment. They received 27 and 34 weeks of training, respectively, in which the order of MOL and PQRST were counterbalanced. Results revealed that the moderately impaired participant's memory for word lists benefitted from the MOL training, but the participants' paragraph learning did not benefit from PQRST training. The severely impaired participant's performance was highly variable throughout, resulting in little change in recall from word lists or paragraphs.

Ehlhardt et al. (2005) investigated the efficacy of instructing adults with severe TBI to use recall and e-mail in a multiple-baseline-across-subjects-designed study. All five participants were many years postinjury and all demonstrated severely impaired memory and executive functions on standard neuropsychological measures. Treatment included the TEACH-M approach, which entails seven steps and learning principles of errorless learning; distributed practice and metacognitive instruction were emphasized. Training was delivered four to five times weekly, ranging from 7 to 15 weeks (as many as required to reach criteria). Four of the five participants completed the training and three of these four participants maintained these steps at 1 month after treatment ended, and all four participants maintained implementation of of the e-mail steps when "altered interface and/or a computer game with no shared features" was added (Ehlhardt et al. 2005). Interviews revealed that all four participants who completed the training endorsed the training. Inter-rater reliability and procedural fidelity

were reportedly strong: baselines were adequate prior to the start of treatment; therefore within-subject experimental control was clearly established.

Hux et al. (2000) examined the efficacy of internal memory strategies (mnemonics and visual imagery) to improve face-name recall in seven individuals with TBI who ranged from 2 to 26 years postinjury. Participants' memory impairment ranged from nonexistent to severe. Intervention was delivered via training sessions that occurred five times per day in one phase, one time per day in another phase, and two times per week in yet another phase using within-participant comparisons. Face-name recall improved more after the intervention was provided one time per day or two times per week as opposed to five times per day, however results were highly variable across individual participants. Authors also reported frequent participant behavior problems.

Manasse et al. (2005) examined the efficacy and effectiveness of a sequential treatment approach that consisted of visual imagery for face-names, followed by real-word training that involved three cuing strategies: name restating, phonemic cuing, and visual imagery. There were five participants with chronic, severe TBI, ranging from more than 1 to 29.5 years postinjury. Treatment was provided in 9 sessions of visual imagery and 30 sessions of real-world intervention. All participants improved in name-face recall after intervention regardless of the kind of cuing, and four of five participants demonstrated more spontaneous use (effectiveness) of therapists' names.

Milders et al. (1998), a pre-post single group study, involved 13 adults with memory problems following closed head injuries and 13 healthy controls matched on age and level of education. Most patients had been discharged from a nearby rehabilitation center. The mean time from injury was about 4 to 5 years, and the mean length of posttraumatic amnesia (PTA) they had suffered was reported as 36 days. The healthy controls were friends or relatives of the patients. Patients were taught strategies to improve the learning of new names and the retrieval of familiar people's names. Strategies were taught in eight, 1-hour sessions delivered one on one over a 4-month period. The importance of applying the strategies in everyday life was repeatedly stressed and homework exercises were encouraged. Pre-post assessments in both groups included the following: three target evaluation tasks that had items not presented in the training (i.e., Name Learning Test, Name-Occupation-Town Learning Test, Famous Faces Naming Test); and two memory tests assumed insensitive or unrelated to the strategies practiced during training (i.e., Digit Span Forwards and Auditory Verbal Learning Task). Performance on two of the three target tasks improved with training compared to controls, but performance on the Name Learning Test did not change in either group. Both groups had similar improvement in the two control memory tests. Limitations included

the small selected sample, an unclear history of the severity and sequelae of TBI in some patients, and narrowly focused outcome measures.

EXTERNAL MEMORY STRATEGIES

External memory strategies may include the use of notebook or other tool to enhance memory abilities. The committee reviewed four RCTs and no nonrandomized, parallel group studies that used external memory strategies; comparator arms included no treatment (n = 1), non-CRT treatment (n = 1), and other CRT treatment (n = 2). The committee also reviewed three pre-post single group designs and one single-subject, multiple baseline experiment. Table 10-3 presents all external memory strategy studies by design, strategy, and treatment comparator.

Controlled Studies

Bergquist et al. (2010) and Bergquist et al. (2009), a small randomized crossover study, enrolled 20 volunteers who had moderate-severe TBI and were more than 1 year postinjury. Participants with a history of ongoing

TABLE 10-3 External Memory Strategies

		Strategy		Treatment Comparator		
Study	Design	Notebook, Diary, Calendar, Other	External Cuing, PROMpting Device(s)	No Treatment	Non-CRT	Other CRT
Bergquist et al. 2009, 2010	RCT	X				X
Ownsworth and McFarland 1999	RCT	X		X		
Schmitter-Edgecombe et al. 1995	RCT	X			X	
Watanabe et al. 1998	RCT	X				X
Bergman 2000	Pre-Post		X			
Gentry et al. 2008	Pre-Post		X			
Hart et al. 2002	Pre-Post	X				
Zenicus et al. 1991	SS/MB	X				

psychiatric symptoms were included as long as symptoms were not severe (e.g., psychotic symptoms) and did not interfere with study participation. Participants also had to have reliable access to the Internet, as the trial compared two Internet-based interventions: an active calendar treatment intervention and a control diary condition. The calendar intervention, which involved an online therapist, focused on developing calendar skills to address difficulties with memory in everyday life and strategies to improve memory functioning. Participants in the diary control condition spent an equivalent amount of time interacting with a therapist online but simply used their calendar to record day-to-day events and not as a compensatory tool. Only 14 of the 20 participants completed the study; 6 of 8 assigned to the calendar intervention, and 2 of 8 assigned to the diary. Outcome measures included self-reported measures that assessed use of compensation strategies (Compensation Techniques Questionnaire) and satisfaction (four questions—satisfaction with therapist, satisfaction with therapy received, emotional distress during therapy, and willingness to receive such therapy again), as well as measures completed by family members (Neurobehavioral Functioning Inventory [NFI] and Compensation Integration Questionnaires [CIQ]). Analytic methods were not well described, particularly regarding missing data for patients who did not complete the trial. Most participants in both groups were satisfied with the Internet-based interventions. No statistically significant differences between groups were found for the four satisfaction questions. Also, no statistically significant differences in functional change between groups were reported after 30 sessions (NFI, CIQ outcomes).

Ownsworth and McFarland (1999) conducted a small RCT in which 20 participants with TBI who were many years postinjury were provided with a diary. Severity of brain injury was not described. Participants were randomized to either use a procedural worksheet during diary use (Diary and Self-Instructional Training) or to use the diary without this self-instruction (diary only), which required the use of higher cognitive skills of self-awareness and self-regulation. The diary-only participants were taught a behavioral sequence to use the diary. During the Diary and Self-Instructional Training session subjects learned how to compensate for everyday memory problems using a small notebook, as an internal strategy to mediate diary use. Some instructions for daily memory checklists were given verbally over the phone (in one session), but the 4-week intervention period mainly involved self-use of diaries. At the end of the intervention period, groups did not differ in mean number of diary entries; however, the diary-plus-self-instruction group maintained their use of the diary strategy to a greater extent than the diary-only group. Using daily checklists, the diary-plus-self-instruction group self-reported these strategies as more helpful and reported less confusion on a questionnaire. Thus, support is provided for

the use of self-instruction when using a memory diary if the purposes are to enhance self-efficacy of strategy use and reduce confusion and moments of disorientation.

Schmitter-Edgecombe et al. (1995) conducted a small RCT in which eight participants with severe TBI who averaged 13 to 16 years postinjury were randomly assigned to a treatment arm or a control condition for a 9-week intervention. The treatment arm consisted of training to use memory notebooks to compensate for memory, whereas the control condition consisted of group meetings to provide psychosocial support. In total, 16 hours of treatment or group support were provided (in 1-hour sessions, twice each week). Memory notebook training was provided in stages of skill-based learning consisting of anticipation, acquisition, application, and adaptation. Didactic instruction and homework, along with weekly goals, were incorporated at each stage in learning activities packets. Participants were taught to use the notebook, identify information, and take notes (Schmitter-Edgecombe et al. 1995). Modifications in notebooks were made based on participants' needs. The control group met in group sessions to discuss social or psychological challenges in everyday living due to their memory impairment (Schmitter-Edgecombe et al. 1995). The primary outcome measures were laboratory-based measures (recall, everyday memory failures [EMFs]), retrospective report of EMFs, symptom distress indicators, and observational reports of EMFs. The study also measured neuropsychological outcomes, but anticipated these would remain unchanged at posttreatment due to the focus on functional everyday memory activities. Pretreatment EMFs established a baseline to reduce error due to individual differences in subjects. On outcome measures for laboratory-based recall, laboratory-based everyday memory, and retrospective report of EMFs, there was no significant different between groups. However, a significant difference on observed EMFs was noted at immediate posttreatment; at 6 month follow-up, these findings retained direction but were no longer statistically significant. These findings provide preliminary evidence for the usefulness of notebook training to decrease EMFs for individuals with severe TBI. The limitation of the trial primarily was due to small size of the sample.

Watanabe et al. (1998), a small RCT, compared the effect on orientation of the presence/absence of a wall calendar in participants' hospital room. All participants were receiving other inpatient rehabilitation, presumably CRT. The study compared temporal orientation (memory for the date) of 30 inpatients on an acute rehabilitation unit who were randomly assigned to groups that either have a wall calendar posted in their room or to not have a calendar. The average age in both groups was in the 50s. Neither time since injury nor severity of injury was reported; however, because participants were reportedly still in PTA, they were likely at least moderately injured and more than 6 months postinjury. The primary out-

come measure was the Temporal Orientation Test (TOT). Results indicated that the presence of a wall calendar had no effect on orientation; indeed, only the emergence out of PTA corresponded to orientation. This relatively weak study found no relationship between the presence of a wall calendar and orientation. The limited information provided on the participants, and the vague description of the intervention, make it difficult to interpret the results of this study for an inpatient population participating in rehabilitation. It is unclear how therapists provided orientation therapy that involved the wall calendar. The older ages of the participants implies that many had strokes, which can result in different kinds of orientation problems (e.g., neglect), which confounds these results. Also, because both groups were actively engaged in inpatient rehabilitation, there were likely numerous commonly shared features of rehabilitation between the two groups.

Other Study Designs

Bergman (2000) conducted a pre-post study involving 41 individuals with chronic cognitive deficits after severe TBI. All were described as having "difficulties with conventional strategies" for aiding memory such as notebooks, calendars, and Post-it reminders. The tested intervention was a "cognitive orthotic," a computer software program designed as a compensatory strategy for aiding weak or ineffective cognitive functions. The underlying foundation for the program was described as "error-free learning, rapid system and skill acquisition, and facilitated generalization." The computer program used six activity modules intended to minimize potential for error, reduce memory burden, maximize ease of memory storage and retrieval, limit preservative tendencies, promote transfer of training, and facilitate task completion through guided sequences. Modules addressed topics such as telephone logs, savings and checking, and appointments. Examiners (neuropsychologists or speech-language therapists) oriented individuals to the program and assessed participants' mastery of the modules. Mastery was defined as the unassisted reliable completion of a targeted task. Reported outcomes were that 36 of the 41 participants achieved mastery of four or more activity modules, and 36 demonstrated rapid achievement of success on initial assigned tasks. Limitations included the absence of a control group, narrowly focused or restricted outcome measures, and an unclear history of the severity and sequelae of TBI in some patients.

Gentry et al. (2008), a pre-post single group study, involved 23 community-dwelling individuals with severe TBI at least 1 year postinjury. All had memory problems that affected ability to perform everyday tasks, such as remembering appointments, managing time and tasks, and managing money and medications. The intervention involved training individuals to use a freely provided personal digital assistant (PDA) as a compensatory

cognitive aid. Training sessions were provided by an occupational therapist in three to six 90-minute home visits conducted within a 1-month period. After training, participants were asked to use their PDAs for an 8-week period. All participants completed the study. Reported outcomes were improvements (pre-post) in assessments of self-rated occupational performance, satisfaction with occupational performance, and in participation in everyday life tasks. The outcomes were measured with standardized tests (Canadian Occupational Performance Measure and Craig Handicap Assessment and Rating Techniques-Revised Measure) and, while self-reported, were agreed upon by a family member or caregiver. Limitations were the absence of a comparison group and perhaps lack of outcome measures assessed by an objective (outside) observer. Generalizability may be limited because all participants were motivated volunteers recruited through fliers who had a working home personal computer and who were able to use a stylus without difficulty.

Hart et al. (2002) investigated the usefulness of a voice organizer in a pre-post design study. The 10 participants, who had moderate-severe TBI and were 3 to 18 years postinjury, were enrolled in a comprehensive TBI rehabilitation program. Case managers or clinicians developed a list of six therapy goals for each client. The goals chosen were considered likely to be discussed in upcoming therapeutic sessions, known to have been forgotten or not followed through by the client in the past, and agreed upon as important by the client and family. Case managers read the individualized goals to clients. Half of the goals that were read and reviewed were randomly assigned to be recorded on a voice organizer for clients while half were not recorded. Clients were given and trained to use devices with the voice recordings. They were prompted by an alarm to listen to the recorded goals three times daily. Seven days after the original session in which goals were recorded, each client's recall for all six goals was tested by a staff member who was blind both to the therapy goals relevant to that client and to the specific goals that had been recorded. Recorded goals were recalled more often than the goals that were not recorded. Clinicians involved in the study thought that participants were more conscious of their recorded goals and more likely to follow through with them. Limitations include the small selected sample and narrow outcome measures that did not assess behavior changes.

Raskin and Sohlberg (1996), a single-subject, multiple baseline experiment, studied the efficacy of prospective memory training with two adults with severe TBI who were, respectively, 11 and 12 years postinjury. Two types of intervention were provided: prospective memory training and repetitive memory drill. Prospective memory was measured using the Patient Reported Outcome Measures (PROM), which measures memory at 1, 2, 10, and 20 minutes, and at 24 hours. Memory for future actions improved

more after prospective memory training than after repetitive drill, although generalization to real-world remembering was variable across participants and type of training. Both participants indicated their preference for prospective memory training during interviews.

Zencius et al. (1991), a single-subject, multiple baseline report, examined the usefulness of memory notebook training for completing homework assignments with four adults with TBI who were also receiving interdisciplinary rehabilitation services. Little descriptive information was provided about the participants other than age and variable test results. After notebook training, three of the four participants improved in completing the number of components to the homework assignments. Without participant or training information, coupled with the ongoing rehabilitation services participants were receiving, these results are difficult to interpret.

COMBINED MEMORY STRATEGIES: INTERNAL AND EXTERNAL

Combined memory strategies may include a blend of both internal and external approaches. The committee reviewed two RCTs and no nonrandomized, parallel group studies that used combined memory strategies; comparator arms included no treatment (n = 1) and other CRT treatment (n = 1). The committee also reviewed one pre-post single group design. Table 10-4 presents all combined memory strategy studies by design, strategy and treatment comparator

Controlled Studies

Berg et al. (1991) (with Milders et al. 1995) enrolled 39 severely injured participants in a small RCT in which they compared the efficacy of a memory strategy program that consisted of instructing two control groups

TABLE 10-4 Combined Memory Strategies

		Strategy		Treatment Comparator		
	Design	Internal	External	No Treatment	Non-CRT	Other CRT
Berg et al. 1991 Milders et al. 1995	RCT	Multiple strategies	Multiple strategies	X		X
Kaschel et al. 2002	RCT	Visual imagery; multiple strategies	Multiple strategies			X
Freeman et al. 1992	Pre-Post	Multiple	Multiple			

on compensatory internal strategies and external aids. Thus, there were three arms in this trial; two that received treatment, the memory strategy rehabilitation group and a "pseudo rehabilitation" group, and one group that did not receive treatment. One of the "pseudo rehabilitation" control groups drilled and practiced (restorative), and the other received no treatment. The memory strategy program emphasized both internal strategies and the use of external memory aids, whereas the "pseudo rehabilitation" control treatment consisted of repetitive drill and practice, and the control group patients were tested according to the time schedule of the trained groups, but received no training. All participants were severely injured and averaged 5 to 6 years postinjury (i.e., in the chronic phase of recovery). Outcomes included self- and other subjective memory questionnaires (including measurements of anxiety related to memory and coping with daily memory problems), and standardized scores (mean sum score, acquisition score, and delayed memory score) from the Rey Auditory Verbal Learning Test, face-name learning, and memory for a shopping list. Immediately after treatment, the subjective ratings of memory problems improved significantly for both the strategy and the drill/practice groups. The strategy group improved on two of three neuropsychological memory measures (sum and delayed memory scores) immediately after treatment, and at follow-up improved significantly in the other neuropsychological memory measure (acquisition). There were no significant improvements found for the drill/practice and the no treatment group. Unfortunately, the authors did not report the reasons for dropouts, nor make adjustments for this in the data analysis; this information may have helped to explain why scores on memory tests appeared to improve over time after the immediate post-treatment results.

Kaschel et al. (2002) conducted a small RCT of 24 patients, including 12 patients with severe TBI who averaged 5 to 6 years postinjury. Participants were randomly assigned to receive visual imagery to improve memory or to receive a typical memory rehabilitation program, which emphasized a combination of compensatory internal strategies and external compensatory strategies. There were 30 treatment sessions in total. Primary outcomes were measures from the Rivermead Behavioural Memory Test (RBMT), the logical memory (stories) subtest from the Wechsler Memory Scale (WMS), and the Appointments test. Secondary outcomes were measures on the Concentration Endurance Test d2, Memory Assessment Clinics ratings scales (MAC-S, MAC-F). Immediate outcomes after intervention revealed that the visual imagery group performed better on the immediate recall of stories (both RBMT and WMS), delayed recall on the RBMT, and delayed (but not immediate) recall on the Appointments test. There were inconsistent treatment effects on the self-reported and other-reported ratings. No treatment

effects were found on the secondary measures. At 3 months after treatment, all treatment effects were maintained.

Other Study Design

Freeman et al. (1992) conducted a pre-post study that enrolled 12 adults in a private rehabilitation program center. All had cognitive deficits and a history of a closed head injury. Of the 12, 6 had been referred for cognitive rehabilitation; they were enrolled in a 6-month rehabilitation program that included a memory module as one of seven modules. The memory module was completed in 2.5 weeks. It was delivered in a 2-hour group setting, three times weekly. During the treatment, trainees and staff repeated various paragraphs and taught skills and techniques to enhance paragraph retention. Skills and techniques included such things as note taking in a memory book, self-monitoring skills, prompts to stop and think, restatement of presented material, and use of imagery. The other six people in the study had been referred for neuropsychological testing only. They received none of the rehabilitation modules but did paragraph memory tests (described below) as part of their neurological assessment at an initial visit and then again 2.5 weeks later. Of note, the mean time since injury for the memory module group was 33 months whereas the mean time since injury for the control group was 12 months. The outcome measure was a memory score based on comprehension and retention of main and secondary ideas presented in a paragraph. The reported outcome was a statistically significant difference between treatment and control posttest memory scores that favored the treatment group. Limitations included the small sample size, differences in characteristics of the intervention and control groups that were not accounted for in analyses, an intervention that was not described sufficiently to be replicable, and a single, limited outcome measure. Whether staff that administered and scored the outcome were the same staff that administered the intervention was not clear.

RESTORATIVE STRATEGIES

Restorative memory strategies aim to reestablish memory functioning following brain injury. The committee reviewed two RCTs that included repetitive drill as a treatment arm; comparator groups were both no treatment and have been previously described in this chapter (see Berg et al. 1991; Tam and Man 2004). The committee also reviewed one pre-post design and one single subject, multiple baseline experiment. Table 10-5 presents all restorative memory strategy studies by design, strategy, and treatment comparator.

TABLE 10-5 Restorative Memory Strategies

		Strategy	Treatment Comparator		
Study	Design	Restorative	No Treatment	Non-CRT	Other CRT
Berg et al. 1991; Milders et al. 1995	RCT	Multiple strategies	X		X
Tam and Man 2004	RCT	Multiple strategies	X		
Raskin and Sohlberg 2009	Pre-Post	Cuing, PROMpting			
Raskin and Sohlberg 1996	SS/MB	Cuing, PROMpting			

Raskin and Sohlberg (1996), a single-subject, multiple baseline experiment, studied the efficacy of prospective memory training with two adults with severe TBI who were 11 and 12 years from injury. Two types of intervention were provided: prospective memory training and retrospective memory drill. Prospective memory was measured using the PROM of the Assessment of Intentional Memory (AIM) scale, which measures memory at 1, 2, 10, and 20 minutes, and at 24 hours. Memory for future actions improved more after prospective training than after the memory drill, although generalization to real-world memory was variable across the two participants and type of training. Both participants validated their preference for prospective memory training during interviews.

In a follow-up pre-post crossover design, Raskin and Sohlberg (2009) provided both prospective memory training and retrospective memory drills to adults with brain injury and healthy adults. Eight adults with brain injury received 1-hour training sessions, twice each week for 6 months. Again, prospective memory was measured using the PROM tasks of the AIM scale, at 2 and 10 minutes. Additional neuropschological tests, memory questionnaires, and a journal/log served as generalization measures. Adults with brain injury improved on prospective memory time and tasks after 2 minutes; however, this group did not show improvement at the longer delay of 10 minutes. On neuropsychological measures immediately post treatment, adults with brain injury improved in attention and executive functions. Generalization to everyday memory performance as measured by a memory questionnaire and memory diaries also improved. Maintenance of prospective memory improvements was demonstrated at 1 year posttreatment. None of the subjects showed improvement for retrospective memory drills. Half of the brain injury group initially enrolled in the study dropped out for various reasons leading to the potential for selection bias.

CONCLUSIONS: MEMORY

The majority of the evidence on the efficacy of memory intervention is with moderate-severely injured individuals who are at a chronic stage of recovery. In the chronic recovery phase, those with impaired ability to learn (store and retrieve) new information, routines, and skills are likely targets for interventions targeting the individual's precise memory impairment. For example, encoding strategies are taught to individuals who have lost the ability to transfer new information into long-term knowledge. Individuals at a subacute phase of recovery also experience memory impairments; however, related attention, information processing, and organization impairments usually impede successful isolation and treatment of memory impairments.

Mild TBI

Internal Strategies

The committee found no evidence that demonstrates the benefit of using internal memory strategies for everyday memory given the absence of patient-centered outcomes.

The committee found limited evidence that the ability to recall new information improves in patients with chronic, mild TBI when they learn to use internal memory strategies such as visual imagery and other encoding strategies. This benefit was short term or immediate as measured by standard memory tests (O'Neil-Pirozzi et al. 2010; Ryan and Ruff 1988).

The committee found limited evidence that in patients with chronic, mild TBI, learning to use internal memory strategies benefits memory long term (O'Neil-Pirozzi et al. 2010).

External Strategies

The committee found no studies that investigated the benefit of using external memory aids for patients with mild TBI.

None of the studies investigated the efficacy of memory intervention for individuals with mild TBI at the subacute recovery stage. Within a short time after injury, most individuals with mild TBI recover and remain asymptomatic. There was limited evidence that individuals with mild TBI in the chronic stage of recovery benefit from learning to use *internal strategies*

such as visual imagery and other encoding strategies (O'Neil-Pirozzi et al. 2010; Ryan and Ruff 1998). In these studies, dosage was provided for 13 to 18 hours, compared to psychosocial support or no treatment. Gains on formal tests of memory immediately after treatment were positive, although only one study provided evidence that these benefits were maintained at 1 month. There is no evidence demonstrating benefit to everyday memory, given the absence of patient-centered outcomes. Future research will be necessary to determine whether or not these strategies improve an individual's ability to learn new information with clear benefit to daily activities (e.g., learning procedure manual instructions, retaining information for an exam). The absence of evidence describing the efficacy of external memory or compensatory strategies for those who have lingering memory impairment after mild TBI should not be equated with negative findings; that is, no current evidence does not mean that individuals with mild TBI do not benefit from using external aids.

The literature suggests that there is limited evidence of a differential benefit of internal memory strategies to patients with mild TBI over those with moderate or severe TBI. Two studies, one RCT and one nonrandomized, parallel group design (O'Neil-Pirozzi et al. 2010; Ryan and Ruff 1998) found that those with mild TBI benefited more than those with moderate or severe TBI. Single-subject, multiple baseline studies found that while individuals with moderate injuries made some improvement in memory, those with severe injuries did not benefit as much (Benedict and Weschler 1992) or did not demonstrate transfer of these skills (Manasse et al. 2005). Even RCTs with good experimental control showed that the generalization of the use of these strategies is insufficiently documented for those with moderate-severe TBI.

Moderate-Severe TBI

Restorative Strategies

The committee found evidence that was not informative that memory intervention restores memory functioning in patients with moderate-severe TBI (Berg et al. 1991; Tam and Man 2004).

The identified evidence did not show a benefit of attempting to *restore* memory in individuals with moderate-severe injuries. Berg et al. (1991) (with Milders et al. 1995) suggests that restoring memory in patients with severe TBI is not efficacious, even though subjectively patients in the repetitive drill and practice arm reported changes in their memory. This RCT found that a comprehensive memory program including internal and external memory strategies improved both memory test scores and patient-

centered measures of improved everyday memory, at least maintained at follow-up. On standard measures of memory, only the strategy group improved. Tam and Man (2004) compared various kinds of computerized intervention, which was provided for 3 to 5 hours. All groups improved memory for the learned content after treatment, although not as much as the feedback group improved. The drill and practice group's self-efficacy ratings of memory did not change. The low dosage of intervention makes these results difficult to interpret.

Internal Strategies

The committee found limited evidence that using internal memory strategies resulted in practical, improvement in everyday activities that involve memory and/or learning. Benefits in patient-centered outcomes were demonstrated by changes in participants' self-efficacy about their memory (Tam and Man 2004), increased knowledge about memory strategies, validated reports by others in the use of strategies, and fewer behavior-based memory problems (Thickpenny-Davis and Barker-Collo 2007).

The committee found limited evidence that showed the majority of treatment effects were maintained at 1-month posttreatment follow-up (Bourgeois et al. 2007; Ehlhardt et al. 2005; O'Neil-Pirozzi et al. 2010; Thickpenny-Davis and Barker-Collo 2007).

The committee found modest evidence that most studies that were compared to no treatment or non-CRT treatment showed immediate benefit of improved memory using internal strategies as measured on standard memory tests (O'Neil-Pirozzi et al. 2010; Thickpenny-Davis and Barker-Collo et al. 2007; Ryan and Ruff 1988). Beneficial treatment effects were difficult to determine in studies comparing memory intervention to other CRT, possibly due to overlapping cognitive processes (Bourgeois et al. 2007; Dirette et al. 1999; Dou et al. 2006; Kaschel et al. 2002; Ruff et al. 1994).

The efficacy of using internal memory strategies to immediately improve memory performance in individuals with moderate-severe TBI on standard memory tests has been shown in several RCTs and a nonrandomized, parallel group design when compared to no treatment or non-CRT treatment (Dou et al. 2006; O'Neil-Pirozzi et al. 2010; Ryan and Ruff 1988; Tam and Man 2004; Thickpenny-Davis and Barker-Collo 2007). Dosage ranged from 13 to 30 sessions. The findings from RCTs that compared internal memory strategies given by instruction to other CRT treatments were less

consistent in finding a benefit to memory above and beyond the other CRT group on standard memory tests (Bourgeois et al. 2007; Dirette et al. 1999; Dou et al. 2006; Kaschel et al. 2002; Ruff et al. 1994). Considering the overlap in cognitive functions, it is challenging to isolate the active ingredient that enhances memory in those in the comparison treatments receiving another form of CRT.

A few RCTs had mixed results when they compared the interface or delivery of instruction of treatment strategies to moderate-severely injured individuals. Delivery methods included computer versus therapist, spaced retrieval instruction versus strategy discussion, and four computerized versions of memory intervention (Bourgeois et al. 2007; Dou et al. 2006; Tam and Man 2004). Although the treatment conditions resulted in improved memory over no treatment or baseline, there were not clear advantages of one instructional practice over another. Pre-post designs and single-subject designed studies add to the evidence base with similar results as the RCTs (Milders et al. 1998). The benefits of improved memory were in general maintained, though not all studies reported maintenance effects.

There is modest evidence that the use of internal memory strategies results in practical improvement in everyday activities that involve memory and/or learning. Two studies reported improved patient-centered outcomes that included changes in self-efficacy about their memory (Tam and Man 2004), increased knowledge about memory strategies, validated reports by others in the use of strategies, and fewer behavior-based memory problems (Thickpenny-Davis and Barker-Collo 2007). Three studies reported that they followed participants after treatment ended and the majority of the treatment effects were maintained (Bourgeois et al. 2007; O'Neil-Pirozzi et al. 2010; Thickpenny-Davis and Barker-Collo 2007).

Comparator: No Treatment or Non-CRT Treatment

Three RCTs (Dou et al. 2006; Tam and Man 2004; Thickpenny-Davis and Barker-Collo 2007) and one nonrandomized, parallel group study (O'Neil-Pirozzi et al. 2010) demonstrated improvement in learning and memory for those who received internal memory strategy training when compared to a no treatment control group. Outcomes included standardized tests of memory. Two of the four studies reported improved patient-centered outcomes that included changes in self-efficacy about their memory (Tam and Man 2004), increased knowledge about memory strategies, validated reports by others in the use of strategies, and fewer behavior-based memory problems (Thickpenny-Davis and Barker-Collo 2007). Two of the three studies that reported treatment effects were maintained at 1 month had no treatment as the control group (O'Neil-Pirozzi et al. 2010; Thickpenny-Davis and Barker-Collo 2007). One RCT provided evidence of

memory intervention when compared to control intervention that was not CRT (e.g., "sham" treatment). Ryan and Ruff (1988) found that the benefit of internal memory strategies was confined to those with mild injuries, not those with moderate-severe injuries.

Comparator: Other CRT Treatment

Five RCTs (Bourgeois et al. 2007; Dirette et al. 1999; Dou et al. 2006; Kaschel et al. 2002; Ruff et al. 1994) and one nonrandomized, parallel study (Goldstein et al. 1996) provided generally positive evidence that internal memory strategies improve aspects of memory above and beyond the control CRT. In Ruff, participants demonstrated changes on memory tests after a memory training module and after an attention module. Kaschel et al. (2002) attempted to investigate the active ingredient of visual imagery from matched participants who were receiving memory rehabilitation involving both external memory compensatory aids and other internal memory strategies. Participants who were trained in visual imagery performed better on several laboratory measures of memory, but not all. Dou et al. (2006) found that both the computer and therapist delivered internal memory programs resulted in similar improvement in memory over those who received no treatment; these results were maintained at 1 month. Dirette et al. (1999) compared to 3 hours of a computer-delivered internal memory strategy program to a "remedial computer program of visual processing" and found no group differences. The low dosage in this study is noticeable compared to the other trials, which ranged from 15 to 30 hours. Bourgeois et al. (2007) investigated the efficacy of spaced retrieval with individuals with severely impaired memory, compared to strategy instruction/discussion over the telephone with the intent to improve the recall and mastery of participants' individualized goals. The spaced-retrieval group was better at reporting their goals and their use than the strategy discussion group, although no differences occurred between groups with generalized strategy use or reported memory problems. Bourgeois et al. (2007) also reported most of the treatment effects were maintained at 1 month. In a small nonrandomized, parallel group study, Goldstein et al. (1996) had mixed results when comparing a computer- to therapist-delivered intervention on how to make associations.

External Strategies or Aids

The committee found modest evidence of the effectiveness of external memory aids (e.g., notebooks, alerting devices) to reduce everyday memory failures for patients with moderate-severe injuries in three RCTs (Bergquist et al. 2009, 2010; Ownsworth and McFarland 1999;

Schmitter-Edgcombe et al. 1995) and other studies (Bergman 2000; Gentry et al. 2008; Hart et al. 2002). Patient-centered outcomes included reduced numbers of memory failures and patient satisfaction.

The committee found modest evidence from RCTs (Bergquist et al. 2009, 2010; Ownsworth and McFarland 1999; Schmitter-Edgcombe et al. 1995) and other studies (Bergman 2000; Gentry et al. 2008; Hart et al. 2002) that showed immediate benefit of using external strategies or aids to compensate for poor memory.

There is modest evidence from three RCTs of the effectiveness of external memory aids to reduce everyday memory failures for patients with moderate-severe injuries in three small to modest-sized RCTs (Bergquist et al. 2009, 2010; Ownsworth and McFarland 1999; Schmitter-Edgecombe et al. 1995). Patient-centered outcomes included use of a compensatory aid, reduced numbers of memory failures, and patient satisfaction. Schmitter-Edgecombe et al. (1995), in a small but well-designed trial, found evidence that therapy to use memory notebooks resulted in compensation for everyday memory failures over those who received psychosocial support. Beyond using the compensatory aides, results suggest that guided self-instruction is associated with participants' reporting the compensatory aid is more helpful and more effective in reducing daily disorientation than being given the aid without instruction (Ownsworth and McFarland 1999). In a telehealth study, Bergquist et al. (2009, 2010) compared dynamic instruction in using a calendar to a control condition (other CRT) in which participants used a diary. Both groups reported satisfaction with the Internet therapy; groups did not differ in self-reported satisfaction or in changes in general overall function on patient-centered outcomes of community integration.

In addition to these RCTs, several studies of other designs found complementary findings, including using cognitive or those strategies to guide the completion of complex, goal-directed activities (Bergman et al. 2000; Gentry et al. 2008; Hart et al. 2002). Therefore, while it would not be expected that external memory aids would actually improve memory; there is evidence that their use is effective in assisting patients to complete everyday, complex activities as indicated in functional, patient-centered outcomes. There is some evidence that patients continue to use compensatory aids several months after treatment ends.

TABLE 10-1 Evidence Table: Memory

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
RCT						
Bergquist et al. 2010 Bergquist et al. 2009	14	Moderate-Severe	This study examined patient satisfaction with a web-based cognitive rehabilitation program previously shown to effect functional improvements.	Y Other CRT Content: Diary condition	• Compensation Techniques Questionnaire • Study Satisfaction Questionnaire	Between the time of assessment and the treatment condition, no significant differences were found in satisfaction. Greater satisfaction upon study completion was additionally found to be correlated with a higher level of calendar use prior to the study's initiation.
Berg et al. 1991 Milders et al. 1995	39	Severe	"Memory strategy training" with several memory tasks chosen by participant with following rules applied: • try to accept that a deficient memory cannot be cured • make a more efficient use of your remaining capacities • use external aids when possible • pay more attention • spend more time • repeat • make associations • organize • link input • retrieval situations	Y No Content and Other CRT Content: Two control groups—one that drilled and practiced (restorative), and one that received no treatment	• Control tasks ▪ Distraction-Reaction Time Task ▪ Reaction Time Task • Effect tasks ▪ 15 Words Test ▪ Face-Name Learning ▪ Shopping Lists	At 4-month follow-up both groups of trainees saw significant, subjective effects of therapy on their everyday memory functioning, rating them as highly positive; only the strategy training group saw significant, objective effects on memory performance scores.

continued

TABLE 10-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Bourgeois et al. 2007	38	NR	This study's objective was to evaluate the effectiveness of an errorless training approach called Spaced Retrieval (SR), delivered via telephone, in improving everyday memory problems.	Y Other CRT Content: Didactic memory strategy instruction	• Cognitive Difficulties Questionnaire (CDS) • Community Integration Questionnaire (CIQ)	Both SR and SI groups experienced a non–statistically significant improvement in their frequency of memory problems; furthermore, the differences between the two from pre-assessment remained, but were still not significant. At 1-month follow-up both groups reported some generalized strategy use to other nontargeted behaviors, but there were no significant results.
Dirette et al. 1999	30	Mild, Moderate, Severe	This study examined the effects of a compensatory intervention compared to a remedial intervention for visual processing deficits.	Y Other CRT Content: Remedial computer work	• Functional computer-based visual processing tasks: PASAT and the "Matching Accuracy Test" segments of The brain Game program ▪ Two data entry tasks ▪ One reading task	Both groups experienced statistically significant improvement on posttests as well as weekly measures; further, 80 percent of both groups used compensatory strategies regardless of the intervention method. Those who used strategies performed better than those who did not.

Dou et al. 2006	37	NR	This study evaluated the effects of a computerized, errorless learning-based memory rehabilitation program in China.	Y Other CRT Content: Non-specific memory training	• Neurobehavioural Cognitive Status Examination (NCSE) • Rivermead Behavioural Memory Test–Cantonese version (RBMT) • Hong Kong List Learning Test (HKLLT)	Though no significant differences were found between patients in computer-assisted memory group (CAMG) and the therapist-administered memory group (TAMG), including a comparison between post training outcome measures and follow-up results, patients in both groups performed better than the Control Group (CG) in the NCSE and RBMT. Compared to the TAMG and CG, the CAMG showed significant improvement in their HKLLT assessment.
Kaschel et al. 2002	24	NR	This study aimed to compare two training programs, with the experimental condition based on imagery training and the other based on pragmatic memory training for the control group.	Y Other CRT Content: Standard of care, with frequency, intensity, individualization of training comparable to treatment group	• "d2" form of the Concentration Endurance Test • Everyday memory test "Appointments" • Memory Assessment Clinics Rating Scales (MAC-S, MAC-F) • RBMT • Wechsler Memory Scale	Imagery training significantly improved delayed recall of everyday relevant verbal materials, such as stories and appointments.

continued

TABLE 10-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Ownsworth and McFarland 1999	20	NR	The aim of this study was to investigate the remediation and assessment of everyday memory problems, using the RBMT and WMS-R to measure global memory performance in 20 subjects.	Y No Content: Control group instructed to use the diary, without treatment	• RBMT • WMS-R	Compared to the Diary Only (DO) group, the Diary and Self-Instructional Training (DSIT) group made diary entries more consistently, reported fewer memory problems, and made more positive ratings associated with treatment efficacy.
Ruff et al. 1994	15	Severe	Two groups received two counterbalanced treatments, attention training compared or memory training, delivered via a computer-based multi-media program called THINKable.	Y Other CRT Content: Attention and memory training, delivered to both groups in a crossover design	• 2+7 Selective Attn Test • Behavioral assessments • Continuous Performance Test • Corsi Block Learning Test • Rey Auditory Verbal Learning Test • WAIS-R	On the computer scores after intervention, there was significant improvement in attention, whereas no significant improvement for memory. On neuropsychological measures, the results were mixed: immediate memory improved while delayed memory did not; only one attention measure improved. Self- and other behavioral assessment of memory-based behavior did change after intervention, whereas only observer rating of attention-related behavior reached significance after intervention.

Ryan and Ruff 1988	20	Mild-Moderate	Memory retraining with visuospatial and verbal representations, using multiple strategies: associational tasks, chaining, rehearsal, visual imagery, multiple associations, ritualized recall.	Y Non-CRT Content: Psychosocial activities with no feedback from therapist	• Benton Visual Retention Test (BVRT) • Rey-Osterrieth Complex Figure Test (CFT) • Ruff-Light Trail Learning Test (TLT) • Selective Reminding Test • Taylor Complex Figure • Wechsler Memory Scale (WMS), Logical Memory Subtest	On neuropsychological measures of memory, both groups improved after treatment; however, those who were mildly injured improved significantly more than moderately injured participants who had received strategy training, moderately injured participants in the psychosocial support group, or mildly injured participants in the psychosocial support group.
Schmitter-Edgecombe et al. 1995	8	Severe	The purpose of this study was to evaluate the effectiveness of a 9-week memory notebook treatment for patients with known memory deficits.	Y Non-CRT Content: Supportive group therapy	• Everyday Memory Questionnaire (EMQ) • Global Severity Index from the *Symptom Checklist 90–Revised* • Logical Memory 1 and 2 scales • Notebook training • RBMT • Visual Reproduction 1 and 2 scales • Weekly learning activities packets (LAPs) • WMS-R	The notebook training group reported significantly fewer everyday memory failures (EMFs) on a daily checklist measure than the supportive therapy group; at follow-up, this finding was no longer significant. For the lab-based memory measures, no significant treatment effects were found at posttreatment or follow-up.

continued

TABLE 10-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Tam and Man 2004	26	NR	The goal of this study was to gain understanding of computer-assisted training effects, using four theoretically different memory retraining strategies, for the treatment of posttraumatic amnesia.	Y No Content: Unspecified; the study indicated treatment was not provided	• Built-up computer performance records • RBMT • Self-efficacy rating scale	Though all four memory training methods showed non-statistically significant positive results compared with the no-treatment control, clinical improvement was found in all four methods, and the Feedback group showed significant improvement in self-efficacy compared to the other groups.
Thickpenny-Davis and Barker-Collo 2007	14	Moderate-Severe	This study aimed to evaluate the effect of an eight-session structured group format memory rehabilitation program on memory function deficits.	Y No Content: Waitlist control	• Behavioral indicators of memory impairment checklist • California Verbal Learning Test (CVLT) • Integrated Visual and Auditory Continuous Performance Test (IVA-CPT) • Memory in Everyday Life and Use of Aids and Strategies Questionnaire • "Memory quiz" (Extent of participants' knowledge about memory and memory strategies) • Visual paired associates (VPA) • Wechsler Memory Scale (WMS) Logical Memory Subtest, revised	Compared to the control, the experimental group improved in many neuropsychological measures of memory (CVLT long delayed free recall, WMS logical memory delayed recall, and response time on the attention test [CPT]), also showing increased knowledge of memory/memory strategies, increased self/observer (significant other) use of memory aids/strategies and decreased self/observer behaviors indicative of memory impairment. Results were maintained at follow-up, with the exception of response time on the attention test and immediate recall of narratives on the WMS.

Watanabe et al. 1998	30	NR	This study compared the effect of the presence or absence of a wall calendar in participants' hospital room on temporal orientation.	Y Other CRT Content: Control received nonspecific cognitive rehabilitation, with no calendar in room	Temporal Orientation Test (TOT) measuring day, date, month, year	Results indicated that the presence of a wall calendar and corresponding orientation therapy had no effect on orientation; only the emergence out of PTA corresponded to orientation.
Nonrandomized, Parallel Controlled Group						
O'Neil-Pirozzi et al. 2010	94	Mild, Moderate, Severe	This study examined the effects of memory training focused on internal strategy use for memory impairment.	Y No Content: Control received no specific intervention	• Hopkins Verbal Learning Test–Revised (HVLT-R) • Rivermead Behavioral Memory Test II (RBMT II)	Memory group intervention participants showed improved memory performance immediately postintervention as well as one month postintervention. Mild and moderately injured participants improved beyond those who were severely injured, even though the severely injured participants still improved beyond severely injured participants who received no treatment.

continued

TABLE 10-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Goldstein et al. 1996	30	NR	This study replicated earlier work that demonstrated the efficacy of two methods of memory training using imagery mnemonics.	Y Other CRT Content: Parallel groups, with one receiving (partly) computerized intervention, one receiving non-computerized intervention	• Free recall of patient-provided list • Number of words recalled on a selective reminding task • Scoring on RIS and FNM tasks	After treatment, both groups recalled significantly more from examiner-provided lists when compared to pretraining, and the computerized group appeared to improve slightly more. On participant-provided lists, pretreatment to posttreatment recall improved significantly, though the computerized group lost its advantage. On name-face learning task, the computerized group had a clear advantage over the original method group both in learning trials and pre- and posttreatment comparisons; the therapist delivery group did not recall significantly more names after treatment.
Pre-Post Single Group						
Bergman 2000	41	NR	This study examined the effect of orientation to a cognitive orthosis (CO); subjects were progressed on specific tasks until they could perform without assistance (mastery).	N	• Appointment Scheduling • Check Writing • Directory • Journal • Savings Deposit/ Withdrawal • Telephone Log	Thirty-six of the 41 participants achieved mastery of four or more activity modules and 36 demonstrated rapid achievement of success on initial assigned tasks.

Freeman et al. 1992	12	NR	This study compared the efficacy of memory remediation treatment, which consisted of compensatory and executive training skills delivered over a 2.5-week period, with no treatment.	N	Identification of key ideas in a paragraph read to the subject	There was a statistically significant difference between treatment and control post-test memory scores that favored the treatment group.
Gentry et al. 2008	23	Severe	This study examined the efficacy of personal digital assistants (PDAs) as a compensatory cognitive aid, used by subjects for 8 weeks after three to six in-home training sessions conducted by an occupational therapist.	N	• Canadian Occupational Performance Measure (COPM) • Craig Handicap Assessment and Rating Technique-Revised (CHART-R)	Self-ratings of occupational performance and satisfaction with occupational performance (COPM), as well as self-rating of participation (CHART-R), showed statistically significant improvement.
Hart et al. 2002	10	Moderate-Severe	This study investigated the usefulness of a portable voice organizer in helping people recall therapy goals and plans previously discussed with their case managers.	N	Number of goals (recorded and nonrecorded) that were remembered	Subjects recalled recorded goals more often than goals that were not recorded; furthermore, recorded goals seemed to be correlated with better awareness or follow-through with therapy objectives.

continued

TABLE 10-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Milders et al. 1998	26	Severe	In this training study, patients were taught strategies to improve the learning of new names and the retrieval of familiar people's names.	N	• Digit Span Forwards • Dutch version of Rey's auditory verbal learning task • Famous Faces Naming Test • Name Learning Test • Name-Occupation-Town Test	Performance on two of the three target tasks improved with training compared to controls but performance on the Name Learning Test did not change in either group. Both groups had similar improvements in the two control memory tests.
Raskin and Sohlberg 2009	8	Mild, Moderate, Severe	Prospective memory training delivered to eight subjects in a within-subjects crossover design. Subjects were expected to perform a specific task, tested at 2 and 10 minutes, with and without external cues. In addition, half of the subjects were tested on retrospective memory.	N	• Boston Diagnostic Aphasia Examination, animal naming • Consonant Trigrams Test • Controlled Oral Word Association Test • PASAT • Randt Memory Test, story recall and picture recognition • Revised Attention Process Test • RBMT • Trail Making Test	Subjects showed improvement on prospective memory time and tasks after 2 minutes, but not at the longer delay of 10 minutes. On neuropsychological measures immediately post treatment, subjects improved in attention and executive functions. Generalization to everyday memory performance also improved, as measured by a memory questionnaire and diaries. Maintenance of prospective memory improvements was demonstrated at one year post-treatment. None of the subjects showed improvement for retrospective memory drills.

Single Subject, Multiple Baseline Experiment Design

Benedict and Wechsler 1992	2	Mild and Moderate	The study examined the efficacy of long-term memory retraining in two adults using two training strategies: method of loci (MOL) and the PQRST verbal strategy.	N	Scores on word-list recall and paragraph recall	The moderately impaired participant's memory for word lists benefitted from the MOL training, but paragraph learning did not benefit from PQRST training. The severely impaired participant's performance was highly variable throughout, resulting in little change in recall form word lists or paragraphs.
Ehlhardt et al. 2005	4	Severe	The TEACH-M program, which facilitates learning and retention of multi-step procedures, was administered to assess participants' ability to learn multi-step procedures utilizing specific cognitive rehabilitation principles.	N	• Number of correct e-mail steps in sequence (out of 7) • Number of correct steps regardless of sequence • Number of training sessions needed for mastery	All four participants replicated treatment effects immediately posttreatment and 30 days thereafter; generalization and social validity data also supported the effectiveness of TEACH-M.
Hux et al. 2000	7	NR	This study examined the efficacy of internal memory strategies, specifically mnemonics and visual imagery, to improve face-name recall in seven subjects ranging from 2 to 26 years postinjury.	N	• Number of faces correctly identified • Number of training sessions needed to reliably identify subset of faces	Sessions held daily and twice a week were found to be more effective than those held five times a day. Mnemonics and visual imagery strategies were effective for four of the participants, irrespective of session frequency.

continued

TABLE 10-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Manasse et al. 2005	5	Severe	The study examined three cueing strategies (name restating, phonemic cueing, and visual imagery) in a real-world context to increase mastery and use of face-name associations in five chronic participants.	N	Number of names mastered (name use, name knowledge seen in each cueing condition)	All participants improved in name-face recall after intervention regardless of the kind of cuing and four of five participants demonstrated more spontaneous use (effectiveness) of therapists' names when given the same number of opportunities.
Raskin and Sohlberg 1996	2	NR	This study was an investigation of prospective memory training using two different types of intervention: prospective and repetitive memory drill.	N	• Performance on criterion standard neuropsychological measures • Performance on prospective memory screening test (Perspective Memory Screening, or PROMS) • Probes of everyday prospective memory	Memory for future actions improved more after prospective memory training than after repetitive drill, although generalization to real world remembering was variable across participants and type of training. Both participants validated their preference for prospective memory training during interviews.
Zencius et al. 1991	4	NR	In this study, the usefulness of memory notebook training for completing homework assignments was examined for four adults, who were also receiving interdisciplinary rehabilitation services.	N	Number of homework assignment components completed correctly: • Meeting a specified person at a certain place and time • Turning in a completed written homework assignment	After notebook training, three of the four participants improved in completing the number of components to the homework assignments.

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11

Multi-Modal or Comprehensive Cognitive Rehabilitation Therapy

OVERVIEW

In cases where an individual has sustained multiple cognitive or behavioral impairments, as is often the case with traumatic brain injury (TBI), a comprehensive treatment program may be ideal. In comprehensive cognitive rehabilitation therapy (CRT) programs (also called multi-modal or holistic), a team of therapists and other rehabilitation providers work together to ensure the most appropriate timing, delivery, and content of therapy for an individual. These treatment programs may occur during inpatient stays, or extend through outpatient programs. In this chapter, the committee reviews the studies on multi-modal/comprehensive CRT, divided by phase of recovery. Controlled studies are divided by comparator arm within these sections, and the committee's conclusions are included at the end of each section.

The committee identified and reviewed six randomized controlled trials (RCTs) of multi-modal or comprehensive (holistic) CRT (Cicerone et al. 2008; Ruff and Niemann 1990; Salazar et al. 2000; Tiersky et al. 2005; Vanderploeg et al. 2008; Zhu et al. 2007). These trials were heterogeneous. Only one trial targeted mild TBI; three focused on the subacute phase while the other three focused on the chronic phase of recovery. Four of the six RCTs had some form of CRT in both trial arms.

Eight additional studies were identified as nonrandomized parallel group controlled studies. Three of the eight included CRT in the comparator group. One study was in the subacute phase, seven were in the chronic

phase, two included both subacute and chronic patients, and one did not report the time since injury. None of the studies was identified as exclusively or predominantly enrolling mild TBI patients. Studies ranged in sample size from 36 to 205 and were equally split between inpatient and outpatient settings. Seven studies were pre-post, single group design without any comparison or control group. However, there was a broad range in the quality of the design, execution, and reporting of the studies. Table 11-1 (at the end of the chapter) presents a summary of all included studies in this review.

SUBACUTE PHASE OF RECOVERY

The committee reviewed three RCTs (Salazar et al. 2000; Vanderploeg et al. 2008; Zhu et al. 2007) of multi-modal/comprehensive CRT in patients in the subacute phase of moderate-severe TBI; one nonrandomized, parallel group study (Bowen et al. 1999) of multi-modal/comprehensive CRT included patients in the subacute phase of recovery from mild, moderate, and severe TBI. All four studies enrolled patients within 6 months of their injury. Most significantly, all three RCTs had some element of CRT in their comparator arms. Thus, the goal of these studies was to determine whether there was a benefit of one form or level of intensity of CRT relative to another, early after injury. These studies were not designed to assess efficacy relative to no treatment or relative to an inert or minimal control condition, such as a waitlist group. Table 11-2 presents all subacute phase studies by design and treatment comparator.

Comparator Group: Non-CRT Content

Bowen et al. (1999), a single, nonrandomized, parallel group study, included 104 patients in the subacute phase with TBI severity ranging from mild to severe. The aim of the study was to evaluate outcomes of services provided by a community-based, interdisciplinary team of specialists—clinical psychologist, occupational therapist, family support nurse—all

TABLE 11-2 Studies in the Subacute Phase of Recovery

		Treatment Comparator		
Study	Design	No Treatment	Non-CRT	Other CRT
Salazar et al. 2000	RCT			X
Vanderploeg et al. 2008	RCT			X
Zhu et al. 2007	RCT			X
Bowen et al. 1999	Parallel		X	

supported by a clinical coordinator. Treatment took place either before discharge from an inpatient hospital stay (mean 5 days postinjury) or after discharge from an inpatient hospital stay (mean 37 days postinjury). Overall, the median contact time with team members was relatively small—fewer than 15 hours for the early group and fewer than 10 hours for the late group. A third group was offered no specialized interdisciplinary team services. All three arms continued to receive existing services or care as usual. Because of the nature of the program, individual-level randomization was deemed infeasible; randomization occurred by 3-month blocks of time and was rotated across the two hospital sites involved in the study. The study included assessment of a broad range of outcomes (e.g., social, cognitive, behavioral, employment, handicap, functional limitations) at 6 and 12 months postinjury. The extent of contact with different team members is well described in the study. There were problems with protocol compliance, in the form of crossovers from original group assignment, which may have been systematic. Using the significance of 0.01 in light of the multiple outcomes, and adjusting for coma duration and age (which differed across the groups), essentially there were no differences in assessed outcomes.

Comparator Group: Other CRT Content

Salazar et al. (2000)[1] conducted an RCT involving 120 active-duty military personnel who had recovered sufficiently from a recent moderate-severe closed head injury (within 3 months of randomization) to participate in a cognitive rehabilitation program or safely return home with a caregiver. All were oriented and had a Rancho Los Amigos cognitive level 7. Most had headaches. About one-third of the participants were described as having aggressive behavior or major depression, although few were taking psychotropic medications. Participants were randomly assigned to a comprehensive, 8-week in-hospital cognitive rehabilitation program or, after receiving some inpatient memory training, were discharged to home for a program of education and counseling via weekly telephone calls from a psychiatric nurse. During the telephone calls, which were described as lasting 30 minutes, nurses inquired about the week's events, offered support and advice in addressing problems, and checked on use of memory aids. Of the 67 participants assigned to the in-hospital program, 60 completed the program; 47 of the 53 assigned to the home program completed the trial. Six patients assigned to home rehabilitation required supplemental therapy. At 1 year posttreatment, more than 90 percent of the participants in both groups returned to work, the primary outcome measure (group difference

[1] The committee reviewed Salazar et al. 2000, with Braverman et al. 1999, and Warden et al. 2000.

was 4 percent [95 percent confidence interval, 5 to 14 percent]). The proportion of participants between groups who were fit for duty was also not statistically different: 73 percent of the inpatient arm versus 66 percent of the home rehabilitation program. A range of neuropsychological tests, as well as behavior, social adjustment (belligerence, social irresponsibility, antisocial behavior, social withdrawal, and apathy), and mood measures did not differ across groups at 1 year, but only 32 of the intensive rehabilitation group and 28 of the home rehabilitation group had those assessments. The reasons for missing data were not reported. A *post hoc* subgroup analyzed the 75 study participants whose period of unconsciousness at the time of injury was more than 1 hour; 28 of 35 (80 percent) of the group randomized to the inpatient program and 23 of 40 (58 percent) of those randomized to the outpatient program were fit for duty at 1 year ($p = 0.05$).

Vanderploeg et al. (2008) conducted a comparative effectiveness study of patients enrolled in four U.S. Department of Veterans Affairs (VA) inpatient TBI rehabilitation programs. Both arms of the study were inpatient rehabilitation; participants received occupational therapy, physical therapy, speech therapy, TBI education, and social support for 2 hours per day. One arm also included 2 hours per day of cognitive-didactic CRT, while the other arm received 2 hours per day of functional-experiential CRT. CRT was given for up to 60 days (33 days was the mean). For both arms, the average quantity of inpatient interventions was 132 hours per patient. The study reported no difference in primary outcomes of independent living or employment, and no difference on any secondary outcome measures including the FIM, measures of mood and behavior, the Disability Rating Scale, or a self-rating of memory. In subgroup analyses, patients younger than age 30 had better school or work outcomes in the cognitive-didactic arm, while those with higher education and older than age 30 did better in the functional-experiential arm on that primary outcome.

Zhu et al. (2007) studied 68 TBI patients with the primary goal of determining whether a higher level of intensity of early inpatient rehabilitation that included CRT produced better outcomes than a lower intensity of the same intervention. Patients were a mean of 20 days postinjury. The intervention took place 4 hours per day, 5 days per week, for up to 6 months or until discharge, if rehabilitation goals were met. The intervention included social skills training, hearing and speech training, and physical therapy, with goals toward achieving independent living and integration into home and community. The comparator arm received the same content of intervention but at only 2 hours per day (versus 4). These investigators found that Functional Independence Measures (FIM) and Neurobehavioral Cognitive Status Examination (NCSE) scores were no different across the high- and low-intensity rehabilitation arms at 6 months, with substantial gains on average in both arms from enrollment to 6 months. However, the

maximum FIM was achieved by the third month in 47 percent of patients in the high-intensity arm compared to 19 percent of the low-intensity arm. This finding is statistically significant and suggests that early intensive inpatient rehabilitation including CRT may hasten recovery, with maintained long-term outcomes. There was no cost analysis so the value (i.e., health benefit relative to cost) is unknown. For example, it is unknown if earlier discharge translated to lower utilization costs.

CONCLUSIONS: SUBACUTE, MULTI-MODAL/COMPREHENSIVE CRT

The evidence is not informative for conclusions about the impact (efficacy) on patient-centered outcomes (quality of life, functional status) of multi-modal/comprehensive CRT in the subacute phase (Vanderploeg et al. 2008).

There is evidence not informative for conclusions about sustainment of treatment effects (through 6 months after treatment) of multi-modal/comprehensive CRT delivered in the subacute phase (Bowen et al. 1999; Salazar et al. 2000).

The evidence is not informative for conclusions about the impact (efficacy) on domain-specific psychometric measures of cognition or functioning of multi-modal/comprehensive CRT in the subacute phase (Zhu et al. 2007).

In summary, the committee identified and reviewed three RCTs of comprehensive or multi-modal CRT in the subacute phase (Salazar et al. 2000; Vanderploeg et al. 2008; Zhu et al. 2007), and one nonrandomized, parallel group study (Bowen et al. 1999). All three of the RCTs compared some form of CRT in all study arms and had no inert, waitlist, or usual care comparison. The nonrandomized, parallel group study included a usual services arm, but that study had challenges to validity due to the quasi-experimental design and crossover; furthermore, the contents of usual services were not reported. Because the three RCTs do not compare CRT to a group receiving non-CRT therapy or usual care, it is not possible to formulate conclusions about efficacy.

Subacute phase patients may not reflect the same patient pool as those who enter the chronic phase and need CRT. Salazar et al. (2000) appeared to have a ceiling effect because 90 percent or more of both treatment groups returned to work, the primary outcome. It is possible that since this study recruited subjects from the subacute phase, a nontrivial proportion might have improved substantially in the first year postinjury regardless

of intervention, and would not have been seeking or referred for CRT in the chronic phase. It is important to be clear that these subacute studies' findings cannot be extrapolated to the population of TBI patients in the chronic phase.

The primary focus of the committee's analysis was assessment of the evidence for efficacy. However, the three RCTs did provide information about two other questions:

1. *Does CRT in the subacute phase affect rate of recovery?* Two RCTs examined this question, but with conflicting results. One RCT (Zhu et al. 2007) found that more intensive rehabilitation led to earlier meeting of milestones for discharge (with outcomes at 6 months being no different). The other (Salazar et al. 2000) found no difference between inpatient and outpatient CRT for *rate* of readiness to return to duty at 1 year. From these two conflicting findings, it is inconclusive as to whether intensity of CRT in the subacute phase is associated with more rapid attainment of clinically meaningful outcomes.
2. *Does CRT delivered in the inpatient versus outpatient setting affect recovery?* One RCT (Salazar et al. 2000) showed no evidence of higher benefit to extending an inpatient, intensive, high-volume CRT program for 8 weeks compared to discharging to a less-intensive, outpatient follow-up program. All participants were eligible for discharge to the community at enrollment. A *post hoc* analysis suggested that those with severe TBI benefitted more from inpatient CRT.

CHRONIC PHASE OF RECOVERY

The committee reviewed three RCTs (Cicerone et al. 2008; Ruff and Niemann 1990; Tiersky et al. 2005) of multi-modal/comprehensive CRT in patients in the chronic phase of TBI. One of the trials compared CRT to a similar volume of a non-CRT intervention (Ruff and Niemann 1990), and another to a waitlist control condition (Tiersky et al. 2005). Cicerone et al. (2008) compared one format of comprehensive CRT to another form of comprehensive CRT to assess relative or comparative effectiveness of alternate comprehensive approaches. Of six nonrandomized, parallel group design studies identified and described in this review of chronic phase TBI patients, three studies compared comprehensive CRT to a non-CRT program, and three were comparative effectiveness studies of alternate CRT approaches. Implications of study results are markedly different for studies that compare CRT to an inert comparison or to a non-CRT comparator group, as these studies provide knowledge about efficacy, versus the stud-

TABLE 11-3 Studies in the Chronic Phase of Recovery

		Treatment Comparator		
Study	Design	No Treatment	Non-CRT	Other CRT
Cicerone et al. 2008	RCT			X
Ruff and Niemann 1990	RCT		X	
Tiersky et al. 2005	RCT		X	
Chen et al. 1997	Parallel		X	
Cicerone et al. 2004	Parallel			X
Goranson et al. 2003	Parallel		X	
Middleton et al. 1991	Parallel			X
Parente and Stapleton 1999	Parallel		X	
Sarajuuri et al. 2005	Parallel		X	
Braunling-McMorrow et al. 2010	Pre-Post			
Cicerone et al. 1996	Pre-Post			
Huckans et al. 2010	Pre-Post			
Klonoff et al. 2007, 2010	Pre-Post			
Mills et al. 1992	Pre-Post			
Murphy et al. 2006	Pre-Post			
Rattock et al. 1992	Pre-Post			
Walker et al. 2005	Pre-Post			

ies that compare alternative forms of CRT. The latter are comparative effectiveness studies, which do not yield knowledge about efficacy but instead show the relative impacts of the two different approaches. Thus, this section of this review is divided into two components: two RCTs (Ruff and Niemann 1990; Tiersky et al. 2005) and four nonrandomized, comparison group studies (Chen et al. 1997; Goranson et al. 2003; Parente and Stapleton 1999; Sarajuuri et al. 2005) that compare CRT to a non-CRT arm; and one RCT (Cicerone et al., 2008) and three nonrandomized, comparison studies (Cicerone et al. 2004; Middleton et al. 1991; Rattok et al. 1992) that compare two alternative forms of CRT. Table 11-3 presents all chronic phase studies by design and treatment comparator.

Comparator Group: Non-CRT Content

The committee reviewed one RCT of comprehensive CRT in patients with chronic TBI (Tiersky et al. 2005). A large majority of this small trial's

participants (29 were randomized; 20 completed the trial) had mild TBI; all enrollees had to be at least 1 year postinjury (mean = 5 years). This study was a pilot trial of an outpatient intervention; no power calculations were reported. The intervention arm received about equal amounts of cognitive remediation (i.e., attention, information processing, memory) and individual cognitive behavioral therapy in two 50-minute sessions, 3 days per week over 11 weeks; the total intervention time is estimated at 55 hours. The comparator group was placed on a waitlist, and received two or three in-person meetings or phone calls with the principal investigator over the 11-week intervention period (2 or 3 hours total); no therapeutic activities were offered in these contacts. Outcomes were measured at 11 weeks, then at 1 and 3 months after treament. The primary outcome measures were the depression, anxiety, and general symptom indexes of the Symptom Checklist-90R, the PASAT (objective measure of attention), a coping measure, and a self-report measure of attention. There was a significant beneficial effect in favor of the intervention ($p < 0.05$) for the general symptom index, depression, anxiety, and the PASAT. Although the two groups did not differ statistically at baseline on a range of characteristics, the sample was small, and they were qualitatively different on several characteristics, for example, baseline General Symptom Index scores were 1.16 for treatment and 1.62 for controls ($p = 0.19$).

In another RCT, Ruff and Niemann (1990) studied 40 patients with severe TBI 1 year postinjury. This outpatient CRT intervention was 8 weeks long and took place 4 days per week, 5 hours per day (for a total of 160 hours). Sessions included 2 weeks each of CRT targeting attention, spatial integration, memory, and problem solving. Also encompassed within the 5 hours of daily rehabilitation programming was a 50-minute group psychotherapy session and 30 minutes of wrap-up. The comparator arm was also 160 hours of treatment in an outpatient setting over 8 weeks. The difference was in the content, as this program included computer/video games, sessions on coping skills, group and didactic sessions on healthy lifestyle, small group discussion forums, lectures and workbook exercises on independence, and art. The comparator arm similarly included 50 minutes daily of group psychotherapy and 30 minutes daily of wrap-up. Cognition was measured in all 40 patients; behavior and adjustment were measured in a subset of 24 patients. Findings showed no between-group differences on outcomes in nine of nine attention measures, five of five spatial measures, five of nine memory measures, and four of four problem-solving measures; performance IQ was also measured. Verbal IQ scores and scores on four of the nine memory measures were better in the CRT arm than the non-CRT comparator arm.

In the Saajuuri et al. (2005) nonrandomized, parallel group study, 19 patients with moderate-severe TBI received an inpatient program that

included both neuropsychological rehabilitation and psychotherapy. The program took 210 hours (7 hours per day, 5 days per week, for 6 weeks). To be included, participants had to be judged as independent in daily life and have "adequate potential to achieve productivity" with "special" rehabilitation. At one rehabilitation facility, 23 patients (three were lost to follow-up) were identified for a comparison group out of a series of 213 patients at a different facility, who had sustained head injuries during the same time frame as those receiving the CRT intervention program; all 23 were judged as meeting the same criteria for the intervention program. The control group received care as usual, including both clinical and rehabilitation care services. A mailed questionnaire 2 years after completing the program (for the intervention group) or a comparable interval (for the comparison group) asked about paid and unpaid work or current student status; 2 of 19 receiving the intervention compared to 9 of 20 of the usual care group were not engaged in any productive activity at follow-up ($p = 0.017$). When categorized by full-time paid employment, only 1 of the 19 intervention compared to 7 of the 20 usual care group met this benchmark.

Chen et al. (1997) enrolled 40 patients in a study that compared hierarchical computer-assisted cognitive rehabilitation delivered in an outpatient setting to "various other therapies including speech therapy and occupational therapy." Twenty patients who had received the computer-assisted cognitive rehabilitation program and had undergone pre-post evaluations of neuropsychological function were drawn from a database at one center; 20 patients from three other centers who had received other services were drawn from those centers' records. The study was small, and the intervention and comparison arm participants differed substantially on several key characteristics including time since injury and length of coma. There were no significant differences between groups in pre-post score changes.

In the Parente and Stapleton (1999) study, outcomes were assessed among 33 TBI patients who had been referred to a rehabilitation program and given a program that included cognitive skills group sessions, computer training, training in use of electronic aids such as tape recorders or personal organizers, interviewing skills training, and peer teaching. Average participation duration was 4 months. However, the analysis sample only included 13 patients who had completed the program at the time the outcome evaluation was conducted. The comparison group was 64 subjects pulled from a database of 568 brain-injured patients who received services during the same time frame; the actual amount and type of services received by these subjects were unknown. While 10 of the 13 (76 percent) who received the intervention program were employed compared to 58 percent of the comparison group, the number in the intervention program analysis is very small, the comparison group could have differed significantly from the intervention group, and what the intervention impact is being compared to

(in terms of content and extent of services that might have included CRT) is completely unknown.

Goranson et al. (2003) retrospectively identified 42 mild TBI patients from existing clinical files. These patients were described as a small group of TBI patients seen at that clinic over 4 years. The study required patients have returned for follow-up outcome data collection at 6 and 18 months after initial collection. The intervention group comprised 21 patients who met the rehabilitation institution's criteria for an outpatient CRT program that targeted attention, memory, reasoning, and problem solving, as administered by providers from multiple disciplines. Treatment was provided for 4 days per week and 5.5 hours per day, for an average of 4 months (range of program duration was 1 to 7 months). Another 21 patients were identified for the comparison analysis, selected to provide a similar distribution on age, education, and gender to the intervention group. Of note, however, most of the patients in the comparator "no rehabilitation" group did not meet inclusion criteria for the CRT program and thus were different from the group that did receive the CRT program. The study sample was in the chronic phase of recovery for mild TBI, on average 12 to 13 months postinjury. Those who received the CRT program had better Community Integration Questionnaire (CIQ) scores on the Home Integration scale at follow-up, adjusting for differences in baseline scores. There were no differences across groups on the CIQ Social Integration or Productivity scores. Again, the study is small, the intervention and comparison groups were not comparable because the majority of the comparison group was ineligible for the CRT program, and the sample selected for the analysis may have been prone to substantial selection bias because it represented a small subset who, for reasons not described, returned to the facility for follow-up outcome measurement.

Comparator: Other CRT Content

In an RCT, Cicerone et al. (2008) compared two alternative approaches to outpatient comprehensive CRT. One group of 34 patients was randomized to receive an intensive outpatient cognitive rehabilitation program, with an emphasis on metacognition and emotional regulation. The program included 11 hours per week of cognitive, communication, and life skill groups plus individual therapy (4 hours per week), over 16 weeks, for a total of 240 hours of outpatient CRT. Another group of 34 study participants were randomized to a different outpatient comprehensive interdisciplinary day treatment of standard neurorehabilitation, which included retraining of discrete cognitive functions through individual therapy and individualized physical, occupational, and speech therapy, as well as counseling and some group sessions. Treatment also took place over 16 weeks, 15 hours per week, for a total of 240 hours of outpatient CRT. The study found that

intensive cognitive rehabilitation yielded better scores on measures of community integration, life satisfaction, and self-efficacy, compared to the standard neuro-rehabilitation arm; neuropsychological functioning improved in both arms, but did not differ across groups at follow-up.

Of the three nonrandomized, parallel group studies comparing alternative forms of CRT, Cicerone et al. (2004) enrolled 56 patients with TBI in a study that compared a 320-hour inpatient cognitive rehabilitation program that included individual and group cognitive remediation (4 days per week, 5 hours per day, 16 weeks) to a 288-hour standard inpatient neurorehabilitation program of physical, occupational, and neuropsychological therapies that "incorporated many of the principles of comprehensive neuro-psychological rehabilitation" but in a less structured, less intense fashion. The intensive CRT treatment arm had significantly better Community Integration Questionnaire scores after program completion, despite being in the chronic phase (mean = 34 months from injury) compared to the less intensive CRT arm, which was in the subacute phase (approximately 5 months postinjury).

Middleton et al. (1991) compared outcomes of two alternative forms of computer-assisted neuropsychological educational treatment at 8 weeks. Both treatment programs had 96 hours of training on attention, concentration, perceptual skills, and problem-solving skills. Of the participants, 18 received an additional 32 hours of computer-assisted attention and memory training, and 18 other participants received instead 32 hours of computer-assisted reasoning and logical thinking training. There is neither a description of how participants were allocated into each group, nor of the process for their selection out of eligible participants. Both groups had statistically significant gains in five of six neuropsychological test measures, but there were no between-group differences at follow-up.

Rattok et al. (1992) enrolled 59 patients with TBI in three different arms; all arms received 140–160 hours of attention training, community activities, and counseling. In addition, one arm received 220 hours of cognitive remediation and small-group interpersonal exercises, one arm received 200 hours of small group interpersonal exercises but no cognitive remediation, and one arm received 200 hours of cognitive remediation but no small group interpersonal exercises. The process for assigning participants to study arms was not described. The 400 hours of CRT were delivered over 20 weeks in an outpatient setting. Among the many outcome measures, no patterns of between-group differences emerged.

Pre-Post Designs

The committee reviewed seven studies of a pre-post design without any comparison or control group (Braunling-McMorrow et al. 2010; Cicerone et al. 1996; Huckans et al. 2010; Klonoff et al. 2007, 2010; Mills et al.

1992; Murphy et al. 2006; Walker et al. 2005). Study participants ranged from having only mild TBI (Cicerone et al. 1996) to only severe TBI (Walker et al. 2005), or included mixed participants. Three studies (Cicerone et al. 1996; Huckans et al. 2010; Walker et al. 2005) had 25 or fewer subjects. Most of these studies examined predictors or covariates of outcomes. Outcomes were measured at 3 months (Walker et al. 2005), through 12 months (Braunling-McMorrow et al. 2010), and through 18 months (Mills et al. 1992) after program completion. Three studies had highly variable follow-up outcome assessment times depending on program completion: Murphy et al. (2006) reported vocational status at discharge from the program, ranging from 1 week to 4.5 years; Cicerone et al. (1996) reported outcomes assessed from 1 to 6 months after treatment; and Klonoff et al. (2007, 2010) reported outcome assessment times at program completion, ranging from 2.8 to 23.5 months.

There was substantial heterogeneity in the content and duration of these CRT programs. Braunling-McMorrow et al. (2010) evaluated a comprehensive, community-based residential rehabilitation program providing multifaceted behavioral and CRT strategies delivered by a multi-disciplinary team. Murphy et al. (2006) evaluated a vocational rehabilitation-focused program that included intensive cognitive rehabilitation followed by placement of participants in actual work settings with a job coach. Klonoff et al. (2007, 2010) assessed work, school, and driving outcomes of a holistic, "milieu-oriented work/school re-entry program." Walker et al.'s (2005) 9-month community-based program including social skills training revolving around a group fundraising program to support an outdoor adventure course activity, practice on the outdoor adventure course, and group meetings to foster individual goal attainment. Cicerone et al.'s (1996) program of neuropsychological and cognitive remediation included a wide range of cognitive domain modalities tailored to the individuals' needs. Mills et al.'s (1992) tailored program "emphasized improvement of the patients' real-life functional abilities and psychological support." The program took place 6 hours daily, 5 days per week, for at least 6 weeks; it involved both patients and family or friends, if appropriate.

CONCLUSIONS: CHRONIC, MULTI-MODAL/COMPREHENSIVE CRT

Mild TBI

There is limited evidence about the impact (efficacy) on patient-centered outcomes of multi-modal/comprehensive CRT delivered to patients with mild TBI in the chronic phase of recovery. One small but well-conducted trial demonstrated meaningful beneficial effects on

patient-centered outcomes (general symptom index, depression, anxiety) (Tiersky et al. 2005).

There is limited evidence about the sustainment of treatment effects on the general symptom index through 3 months posttreatment of multimodal/comprehensive CRT delivered to patients with mild TBI in the chronic phase of recovery (Tiersky et al. 2005).

There is limited evidence about the impact (efficacy) on psychometric measures of cognition of multi-modal/comprehensive CRT delivered to patients with mild TBI in the chronic phase of recovery (Tiersky et al. 2005).

Moderate-Severe TBI

The evidence is not informative about the impact (efficacy) on patient-centered outcomes (quality of life, functional status) of multimodal/comprehensive CRT in patients with moderate-severe TBI in the chronic phase of recovery.

The evidence is not informative about the sustainment of treatment effects (through 6 months after CRT) of multi-modal/comprehensive CRT delivered to patients with moderate-severe TBI in the chronic phase of recovery.

The evidence is not informative about the impact (efficacy) on psychometric measures of cognition for multi-modal/comprehensive CRT in patients with moderate-severe TBI in the chronic phase of recovery.

The committee found a paucity of studies of efficacy of comprehensive CRT, and the two RCTs of efficacy that the committee identified were small and intended as pilot studies. The lack of large trials with an inert or waitlist comparison group is the primary reason for the conclusions. In brief, there were a total of three RCTs and six nonrandomized, parallel group design studies of comprehensive CRT identified in the review. However, one of the three RCTs and three of the nonrandomized, parallel group studies were comparative effectiveness studies of alternative approaches to CRT and did not address efficacy. These trials compared one or more extensive programs of CRT; the amount of services in these programs ranged from a minimum of 96 hours to a maximum of 400 hours across all arms including the control arms.

The two efficacy RCTs of comprehensive CRT were small pilot studies, had no power calculations, and targeted different groups of TBI patients.

One of the two RCTs (Tiersky et al. 2005) included patients with predominantly mild TBI in the chronic phase demonstrated meaningful beneficial effects; notably, it was the sole RCT with an inert comparator arm—patients in that arm were waitlisted for the program. Therefore, there is preliminary evidence that an 11-week outpatient program of about 55 hours of both CRT and cognitive behavioral therapy is beneficial in patients with mild TBI in the chronic phase. However, while showing favorable findings on several primary outcomes, the study was a pilot, exploratory trial; no larger, follow-on trials were identified in this literature review. The second efficacy trial (Ruff and Niemann 1990) found few differences across CRT and non-CRT arms in a population with moderate-severe TBI, the non-CRT program was intensive and certainly included services and elements that could have also had a beneficial effect on the outcomes studied. In addition, the non-CRT arm received 160 hours of services over 8 weeks, an amount against which the lack of evidence of large benefit of CRT in this study must be taken into account. Because the control group received a substantial amount of rehabilitation and social services, the ability to detect a difference on clinical outcomes between the CRT arm and the control arm may be reduced. This study's findings were not judged as evidence against efficacy of comprehensive CRT. The three nonrandomized, parallel group studies that had at least one non-CRT comparison group were small and had considerable design limitations. These conditions preclude findings from those trials having much bearing on interpretation of this literature in weighing whether or not there is benefit from comprehensive CRT for patients with TBI in the chronic phase.

About half of the studies the committee identified on comprehensive CRT did not answer questions about efficacy but rather compared one or more extensive programs of CRT; the amount of services in these programs ranged from a minimum of 96 hours to a maximum of 400 hours across all arms. Comparative effectiveness studies of comprehensive CRT may be premature without preceding efficacy trials of the interventions applied in each arm. Furthermore, without assessment of utilization and cost, the relative value (extent of health benefit relative to cost) of the programs being compared in these studies cannot be determined.

TABLE 11-1 Evidence Table: Multi-Modal/Comprehensive CRT

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
RCT						
Cicerone et al. 2008	68	Moderate-Severe	Compared one format of comprehensive neuropsychologic (NP) CRT to another form of standard, multidisciplinary CRT to assess relative or comparative effectiveness of alternate comprehensive approaches.	Y Other CRT Content: Standard, multidisciplinary neuro-rehabilitation	• Primary outcomes: ▪ CIQ (community integration) ▪ PQOL (life satisfaction) • Secondary outcomes: ▪ NP functioning • Trail Making Test • Controlled Oral Word Association Test • Booklet Category Test • California Verbal Learning Test-II • Rey Complex Figure ▪ Perceived self-efficacy ▪ Community-based employment • Vocational Integration Scale	While both groups saw NP improvement, intensive CRT subjects, compared to the standard CRT group, saw greater improvement on the CIQ, PQOL, and self-efficacy for the management of symptoms. At 6-month follow-up, these gains were maintained. The standard CRT patients, however, showed increased productivity at 6 months, correlated with the need for continued remediation.
Ruff and Niemann 1990	24	NR	The effectiveness of cognitive remediation versus day treatment was compared in this study of emotional and psychosocial adjustment in subjects.	Y Other CRT Content: Sessions emphasizing psychosocial adjustment, leisure, and activities of daily living	Katz Adjustment Scale (KAS) subscales: • Social Obstreperousness • Acute Psychoticism • Withdrawn Depression	There was no significant difference between groups, with both groups reporting decreased symptoms of psycho-emotional distress, i.e., lessened social withdrawal and depression.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Salazar et al. 2000 Braveman et al. 1999 Warden et al. 2000	120	Moderate-Severe	Comparing in-hospital to at-home rehabilitation services for 120 active-duty military personnel who had recovered sufficiently from a recent moderate-severe closed head injury (within 3 months of randomization) to participate in a cognitive rehabilitation program.	Y Other CRT Content: Home-based rehabilitation with TBI education and individual counseling from a psychiatric nurse, educational materials, and recommended strategies for enhancing cognitive and organizational skills	• Auditory Consonant Trigrams • Buschke Selective Reminding Test • Halstead-Reitan Neuropsychological Impairment Index • Katz Adjustment Scale subscores • PASAT • Return to gainful employment and fitness for military duty at 1-year follow-up • Trahan Continuous Visual Memory Test • Wechsler Memory Scale Revised • Wisconsin Card Sorting	At 1-year follow-up, there was no significant difference between the in-hospital CRT program and home-based CRT program groups in return to gainful employment or fitness for duty; furthermore, there were no significant differences in cognitive, behavioral, or quality-of-life measures. A post hoc subset analysis showed that, in patients who were unconscious for more than an hour, the in-hospital group had a greater return-to-duty rate.

Tiersky et al. 2005	20	Mild, Moderate	Tested the efficacy of a comprehensive neuropsychologic rehabilitation program with cognitive remediation coupled with cognitive behavioral therapy sessions.	Y No Content: Wait list	• Neuropsychologic functioning measures: ▪ PASAT ▪ RAVLT ▪ Assessment of Client Functioning Inventory (ACFI) ▪ Attention Questionnaire • Psychosocial/affective functioning measures: ▪ Coping Response Inventory (CRI) ▪ Symptom Checklist–90 Revised (SCL–90 R) • Measure of community participation: CIQ	The treatment group improved significantly in emotional functioning, which included reduced anxiety and depression, compared to the control; 1-month and 3-month follow-ups showed the greatest improvements. While performance on a divided auditory attention measure improved as well, no changes were observed in community integration scores.
Vanderploeg et al. 2008	360	Moderate-Severe	Evaluated two different cognitive rehabilitation approaches, cognitive didactic and functional-experimental, to determine efficacy overall and relative effectiveness to specific subpopulations.	Y Other CRT Content: Cognitive didactic or functional-experimental	• Primary outcome measures at 1-year follow-up: ▪ Functional independence in living ▪ Return to work and/or school • Secondary outcome measures: ▪ FIM ▪ Disability Rating Scale score ▪ Neurobehavioral Rating Scale	The study found no difference in primary outcomes of independent living or employment, and no difference on any secondary outcome measures including the FIM, measures of mood and behavior, the Disability Rating Scale, or a self-rating of memory. In subgroup analyses, patients younger than age 30 had better school or work outcomes in the cognitive-didactic arm, while those with higher education and older than age 30 did better in the functional-experiential arm on that primary outcome.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Zhu et al. 2007	68	Moderate-severe	Evaluated the benefit of cognitive rehabilitation therapy, comparing varied intensity levels of training, on functional outcome.	Y Other CRT Content: Fewer hours of rehabilitation, compared to the treatment group.	• Primary outcome measure: FIM • Secondary outcome measures: ▪ Glasgow Outcome Scale (GOS) ▪ Neurobehavioural Cognitive Status Examination (NCSE)	Though FIM and NCSE scores were no different across the high- and low-intensity rehabilitation arms at 6 months, with substantial gains on average in both arms from enrollment to six months, the maximum FIM was achieved by the third month in 47 percent of patients in the high-intensity, compared to 19 percent of the low-intensity arms. This finding is statistically significant, suggesting that early intensive inpatient rehabilitation including CRT may hasten recovery, with similar longer-term outcomes.

Nonrandomized, Parallel Controlled Group

Bowen et al. 1999	104	Moderate-severe	Evaluated whether a community-based, interdisciplinary team (e.g., clinical psychologist, occupational therapist, and family support nurse) in addition to usual-care services was more beneficial for improving outcome than usual services alone. Based on a prespecified timetable, the study also aimed to determine whether early treatment was better than later intervention in 104 subjects assigned to a treatment group.	Y Other CRT Content: Usual care, or non-interdisciplinary services (occupational therapy alone)	• Wimbledon Self-Report Scale • Katz Adjustment Scale, modified form R1 (KAS-R1) • Logical Memory 1 • Logical Memory 2 • Occupational status • Functional Limitations Profile • International Classification of Impairments, Disabilities and Handicaps (ICIDH) ▪ Physical Independence ▪ Mobility	After adjusting for potentially confounding factors, the investigators found a statistically insignificant superior outcome for both intervention groups, compared to the control group, in some but not all areas.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Chen et al. 1997	40	NR	Examined the effectiveness of computer-assisted cognitive rehabilitation (CACR) involving a hierarchical sequence of training steps beginning in fundamental functions and advancing to more complex cognitive processes.	Y Other CRT Content: Control group received no or low doses of CACR, but did receive other therapies, like speech therapy and occupational therapy	• WAIS-R subtests: ▪ Information ▪ Vocabulary ▪ Digit span, symbol ▪ Arithmetic ▪ Comprehension ▪ Similarities ▪ Picture completion ▪ Picture arrangement ▪ Block design ▪ Object assembly • Category test • Trail Making Test • Wisconsin Card Sorting test • WMS and WMS-R • Digit span forward, backward • Logical memory immediate, delayed • Visual reproduction immediate, delayed • Paired associates immediate, delayed	CACR made significant gains on the neuropsychological test on 15 measures, compared to seven by the comparison group. In contrast, the investigators found no significant differences between groups on posttreatment gains.

Cicerone et al. 2004	56	Mild, Moderate, Severe	This study compared the effectiveness of an intensive cognitive rehabilitation program (ICRP), a highly structured program integrating cognitive and psychosocial interventions.	Y Other CRT Content: Standard neurorehabilitation including physical, occupational, and speech therapies, as well as neuropsychologic treatment	• CIQ • Quality of Community Integration Questionnaire (QCIQ) • Trail Making Test • California Verbal Learning Test • Rey Complex Figure • COWAT • Category Test	Both groups improved significantly on the CIQ, with the ICRP participants twice as likely to show clinical benefits, compared to the SRP group. ICRP participants, as well as those with clinically significant improvement on the CIQ, showed significant overall improvement in neuropsychologic functioning.
Middleton et al. 1991	36	NR	Investigates outcomes following computer-delivered cognitive rehabilitation therapy, comparing two forms of computer-assisted neuropsychological treatment targeting attention and memory skills or reasoning and logical thinking skills.	Y Other CRT Content: Control received computer-assisted training on reasoning and logical thinking skills	• WAIS-R, Digit Span • Wechsler Paired Associates • Knox's cube • Block Counting • Concept formation • Shipley Abstraction	There was significant improvement on five of six measures by both groups at 8-week follow-up; no differential effect was observed in the treatment group.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Parente and Stapleton 1999	33	NR	In a pilot study, evaluated the effectiveness of the Cognitive Skills Group (CSG) providing thinking skill training as a precursor to vocational placement. The sequence of topics include problem solving, concentration/ attention, decision making, remembering faces and names, study skills, functional mnemonics, prosthetic memory devices, social cognition, organizational skills, goal setting, non-verbal perception, specific study skills, and test-taking strategies.	Y Other CRT Content: Similar services but not within CSG	Return to work	Participants in the CSG had a 76 percent vocational rehabilitation rate, i.e., placement in competitive employment; 58 percent of the baseline participants returned to work.

Rattok et al. 1992	59	severe	Assessed three groups with varying treatment combinations of attention training, cognitive remediation, small-group interpersonal exercises, community activities, and personal counseling. Each group received a total of 400 hours of training. Cognitive remediation involved task and curing hierarchies, constructional praxis, visual information processing, and logical reasoning.	Y Other CRT Content: Group 1 received cognitive remediation with small-group interpersonal exercises; Group 2 stressed small-group interpersonal exercises; Group 3 involved cognitive remediation without small-group time; all three groups received attention training.	• Orientation Remedial Module (ORM) • Purdue Pegboard • Visual processing skills • Academic skills • WAIS – verbal, performance • Psychomotor dexterity • Higher order and conceptual skills	All three treatment mixes were equally effective in all areas, with some mixes producing superior results to others in some respects (e.g., with regard to intra- and interpersonal functions, the mixes that emphasized group interventions were superior to Mix 3 in some respects).
Sarajuuri et al. 2005	39	Moderate-Severe	Evaluated outcome following a comprehensive, 6-week neurorehabilitation program with psychotherapy and vocational interventions as well as follow-up support.	Y Other CRT Content: Conventional care and rehabilitation	Structured self-report questionnaire: • Gainful work (full or part time) • Education/studying • Household management • Supported or sheltered work • Work trials • Productive but nongainful work (full or part time) • Volunteer work	At two-year follow-up, the treatment group improved significantly more than the control; 89 percent of treated patients were productive, compared with 55 percent of the control group.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Pre-Post Single Group						
Braunling-Mcmorrow et al. 2010	205	Severe	Investigators examined the effect multifaceted rehabilitation services had on functional outcomes for participants with major physical and cognitive difficulties (n = 129) and those with behavioral complications (n = 76).	N	Functional Area Outcome Menu: • Behavioral and Emotional Status • Community Participation • Educational Endeavors • Global Quality of Life • Intimacy/Relationships • Invovement in Vocational or Educational Endeavors • Level of Awareness • Level of Independence • Level of Self-Managed Health • Residential status • Vocational Endeavors	There were significant functional gains of approximately 1.5 levels, using the rehabilitation treatment model, for neuropsychologically impaired participants, both with and without related behavioral and substance problems.

Cicerone et al. 1996	20	Mild	This investigation was a retrospective analysis of a neuropsychological rehabilitation program for 20 patients who were part of a larger sample, referred for treatment due to postconcussive symptoms and functional disability.	N	• Attention ▪ Digit Span, Forward and Backward ▪ Trail Making Test ▪ Continuous Performance Test of Attention ▪ PASAT • Memory ▪ Logical Memory I and II ▪ California Verbal Learning Test ▪ Rey Immediate Recall • Higher cognitive function ▪ Rey Copy ▪ WCST Perseveration ▪ Category Test ▪ Mazes ▪ Verbal Fluency	Neuropsychological rehabilitation led to improved cognitive functioning and a reduction of post-concussive symptoms for those participants able to resume productive functioning; these improvements most affected areas of complex attention and information-processing speed. Participants who were not able to resume productive functioning showed decline in functioning on various measures at 1- and 6-month follow-up.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Huckans et al. 2010	21	Mild	Investigators piloted a Cognitive Strategy Training (CST) group treatment to examine if an increase in compensatory strategies use was observed; they also examined the effect of CST on self-reported psychiatric symptoms, cognitive symptoms, and life satisfaction.	N	• Beck Depression Inventory • Cognitive Symptom Severity • Community Integration Questionnaire • Frequency of Cognitive Strategy Usage Scale (FCSUS) • Memory Compensation Questionnaire (MCQ) • Memory Questionnaire • PTSD Checklist • Satisfaction with Life Scale • Severity of Dependence Scale • TBI self-efficacy scale • Usefulness of Cognitive Strategy Scale (UCSS)	There was a significant increase in compensatory strategies (MCQ), use of class strategies and day planners (FCSUS), internal cognitive strategies, and use of extensive cognitive aids. Secondary analyses showed significantly lower levels of depression, lower levels of memory and cognitive impairment, no change in PTSD symptoms, no change in community integration levels, and a trend toward increased self-efficacy.
Klonoff et al. 2010	103	Mild, Moderate, Severe	Examines cognitive retraining offered within a therapeutic milieu and driving outcomes, the relationship between metacognitive processes and clearance to drive, and the relationship between a patient's working alliance (WA) and driving status at discharge.	N	• Cognitive Retraining Behavior Checklist (CRBC) • Digit Symbol • Driving status • Letter Scan (letter H) • Matching Shapes • Word Fluency • Working Alliance (WA) scores	In all participants, the Matching Shapes cognitive test showed a significant difference between driving groups: drivers rated better on organization, independence, use of compensations than non-drivers, and drivers had higher mean and discharge WA ratings.

Klonoff et al. 2007	101	Mild, Moderate, Severe	Examines the effectiveness of cognitive retraining exercises within a milieu-based rehabilitation on work or school status.	N	• Cognitive Retraining Behavior Checklist (CRBC) • Digit Symbol • Driving status • Letter Scan (letter H) • Matching Shapes • Word Fluency • Working Alliance (WA) • Work/school status	More than 80 percent of participants returned to work or school associated with better cognitive performance in tasks requiring information processing speed, visual scanning, visuospatial skills, and memory.
Mills et al. 1992	42	Severe	Examines outcomes of a 6-week, structured outpatient rehabilitation program, individualized to each patient, including psychological support and emphasizing improvements in real-world functional abilities. Evaluations included family and patient interviews to determine day-to-day functioning. Follow-up evaluations were conducted at 6, 12, and 18 months post treatment.	N	• Functional evaluation ▪ Identifying community resources ▪ Consumer skills ▪ Health ▪ Leisure activities ▪ Safety awareness ▪ Self-care ▪ Social communication ▪ Telephone skills ▪ Time management ▪ Use of public transportation • Individual treatment goals • Speech pathology evaluation	Patients' functional outcomes improved significantly post treatment; the overall percentage of goals achieved was 67.5 percent. A positive correlation between the initial functional evaluation and cognitive assessments was reported, however there was no significant correlation between the change in functional and cognitive outcomes posttreatment, although a trend was indicated. The number of days in treatment correlated with functional improvement.

continued

TABLE 11-1 Continued

Study	N	TBI Severity Level	Brief Narrative	Comparator	Outcome Measures	Findings
Murphy et al. 2006	232	Mild, Moderate, Severe	Evaluates a rehabilitation program to contain elements of group-based training, followed by work site-based rehabilitation including variable amounts of hospital- or community-based neurological rehabilitation. As such, the program was designed to include elements of cognitive rehabilitation as well as site-specific work placement training and rehabilitation.	N	• Paid competitive employment • Education or training • Voluntary work • Discharge to other services • Client withdrew • Discharged for other reasons	Overall, 72 percent of subjects resumed independent activity, such as paid competitive employment, education or training, or voluntary work. Of the remaining participants, 15 percent were referred to further rehabilitation services, and 13 percent of the sample withdrew. The authors reported that there was no significant difference on severity of injury relative to outcome.
Walker et al. 2005	11	Severe	A pilot study to evaluate an extensive, three-stage program that ultimately focused on goal identification and achievement through tasks analysis and problem solving in goal areas.	N	• Individual goals related to: ▪ Employment ▪ Study ▪ Driving ▪ Leisure ▪ Independence • Psychological measures: ▪ Depression, Anxiety, and Stress Scales ▪ General Well-Being Questionnaire ▪ European Brain Injury Questionnaire, family rating	At least one goal was achieved by 10 of the 11 participants, with overall, 21 of 26 goals attained. There were no significant differences on psychological measures.

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12

Telehealth Technology

OVERVIEW

Telehealth technologies provide opportunities to increase access to healthcare for individuals who are not located in proximity to high-quality care. The Centers for Medicare & Medicaid Services defines *telemedicine* as two-way audio and video interactive communication, which is specifically covered by the Military Health System, when appropriate and medically necessary for beneficiaries. The application of telecommunication technologies allows providers and healthcare systems to create new methods or more efficient structures for the delivery of care. In this chapter, the committee reviews the studies on cognitive rehabilitation therapy (CRT) interventions for a range of deficits due to traumatic brain injury (TBI) applied through telehealth technology applications.

CRT APPLIED THROUGH TELEHEALTH TECHNOLOGY

The committee reviewed six randomized controlled trials (RCTs) (Bergquist et al. 2009, 2010; Bourgeois et al. 2007; Dou et al. 2006; Ownsworth and McFarland 1999; Salazar et al. 2000; Soong et al. 2005) and four feasibility or pilot studies (Bergquist et al. 2008; Diamond et al. 2003; Egan et al. 2005; Melton and Bourgeois 2005) that involved a telehealth technology whereby parts of the intervention were delivered remotely. Five of the studies did not meet eligibility criteria because they either did not evaluate a CRT intervention (Egan et al. 2005), they evaluated a limited outcome related only to feasibility or the task being taught

(Bergquist et al. 2008; Diamond et al. 2003; Melton and Bourgeois 2005), or the etiology of the brain injury of participants was not specified as traumatic (Soong et al. 2005). Studies included in the telehealth technology review are not mutually exclusive from trials included in the evaluations of other domains.

Of the remaining five studies, one was a small, randomized crossover study that involved 20 volunteers with a history of moderate-severe traumatic brain injury (TBI) at least 1 year prior to study entry (Bergquist et al. 2009, 2010). Individuals with a history of ongoing psychiatric symptoms were included as long as symptoms were not severe (e.g., psychotic symptoms). Participants, who had to have reliable access to the Internet, were randomized to an active cognitive rehabilitation intervention or to a control group. After completing 30 instant messaging sessions with online therapists, participants were crossed over to the alternate group for 30 more sessions. The active intervention, which involved an online occupational therapist with expertise in cognitive rehabilitation, focused on developing calendar skills to address difficulties with memory in everyday life and on developing strategies to improve memory functioning. The control group also involved interaction with the online therapist, but participants in this group were instructed primarily to use their calendar to record day-to-day events rather than using calendars as a compensatory tool for memory impairments. Only 14 participants completed the study. Outcome measures were self-reported measures that assessed use of compensation strategies (Compensation Techniques Questionnaire) and satisfaction with therapy, and measures completed by family members (Neurobehavioral Functioning Inventory and Compensation Integration Questionnaires). All participants reportedly learned to use the instant messaging system. Most individuals in both groups were satisfied with their Internet-based interventions. No statistically significant differences in change in daily function were reported between groups after 30 sessions.

Another modest-sized trial involved adults with persisting memory problems several years after a documented closed head injury (Bourgeois et al. 2007). The trial also required a family member to participate with the patient. Participant-caregiver pairs were assigned to either spaced retrieval training or a didactic control strategy using stratified pairing based on race and sex (quasi-experimental). Both treatments were delivered via telephone by clinician trainers. After initial face-to-face assessments of cognitive difficulties and social participation activities, the trained discussed treatment goals with the client and caregiver, and the group selected the three most troublesome areas to work on during training. The trainer then provided memory logs and asked patients and caregivers to record the frequency with which each problem occurred over the next week. The trainer called participants the following day to make sure that instructions and data collection

methods were understood. The trainer then called participants four to five times each week for 30-minute sessions. Participants in the spaced retrieval group received an instructional technique focused on selected goals. The therapist modeled correct responses to questions related to the goals and instructed the participants not to struggle to retrieve responses, but to respond immediately. Participants in the control arm received the same total amount of therapy time and sessions that focused on memory strategies such as association, verbal rehearsal, imagery and written reminders. Outcomes included goals mastered, generalization, the frequency of reported memory problems, a cognitive difficulties scale, and community integration and quality of life measures. Immediately and at 1 month posttraining, the space retrieval group (and their caregivers) reported more treatment goal mastery and use than the didactic instruction group (and their caregivers). Both groups reported some generalization to other nontargeted behaviors, but these improvements were not statistically significantly different between groups. There were no reported important or statistically significant improvements in quality of life for either group. One limitation was that data about "objective, observable behaviors" related to selected goals was obtained from memory logs, and those data were sometimes incomplete. Of the 51 pairs who agreed to participate, only 38 completed the study: 22 spaced-retrieval training pairs and 16 didactic control pairs.

Another small randomized trial involved 20 patients, most of whom had sustained a brain injury from a motor vehicle accident many years before (Ownsworth and McFarland 1999). The severity of the brain injury was not described. The trial compared two different approaches to training individuals to use a dairy to compensate for memory problems (a diary only approach and a diary and self-instructional approach that taught compensation using higher cognitive skills of self-awareness and self-regulation). In one session, some instructions for daily memory checklists were given verbally over the phone to both groups, but the 4-week intervention period mainly involved self-use of diaries. Follow-up phone calls to monitor progress or provide additional instruction were not included during the intervention phase of the study. Findings showed that the self-instruction group consistently made more diary entries and reported less memory problems than the diary only group.

Another trial involved 30 patients with memory disorders and a history of TBI who had had neurosurgery several months prior (Dou et al. 2006). Patients who had a history of previous psychiatric problems or who were computer phobic were excluded. Participants were randomly assigned to one of the following three groups: computer assisted memory training, therapist assisted memory training, and no specific memory training (the control group). In the computer assisted training, patients were asked to identify or define the information they needed help from a therapist to

learn. The computer provided the necessary information for the patients to generate correct decisions through an errorless approach. The patients were not encouraged to engage in guesswork and were told to consider alternatives to and the consequences of an intended action. The therapist assisted training covered similar content, but the content was presented as a picture album and therapists gave directions face to face. The training consisted of 20 45-minute sessions occurring 6 days a week. Training was aimed at compensatory techniques related to memory, management of typical daily tasks, and utilizing typical component memory skills. One month after treatment, both treatment groups improved on two outcome assessments (Neurobehavioral Cognitive Status Examination, Rivermead Behavioural Memory Test) compared to the control group, though both treatment groups improved similarly.

The largest trial involved 120 active-duty military personnel who had recovered sufficiently from a recent moderate-severe closed head injury (within 3 months of randomization) to participate in a cognitive rehabilitation program or safely return home with a caregiver (Salazar et al. 2000, with Braverman et al. 1999 and Warden et al. 2000). All were oriented and had a Rancho Los Amigos cognitive level of 7. Most had headaches. About a third of the participants were described as having aggressive behavior or major depression, though few were taking psycho-trophic medications. Participants were randomly assigned to a comprehensive 8-week in-hospital cognitive rehabilitation program or a limited educational and counseling home rehabilitation program with weekly telephone support from a psychiatric nurse. During the telephone calls, which were described as lasting 30 minutes, nurses inquired about the week's events and offered support and advice in addressing problems. Of the 67 participants assigned to the in-hospital program, 60 completed the program; 47 of the 53 assigned to the home program completed the trial. Six patients assigned to home rehabilitation required supplemental therapy. Cognitive behavioral function assessed with various measures was similar for both groups at baseline and at 1-year follow-up. More than 90 percent of the participants in both groups had returned to work (the primary outcome measure) 1 year after treatment (the difference between groups was 4 percent, [95 percent confidence interval, 5 to 14 percent]). Quality of life measures including belligerence, social irresponsibility, anti-social behavior, social withdrawal, and apathy were reported as not statistically significantly different between groups at 1 year, but only 32 of the intensive rehabilitation group and 28 of the home rehabilitation group completed those assessments.

CONCLUSIONS: TELEHEALTH TECHNOLOGY

This scant evidence base shows that telehealth technologies, including telephone and two-way messaging, are feasible means of providing at least part of CRT for some patients. No studies evaluated the use of telemedicine, as defined by the Centers for Medicare & Medicaid Services as two-way audio and video interactive communication. Overall evidence is insufficient to clearly establish whether telehealth technology delivery modes are more or less effective or more or less safe than other means of delivering CRT. However, when combined as part of a broader CRT program, telehealth technologies, including telephone calls, can contribute to outpatient treatment programs with comparable results to inpatient programs for selected individuals.

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13

Adverse Events or Harm

OVERVIEW

The potential for introducing harm or causing adverse event may occur during any form of treatment. The relationship between potential adverse events or harm is traditionally considered relative to pharmacologic agents, and the clinical trial process attempts to ensure the safety of a new drug or medical device. However, rehabilitation may cause adverse events or harm in patients as well. The rehabilitation process includes many phases, such as screening and diagnostic testing, goal setting, one or many intervention, and follow-up evaluation; at each point, there is an opportunity to expose patients to potentially harmful practices or information. For example, a patient may sustain an injury during a particular rehabilitation strategy, or a rehabilitation therapist might focus on a patient's challenges rather than successes, unintentionally harming the patient's emotional well being and minimizing the potential for future success. Capturing data about the occurrence of adverse events or harm is important for all types of treatment. The committee reviewed only the randomized controlled trials (RCTs) on cognitive rehabilitation therapy (CRT) for reported information about the potential for adverse events or harm. This chapter includes a discussion of those studies.

POTENTIAL FOR ADVERSE EVENTS OR HARM FROM CRT

None of the RCTs that met inclusion criteria explicitly conceptualized or assessed potential risks of therapy, such as major inconveniences, unin-

tended negative consequences, or exacerbation of a concomitant condition (e.g., posttraumatic stress disorder). None of the trials reported data about any serious adverse events, including acts of aggression, suicide, or death.

Several of the trials that evaluated multi-modal/comprehensive therapy assessed measures such as anxiety and depression that theoretically could be improved or worsened with some forms of CRT (Ruff and Niemann 1990; Salazar et al. 2000; Tiersky et al. 2005; Vanderploeg et al. 2008). Ruff and Niemann's (1990) small trial included 24 patients with chronic, moderate-severe traumatic brain injury (TBI). The trial compared a multi-modal, structured cognitive outpatient retraining program with therapy focusing on psychosocial functioning and activities of daily living (ADLs). Although the investigators had hypothesized increased emotional distress with cognitive rehabilitation, they found neither group perceived any changes in emotional or psychosocial functioning, though individuals in the second group tended to rate themselves more obstreperous after treatment. Salazar et al. (2000) and colleagues'[1] single-center trial of patients with TBI in the subacute phase reported increased numbers of patients with major depression (19 at baseline, 27 at 1-year follow-up) and generalized anxiety (10 at baseline, 20 at 1-year follow up) among the 53 active-duty military personnel with moderate-severe TBI randomized to home rehabilitation with telephone support. No such increases were seen among the 67 individuals randomized to intensive in-hospital rehabilitation (depression 18 at baseline and 16 at follow up; anxiety 9 at baseline and follow-up). Incomplete follow-up at 1 year (34 of 53 home rehabilitation patients and 42 of 67 in-hospital rehabilitation patients) and possible differential surveillance and ascertainment limit the interpretation of these findings. Tiersky et al.'s (2005) small, single-blind trial found that individuals with mild TBI in the chronic phase who were randomized to neuro-psychologic rehabilitation reported less anxiety and depression (measured with SCL-90R) at 3 months than those randomized to a waitlist group. Vanderploeg et al.'s (2008) multi-center trial involving veterans with moderate-severe TBI in the subacute phase who were treated in acute inpatient rehabilitation programs reported no differences in worry, depression, or irritability at 1 year between groups randomized to cognitive didactic versus functional-experiential rehabilitation.

RCTs that evaluated single modality interventions most often used modality-specific outcomes and did not assess outcomes that could have detected any psycho-emotional distress related to the rehabilitation therapy. Only the Salazar trial reported estimated costs of CRT. The additional rehabilitation cost estimated for each patient in the intensive in-hospital group

[1] The committee reviewed Salazar et al. 2000, with Braverman et al. 1999 and Warden et al. 2000.

was $51,840 (based on standard WRAMC physiatry service costs of $864 per day) whereas the home program rehabilitation total cost was $504 per patient (Salazar et al. 2000).

CONCLUSIONS: ADVERSE EVENTS OR HARM

The committee found that evidence about any potential downsides and risk for harm associated with CRT is scant. Although the limited available evidence suggests no great concern regarding risk for harm, future studies that evaluate CRT should include and report measures that assess such risks.

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PART III: RECOMMENDATIONS

14

Directions

Since cognitive rehabilitation therapy (CRT) was first described in published literature, its clinical application and efforts to document efficacy of CRT treatments through research have been ongoing. Innovative interventions aimed to address specific cognitive impairments and whole-person functioning have been characteristic of this field. However, limited empirical research and inadequate standardization currently restrict the ability to formulate evidence-based practices. This current state of knowledge will therefore, benefit from increased organization and funding of both interventional studies and observational analyses. Both approaches, to be optimally productive, must address the challenges in obtaining more useful and interpretable data on the patients treated or enrolled in studies, on the CRT treatments they receive, and on the outcomes they experience.

SYNTHESIS OF EVIDENCE REVIEW

The committee found published data signaling the benefit of some forms of CRT for traumatic brain injury (TBI). However, the evidence for the therapeutic value of CRT is variable across cognitive domains and is currently insufficient overall to provide definitive guidance for translation into clinical practice guidelines, particularly with respect to selecting the most effective treatment(s) for a particular patient. This limitation results from the heterogeneity of TBI as well as a lack of operational definitions of different forms of CRT, small samples typical of most CRT studies, and the variety of premorbid conditions, comorbidities, and environmental factors that may moderate the value of a given form of CRT. Table 14-1

TABLE 14-1 Overall Conclusions by Cognitive Domain and Multi-Modal/Comprehensive CRT

Domain	Attention		Executive Function		Language and Social Communication	Memory					Multi-Modal/ Comprehensive CRT		
Subdomain			Awareness	Non-Awareness									
TBI Severity	Moderate-Severe		Moderate-Severe		Moderate-Severe	Mild	Moderate-Severe				Moderate-Severe	Mild	Moderate-Severe
Recovery Phase	Subacute	Chronic	Chronic		Chronic	Chronic					Subacute	Chronic	
Approach	R	R	R	R/IC/EC	R	IC	EC	R	IC	EC	M	M	M
Patient-Centered Outcomes	0	+	0	+	0	0	N/A	0	+	++	0	+	0
Long-Term Treatment Effect	+	0	0	0	+	+	N/A	0	+	N/A	0	+	0
Immediate Treatment Benefit	+	+	+	+	++	+	N/A	0	++	++	0	+	0

NOTES: EC = external compensatory strategy; IC = internal compensatory strategy; M = mixture of treatment approaches; R = restorative strategy; Evidence Grades: 0 no or not informative, + limited, ++ modest, +++ strong. Multiple treatments intended to target cognitive (non-awareness) aspects of executive function were examined in single studies. The treatments varied in their approach from more restorative (e.g., categorization training) to internal compensatory (e.g., Goal Management Training) to external compensatory (e.g., neutral alerting tones). The evidence grading reflects the lack of replication of any single approach.

provides an overview of the committee's conclusions based on the review of literature of modular, domain-specific treatments as well as multimodal/comprehensive CRT programs.

In most cases the evidence provides limited, and in some cases modest, support for the efficacy of CRT interventions. The committee defined limited evidence as "Interpretable results from a single study or mixed results from two or more studies" and modest evidence as "Two or more studies reporting interpretable, informative, and largely similar results" (see Box 6-2 for all evidence grades and definitions). **The committee emphasizes that conclusions based on the limited evidence regarding the effectiveness of CRT does not indicate that the effectiveness of CRT treatments are "limited"; the limitations of the evidence do not rule out meaningful benefit.** ***In fact, the committee supports the ongoing clinical application of CRT interventions for individuals with cognitive and behavioral deficits due to TBI.*** To acquire more specific and meaningful results from future research the committee has laid out a comprehensive research agenda to overcome challenges in determining efficacy and effectiveness. One way policy could reflect the provision of CRT is to facilitate the application of best-supported techniques in TBI patients in the chronic phase (where natural recovery is less of a confound), with the proviso that objectively measurable functional goals are articulated and tracked and that treatment continues only so long as gains are noted.

In reviewing the evidence regarding the efficacy and effectiveness of CRT, the committee found no studies addressing cognitive deficits in the acute phase of recovery following TBI, few studies addressing cognitive treatment for individuals with mild injuries—those that did were only in the chronic phase; and few studies addressing treatment of those with moderate to severe injuries in the subacute phase. Table 14-2 provides the committee's definitions for acute, subacute, and chronic recovery phases. The dearth of evidence in these areas is multi-factorial, but the committee recognized specific practical and methodological limitations. One limitation is that objective measures sensitive to the cognitive complaints of patients with mild TBI are lacking in many instances and the use of subjective self-report measures as an alternative is problematic when studying treatments that cannot be blinded. Also, studies of subacute treatments require rela-

TABLE 14-2 Definitions of Acute, Subacute, and Chronic TBI Recovery

	Mild TBI	Moderate-Severe TBI
Acute	< 3 months	Acute hospital care
Subacute	> 3 months < 6 months	Inpatient rehabilitation
Chronic	> 6 months < 12 months	Outpatient rehabilitation

tively large samples because the ability to gauge the impact of a treatment regimen in individual patients is diminished in the context of rapid and variable natural recovery. Thus, in practice clinicians may defer substantial resource investment in CRT to later stages of TBI when it becomes clear which problems and impairments will persist long term.

Evidence supporting the efficacy of CRT in the chronic phase of TBI for patients with moderate-severe injuries varies by cognitive domain and specific CRT treatment modality. Of note, patients with moderate to severe injuries in the chronic phase typically have deficits that can be objectively measured and have a slower rate of natural recovery. These patients are unlikely to improve substantially without intervention; thus, observations of clinical outcomes in the chronic phase of TBI are a more useful source of evidence than in more variable, earlier phases of recovery. However, currently even the most promising treatments lack sufficiently powered trials to answer important practical questions, including (1) which patient characteristics are associated with best response from a given treatment, (2) what are the lasting benefits of treatments that have initially positive results, and (3) to what degree does generalization occur of trained tasks to real-world tasks (for modular treatments) or to global impact on community integration and quality of life (for comprehensive treatment programs).

RECOMMENDATIONS

Considering the dearth of conclusive evidence identified to date, the committee recommends an investment in research to further develop CRT. The committee interpreted its charge as assessing the current state of the evidence. The committee was not asked to develop policy guidelines or make clinical practice recommendations, but to reach evidence-based conclusions that would inform policy decisions. In most cases the evidence provides limited, and in some cases modest, support for the efficacy of CRT interventions. However, the limitations of the evidence do not rule out meaningful benefit. In fact, the committee supports the ongoing clinical application of CRT interventions for individuals with cognitive and behavioral deficits due to TBI. To acquire more specific/meaningful results from future research the committee has laid out a comprehensive research agenda to overcome challenges in determining efficacy and effectiveness. However, these recommendations are possible because the evidence review signals some promise. Compared to pharmacological studies, which are more conducive to controlled environments, the committee acknowledges the difficulties associated with research for all forms of rehabilitation. Complexity of patient, injury or disease, and environmental characteristics, among other factors, require variability in possible treatment approaches; these complexities create inherent challenges with rehabilitation research in

general. Therefore, the committee did not identify methodological issues in this report to hold CRT research to a higher standard than rehabilitation research at large; it serves merely as a overt discussion of the issues that cloud determination of efficacy and effectiveness. To improve future evaluations of efficacy and effectiveness of CRT for TBI, larger sample sizes and volume of data are required, particularly to answer questions about which patients benefit most from which treatment(s). This requires more extensive funding of experimental trials and a commitment to "mining" clinical practice data in the most rigorous way possible. For such approaches to be most informative, the variables that characterize patient heterogeneity, the outcomes that are used to measure impact of treatment, and the treatments themselves need to be defined and standardized. In addition, more rigorous review of potential harm or adverse events related to specific CRT treatments is necessary.

Nascent efforts at standardization are underway across multiple civilian and military funding agencies. These efforts should take place in collaboration. The National Institutes of Health (NIH) common data element (CDE) initiative, a National Institute on Disability and Rehabilitation Research (NIDRR)–supported center on treatment definition, and several practice-based evidence studies are helping to better characterize TBI patients, treatments, and relevant outcomes. Practice-based evidence studies include the Congressionally Mandated Longitudinal Study on TBI (e.g., 15 Year Longitudinal Study of TBI Incurred by Members of the Armed Forces in OIF/OEF), DVBIC Study on Cognitive Rehabilitation Effectiveness for Mild TBI (SCORE!), Millennium, and TBI Model Systems. These cohorts involve collaborative efforts between the U.S. Department of Defense (DoD) and U.S. Department of Veterans Affairs (VA) via the Defense and Veterans Brain Injury Center (DVBIC). Furthermore, the recently funded Federal Interagency Traumatic Brain Injury Research (FITBIR) database will be collecting uniform and high-quality data on traumatic brain injury, including brain imaging scans and neurological test results. The committee recognizes the ongoing emphasis from both government agencies to enhance collaboration on TBI and improve psychological health of service members and veterans through the VA/DoD Joint Executive Council Strategic Plan to integrate health care services (VA/DoD 2009). This collaboration is especially important in evaluating transitions in care and long-term treatment for injured soldiers as they move out of the Military Health System (MHS) and into the Veterans Health System, run by the VA. For example, it will be important to study how CRT may benefit aging veterans who experience long-term outcomes of TBI, such as cognitive decline associated with dementia.

Because CRT is not a single therapy, questions of efficacy and effectiveness need to be answered for each cognitive domain and by treatment

approach. Nevertheless, within a specific cognitive domain, there must be sufficient research and replication for conclusions to be drawn. Standard definitions for intervention type, content, and key ingredients will be critical to developing evidence-based practice standards. The documentation of interventions in practice and more frequent use of manual-based interventions in research will help validate measures of treatment fidelity. For example, while there is evidence from controlled trials that internal memory strategies are useful for improving recall on decontextulized, standard tests of memory, there is limited evidence that these benefits translate into meaningful changes in patients' everyday memory either for specific tasks/activities or for avoiding memory failures. Therefore, an increased emphasis on functional patient-centered outcomes would allow for a more meaningful translation from cognitive domain to patient functioning. The committee acknowledges that efforts are underway to facilitate manualization of treatments, including the "Cognitive Rehabilitation Treatment Manual" by the Brain Injury Special Interest Group of the American Congress of Rehabilitation Medicine, and the "Executive Plus" treatment manual developed by the Mount Sinai Brain Injury Research Center. These are promising efforts to build upon, an effort this report supports.

The committee recommends the Department of Defense (DoD) undertake the following:

- *Include measures in experimental and observational data sets that characterize important dimensions of patient heterogeneity and factors affecting recovery and response to CRT;*
- *Improve standardization of CRT treatments as well as TBI patient characteristics and relevant outcome measures in clinical practice and research;*
- *Develop a common registry or linked registries encompassing de-identified data of large numbers of consenting patients to facilitate data mining and the rationale for testing new interventions; and*
- *Prospectively follow any policy changes in coverage for CRT in the Military Health System.*

Due to the pressing nature of the problem—TBI affects many thousands of individuals, particularly U.S. service members, every year—these efforts should take advantage of current momentum in TBI research to improve the field of CRT research via existing cohorts. The committee developed and designed the layout of these recommendations systematically, to sequentially address fundamental flaws in CRT research. For example, developing a common registry to prospectively facilitate data mining should not be undertaken before there are agreed-upon definitions of patient characteristics, outcome measures, and CRT interventions, which cannot be accomplished

without accounting for and recognizing TBI-related heterogeneity, factors affecting recovery, and response to CRT.

Recognize Heterogeneity, Factors Affecting Recovery, and Response to CRT

An individual's response to CRT may be affected by preinjury status, comorbid conditions, environmental factors, injury severity, impairment severity, and mechanism of injury. For example, it may be that certain types of memory remediation work best for individuals with moderate-severe injury, focal memory impairments, and a supportive home environment. Or, treatment impact may vary with the presence of a sleep disturbance or the extent of family support to enhance participation in or reinforcement of the intervention. Researchers and clinical providers should collaborate to identify the many variables that influence response to therapy interventions. Relatively large samples are therefore necessary to ascertain the interventions that are most effective for specific patients and their special needs and circumstances. To enhance the understanding of the optimal treatment candidates for various forms of CRT, and their relative value in affecting different outcome targets, DoD should collaborate with other rehabilitation research organizations to capture relevant patient characteristics and outcome measures, which can facilitate comparison of results across studies and treatments and support formal meta-analyses.

Categorizing participants by injury severity and recovery phase may be important to create useful categories, group studies, and draw related conclusions. However, in research or treatment of cognitive deficits following TBI, clinicians and researchers are generally more attentive to *severity of the deficit* rather than *severity of injury*. Likewise, in application and research, clinicians and researchers focus more on clinical indicators of treatment need and readiness for treatment than the absolute time since injury. Therefore, in some cases, the severity of injury classification does not correspond with the severity of deficit requiring rehabilitation. For example, a moderate or severe TBI can result in chronic but mild, moderate or severe cognitive impairments. Likewise, a mild TBI can result in mild but very disabling cognitive impairments that interfere with one's ability to participate in society.

Environmental and social factors, particularly family support, are especially influential in recovery from TBI. Engaging and mobilizing the patient's family may be accomplished by a range of efforts. Caregivers are directly affected by their family members' disability and play key roles in motivation, treatment participation, compliance, and follow-up. Thus, education and support for family members and other caregivers are essential in CRT treatment. However, the roles of family and caregivers in CRT

treatments for TBI are rarely defined systematically and vary by intervention, study, and rehabilitation program. DoD should encourage family or caregiver involvement, especially where interventions or rehabilitation programs may require significant support for the treated individual within or beyond the treatment facility. Investigators should consider the important role of caregivers as interventions or rehabilitation programs are tested in controlled environments. DoD should consider the incurred costs of CRT to family members, in part related to the burdens of taking time away from work and traveling to rehabilitation facilities, and thus may want to increase support for families/caretakers as part of the recovery process.

Promote Standardization and Operationalization of Patient Characteristics, Outcome Measures, and CRT Interventions

Research to document efficacy of CRT will benefit from greater operational definition of the CRT interventions being evaluated. Given that no current treatment taxonomy is sufficiently mature to allow feasible coding of treatment A versus B versus C in practice, the most realistic short-term approach to defining and standardizing specific CRT interventions is to develop treatment manuals and adherence measures to verify that the defined treatment is being administered to patients. Developers of CRT treatments and others experienced in their use, along with civilian and military funding agencies, should collaborate to codify and make widely available these operationally defined treatments (e.g., specific manual-based forms of CRT), which can be tested in clinical trials. Likewise, collaboration should achieve consensus for recommendations on variables that describe patient characteristics and clinical outcomes. To enforce newly established standards, funders can promote these standardized practices by requiring research uniformity in research proposals. Likewise, professional organizations may consider providing continuing education only to those practitioners and providers meeting standard criteria.

Recommendation 14-1: DoD should work with other rehabilitation research and funding organizations to

1. **Identify and select uniform data elements characterizing TBI patients including cognitive impairments (to supplement measures of injury severity) and key premorbid conditions, comorbidities, and environmental factors that may influence recovery and treatment response;**
2. **Identify and select uniform TBI outcome measures, including standard measures of cognitive and global/functional outcomes; and**

3. **Create a plan of action to**
   a. **Identify currently feasible methods of measuring the delivery of CRT interventions,**
   b. **Advance the development of a taxonomy for CRT interventions that can be used for this purpose in the future, and**
   c. **Advance the operationalization of promising CRT approaches in the form of treatment manuals and associated adherence measures.**

Advancing the evidence about CRT requires enlarging the sample size of patients studied in similar ways, by investing in larger studies or ensuring the collection of comparable data across multiple smaller studies and observational data sets. The necessary data include variables that capture characteristics of patients that are relevant to predicting their outcomes and their response to treatment, variables that capture a range of outcomes that shed light on the impact of CRT, and variables that capture the type and dose of CRT interventions that patients receive. Measures of many of the relevant patient characteristics are already available, but comparable measures are not being collected across studies. Measures of the relevant outcomes are also available, and the NIH's CDE effort has already made some progress in suggesting specific consensus outcome measures for patients with TBI. Outcome measures incorporated into CRT research remain variable. Therefore, in the areas of patient characteristics and outcomes, progress can be made by striving for consensus on the available measures that are most useful to incorporate into CRT data collection efforts over time.

In the case of variables that define CRT interventions received, however, the field is not nearly as well developed. There is no current taxonomy that defines or names in standardized fashion different forms of CRT in ways that are likely to map onto their efficacy and effectiveness, and thus no straightforward process for recommending treatment-related variables for incorporation into studies and registries. Thus, advancing the process of standardized treatment data collection will evolve over time and may involve (1) considering what measures are currently available that are likely to be useful in this effort, (2) developing a consensus agenda of the work needed to advance CRT treatment definition, and (3) distilling promising forms of CRT into treatment manuals with associated adherence measures, so that the delivery of these well-defined packages can be documented. As a way to make these improvements, the committee recommends that DoD convene a conference to achieve consensus among multiple agencies and professional organizations providing or endorsing CRT. The conference participants should be given specific goals to finalize the selection of patient

characteristics and outcome variables to be included in experimental and observational CRT research, and to plan a strategy to advance the common definition and operationalization of CRT interventions.

Recommendation 14-2: DoD should convene a conference to achieve consensus among a multiagency (e.g., VA, NIH, and NIDRR), multidisciplinary team of clinicians and researchers to finalize the selection of patient characteristics and outcome variables to be included in experimental and observational CRT research, and to plan a strategy to advance the common definition and operationalization of CRT interventions.

In addition, researchers and clinicians should reach consensus on the appropriate timing of CRT in the course of recovery following TBI. Current data examine the application of CRT in subacute and chronic phases of mild or moderate/severe TBI, with no parallel identified evidence base for review of CRT delivered during the acute stage. This may in part be due to spontaneous resolution of short-term impairments without rehabilitation. Formal analyses to identify early predictors of spontaneous recovery should be undertaken to best identify patients who are at risk for long-term impairments and who are good candidates for CRT. Data are needed to enforce or dispel the current idea that rehabilitation programs should ideally begin treatment only in subacute and chronic phases of TBI.

Develop a Registry Among Existing Cohorts

The treatment and time course of TBI among military personnel, including its sequelae and recovery, prompt the cooperative engagement of government agencies and other research organizations to advance evidence-based decision making pertaining to the value of specific interventions for TBI, particularly within the military setting. Ongoing research provides an opportunity to bridge substantial knowledge gaps that require continual compilation and analyses of the results as well as publication of interim findings and data sharing.

Throughout its deliberations, the committee had the opportunity to hear from researchers actively engaged in studies of CRT for the treatment of individuals with TBI. Ongoing and new studies provide an opportunity to increase standardization, identify factors that characterize the course of TBI and factors that may affect recovery, and evaluate individual CRT approaches compared to comprehensive or multi-modal treatments. Furthermore, such studies provide an opportunity for DoD and allied agencies (e.g., NIDRR, NIH, VA) to better understand the evolving field of CRT and make judgments regarding efficacy of both modular and comprehensive treatments.

Longitudinal patient registries represent an evolving resource that will make observational studies of comparative effectiveness more feasible and informative. Such deidentified but coded registries go beyond administrative claims data, which typically lack sufficient clinical data about disease severity. Larger integrated health care delivery systems are creating registries with the aid of electronic medical records that link administrative claims data with clinical, pharmacy, and laboratory data, and, increasingly, with patient-reported data that are collected in a systematic fashion. Clinical trials are typically of relatively short duration but contain a wealth of well-characterized data and should be included in the proposed longitudinal registries.

Recommendation 14-3: DoD should incorporate the selected measures of patient characteristics, outcomes, and defined CRT interventions into ongoing studies (e.g., DVBIC: SCORE trial, Millennium, TBI Model Systems) and develop a comprehensive registry encompassing the existing cohorts and deidentified MHS medical records to allow ongoing evaluation of CRT interventions.

There are many strategies for establishing a registry, but existing studies or cohorts that might be adapted for this purpose include the Congressionally Mandated Longitudinal Study on TBI, DVBIC SCORE trial, Millennium, and TBI Model Systems. CRT for TBI ideally would take into account subgroup-level results, given the heterogeneity of populations and forthcoming advances in disease mechanisms/markers (Kent et al. 2010). Randomized trials large enough to conduct such analyses will be expensive and take years; a prospectively designed registry could potentially yield results on subgroups more rapidly to help the inform research community about who would most benefit from CRT. A registry could be used to analyze current implementation of CRT as well as the associated outcomes. This information should prospectively capture additional data elements. The registry should include data from (1) operationally defined categories or taxonomy of CRT treatments (as described in Recommendations 14-1 and 14-2), and (2) providers of CRT-consistent care, such as physical therapists, occupational therapists, speech therapists, or others.

The different labels and billing codes currently used by various providers (e.g., occupational therapists, physical therapists, and speech-language pathologists) makes it difficult or impossible to identify and track current CRT usage patterns. Operationally defined CRT treatments (i.e., manual-based interventions) will not clear up the ambiguity of services provided via occupational therapy (such as "dressing training") versus CRT. However, operationally defined CRT treatments will improve identification and tracking of (1) restorative programs (these treatments usually involve "ar-

tificial" tasks so they cannot be labeled as "dressing training"), and (2) large, organized programs of compensatory CRT treatments. Once a more comprehensive taxonomy of rehabilitation treatments is available, embedded CRT activities provided via occupational therapy, physical therapy, or speech-language pathology will be easier to identify due to the services provided (e.g., training, learning, adapting, and compensating).

Recommendation 14-4: Using these data sources, DoD should plan to prospectively evaluate the impact of any policy changes related to CRT delivery and payment within the MHS with respect to outcomes and cost-effectiveness.

Prospectively planned analyses of clinically rich data sets are increasingly used to monitor and evaluate the implementation and impact of clinical and policy interventions in health care. These registries provide the opportunity to reassess effectiveness—including both benefits and harms—of interventions as they move into routine care from settings and populations in which they have been tested for efficacy. Because little research exists on dissemination of evidence-based CRT therapies, DoD should evaluate the impact of policy changes about evidence-based CRT interventions delivered in the MHS. DoD can shape and monitor implementation rollout, and plan a prospective evaluation of the utilization, health, and financial impacts of any coverage policy change.

Advance Current Research

To continue efforts to document efficacy and effectiveness of CRT, research should be designed to address the effects of CRT across various levels of TBI severity and recovery among individuals capable of participating in this therapy, especially service members and veterans. Current efforts should provide valuable information about CRT efficacy and effectiveness. For example, the ongoing SCORE! trial includes four arms. The treatment group (with CRT) will be compared to a no-treatment group (to determine efficacy) and other forms of CRT group (to determine effectiveness). As discussed previously, the potential moderating effects of premorbid conditions (e.g., attention deficit hyperactivity disorder [ADHD], learning disabilities), comorbidities (e.g., posttraumatic stress disorder [PTSD], depression), and social environmental context (e.g., family support) on response to CRT should be studied. Investigative attention should be devoted to evaluating the generalization of the effects of CRT across various settings, as well as the persistence of any improvements over time. There are several promising efforts under way or planned, as indicated by the table of ongoing or re-

cently completed clinical trials found in Appendix C of this report. Ideally, study designs will include

- an emphasis on functional patient-centered outcomes;
- defined control groups of ideally wait-list or usual care comparisons; and
- sample sizes sufficiently large to inform analyses of the impact of heterogeneities (covariates) within the TBI population on treatment outcome; or
- novel, adaptive designs (to surmount sample size issues).

DoD should continue to facilitate development of existing, early stage research. Early research may be most efficiently compared to no treatment or a wait-list control, since this does not require design of plausible but inert comparison treatments, and avoids the risk of comparing two effective treatments. Once a treatment is shown to be superior to no treatment, research designs may include increasingly precise comparisons to define the ingredients that account for impact. Such treatments should be distilled into treatment protocols or manuals in consultation with their original developers and/or researchers and clinicians experienced in these approaches, and accompanied by adherence measures that ensure these treatments' faithful delivery.

Once a set of effective modular treatments is assembled, a comprehensive program could then be built from the set. The protocol would ideally incorporate assessment and treatment selection criteria to determine which patients should receive which modules, as well as assessment of the impact of the program on important aspects of activity and participation. A research program of this magnitude requires substantial and sustained investment, and most likely a multicenter research system to recruit sufficient patients for study.

Recommendation 14-5: DoD should collaborate with other research and funding organizations to foster all phases of research and development of CRT treatments for TBI, from pilot phase, to early efficacy research (safety, dose, duration and frequency of exposure, and durability), to large-scale randomized clinical trials, and ultimately, effectiveness and comparative effectiveness studies.

Modeling, observational studies, randomized controlled trials (RCTs), and systematic reviews are the types of research approaches used for comparative effectiveness and implementation research. Well-controlled trials of CRT will help provide more definitive evaluations of CRT efficacy in

ameliorating cognitive deficits due to TBI, as will large observational studies that capitalize on existing registries and cohorts, including long-term follow-up of clinical trial populations. Observational studies are potentially less expensive to perform than RCTs; however, observational studies require sufficient sample size and duration to account for variability of injury severity and other factors that influence treatment choice and outcomes. The Patient Centered Outcomes Research Institute, established in 2011, includes a Methodology Committee charged with identifying areas of methodological research to improve the quality of findings from comparative effectiveness studies, particularly observational study designs. Meaningful analysis requires accounting for these factors and comparing outcomes of different treatment approaches. Periodic evaluation of accrued evidence should accompany efforts to improve the size and quality of studies, since the value of a systematic review of evidence depends on the quality of studies being assessed.

CONCLUSION

Members of the military and civilians commonly experience TBI, which often results in significant cognitive, physical, or psychosocial deficits requiring rehabilitation. These recommendations aim to assist DoD and allied agencies in addressing this increasing and significant problem for U.S. society. Conclusive evidence of efficacy, and particularly effectiveness, is lacking for all forms of CRT even though some forms have modest amounts of evidence.

In reviewing the evidence, the committee found no studies addressing cognitive deficits in the acute phase of recovery following TBI, few studies addressing treatment of those with moderate-severe injuries in the subacute phase, and few studies addressing cognitive treatment for individuals with mild injuries overall. Evidence supporting the efficacy of CRT in the chronic phase of TBI for patients with moderate-severe injuries varies by cognitive domain and specific CRT treatment modality. Because the noted limitations of the evidence often were secondary to the methodological shortcomings of the studies reviewed, and do not rule out meaningful benefit of CRT for TBI, *the committee supports the ongoing clinical application of CRT interventions for individuals with cognitive and behavioral deficits due to TBI.* With thoughtful consideration of the challenges it faced throughout the study process, and in light of the lack of conclusive evidence, the committee has identified these recommendations as a way forward for the Military Health System.

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Appendixes

Appendix A

Comparative Effectiveness and Implementation Research for Neurocognitive Disorders: Concepts Relevant to Cognitive Rehabilitation Therapy for Traumatic Brain Injury

TASKS RELATED TO COMPARATIVE EFFECTIVENESS RESEARCH

The Institute of Medicine (IOM) Committee on Cognitive Rehabilitation Therapy (CRT) for Traumatic Brain Injury (TBI) was asked to determine if there is sufficient evidence to support widespread use of CRT interventions in the Military Health System (MHS), including TRICARE coverage. In the Statement of Task, the committee was charged with assessing the literature not only for efficacy but also for effectiveness ("the committee will consider comparison groups such as . . . other non-pharmacological treatment") as well as any evidence of harm or safety issues. Thus, subtasks 1 through 3 of the Statement of Task to the committee include requests for analysis of any existing literature that directly compares alternative treatment approaches. Such an analysis directly falls within the definition of comparative effectiveness research (IOM 2009).

A primary tenet of comparative effectiveness research is to evaluate which preventions and treatments work for which patients. This tenet reflects "the growing potential for individualized and predictive medicine—based on advances in genomics, systems biology, and other biomedical sciences—through the analysis of subgroups with demographic, ethnic, physiologic, and genetic characteristics that could be useful factors in clinical decisions" (IOM 2009). CRT interventions are multi-faceted, and by definition, *tailored to the particular individual*. Interventions intend to address not only specific domains of cognitive impairment, but also potential mediators and moderators of a CRT intervention's effect (Figure A-1). These mediators or moderators may include characteristics unique to the

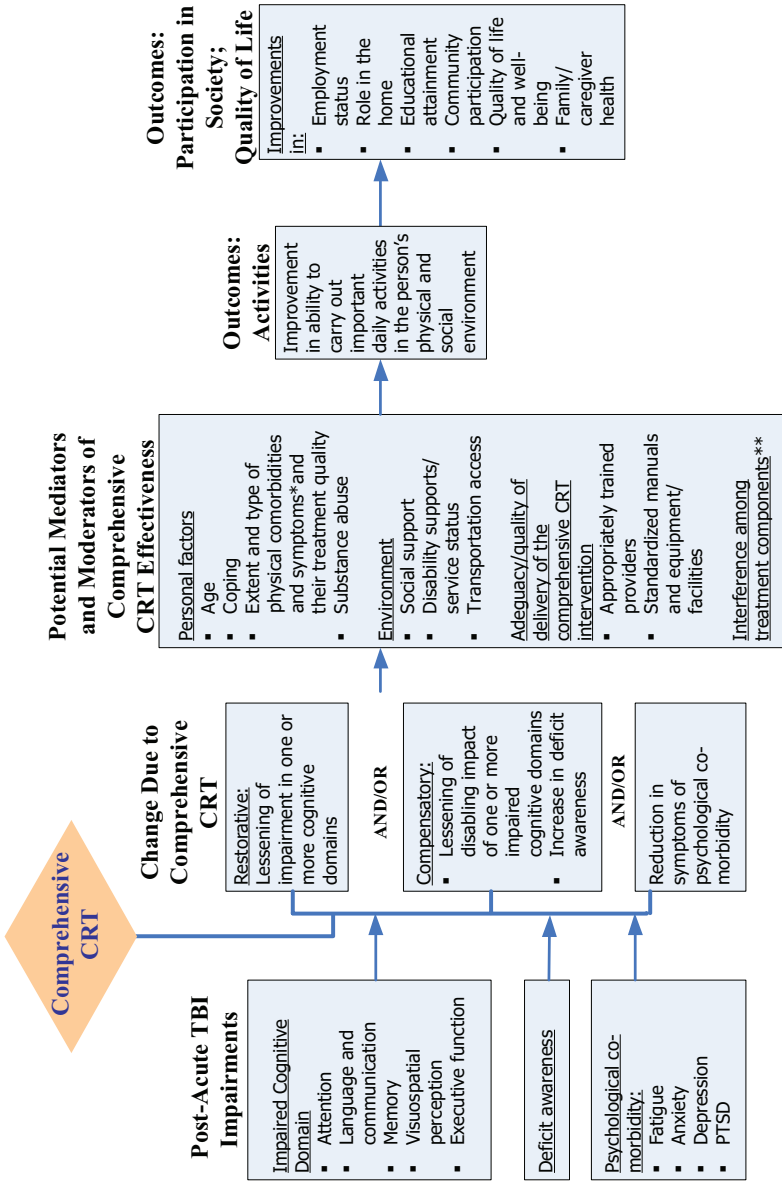

FIGURE A-1 Model for multi-modal/comprehensive CRT.
* For example: visual impairment, headache, dizziness.
** For example: side effect of medication for depression interferes with attention.

individual, the type and extent of comorbidities, or the type and one or more cognitive deficits. Furthermore, the unique characteristics of the individual may reflect preexisting conditions or factors unrelated to TBI, such as presence of a sleep disturbance or extent of family support to enhance participation in or reinforcement of the intervention.

TASKS RELATED TO IMPLEMENTATION RESEARCH

The committee was also asked to assess adequacy of the "training, education, and experience" of providers of CRT, which falls within the scope of implementation research. Such research aims to analyze whether clinical interventions with evidence of efficacy are being delivered in real-world, nonexperimental settings by usual providers, and if so, whether the interventions continue to have a net health benefit. Thus, implementation research not only observes levels of care and barriers to provision of high-quality care, but also designs and evaluates policy or health care delivery system interventions that may improve the uptake or delivery of a clinical therapy. In that way, the health benefit of a therapy—across a population—is maximally achieved in the context of its value. This issue is particularly relevant to CRT, since such interventions are more complex than delivery of a drug and require

1. Availability of specific protocols and tools for delivering a particular CRT intervention,
2. Adequately trained CRT providers, and
3. A context that maximizes sufficient participation by the patient to achieve the benefit of the CRT.

TRANSLATING EVIDENCE INTO PRACTICE THROUGH PHASED IMPLEMENTATION AND EVALUATION

The IOM Clinical Research Roundtable developed a now widely accepted conceptual model of the research stages (Sung et al. 2003). As depicted in Figure A-2, research stages include discovery of disease mechanisms in the laboratory, development of efficacious therapeutics, and translation of evidence-based therapies into widespread practice. To translate evidence-based therapies to care generally calls for a *phased series of studies,* due to the need to reengineer or redesign the way care is usually delivered. These kinds of behavior or organizational changes are often complex, and initial implementation approaches require extensive investigator involvement in design and oversight of the change process. Strategies that are successful in more tightly controlled environments must become broadly disseminated in heterogeneous care settings, with less investigator involvement.

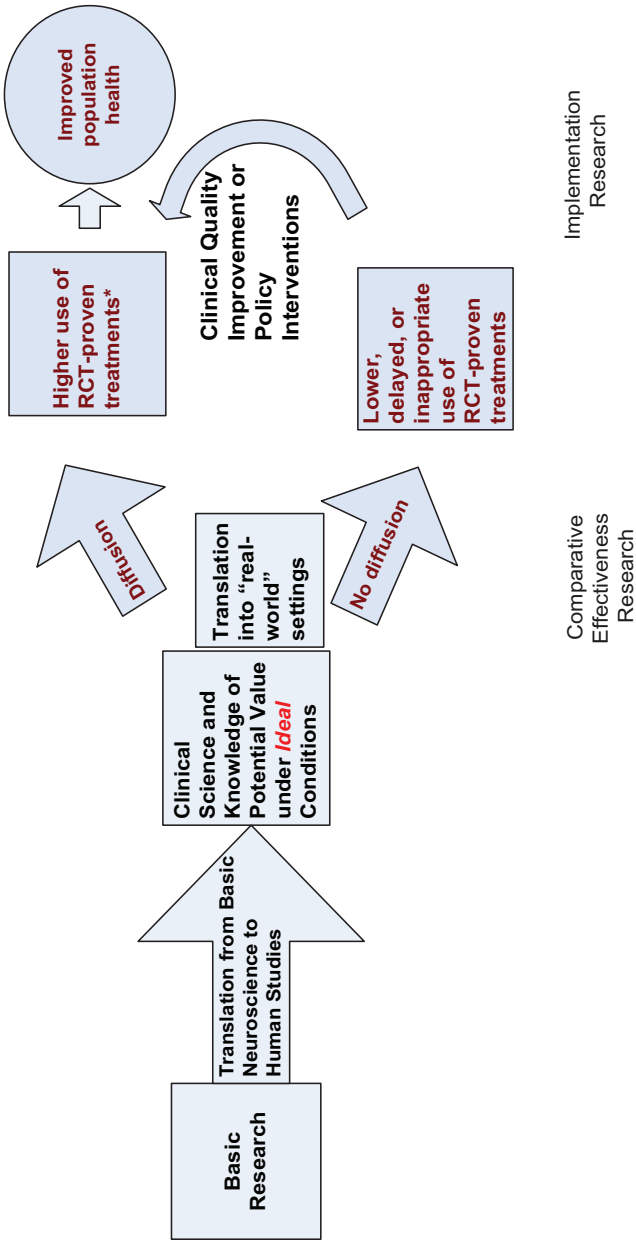

FIGURE A-2 Clinical research continuum.
SOURCE: Vickrey et al. (submitted).

Furthermore, change strategies apply evaluations later in the process, focusing on a qualitative analysis of how and how well the intervention is implemented, and whether the intervention continues to have beneficial impact (Figure A-3) (Stetler et al. 2008). These kinds of evaluations are particularly relevant for nonpharmacological interventions like CRT. For an example beyond TBI literature, interventions to facilitate behavioral or lifestyle changes in diet and physical activity for hypertension control utilize these evaluations (Appel et al. 2003).

CRT FOR TBI AND COMORBIDITIES COMMON IN THE MILITARY SETTING

The literature reviewed for this report illustrates that TBI occurring in a military context is commonly accompanied by comorbidities, including symptoms of psychological distress and possible co-occurring diagnoses of depression, posttraumatic stress disorder (PTSD), or anxiety disorder. Physical comorbidities also may exist, including pain, fatigue, sleep disturbance, visual impairment, or effects of polytrauma from blast injuries. The recognition and management of these comorbidities will impact end-indicator outcomes such as health-related quality of life or employment;

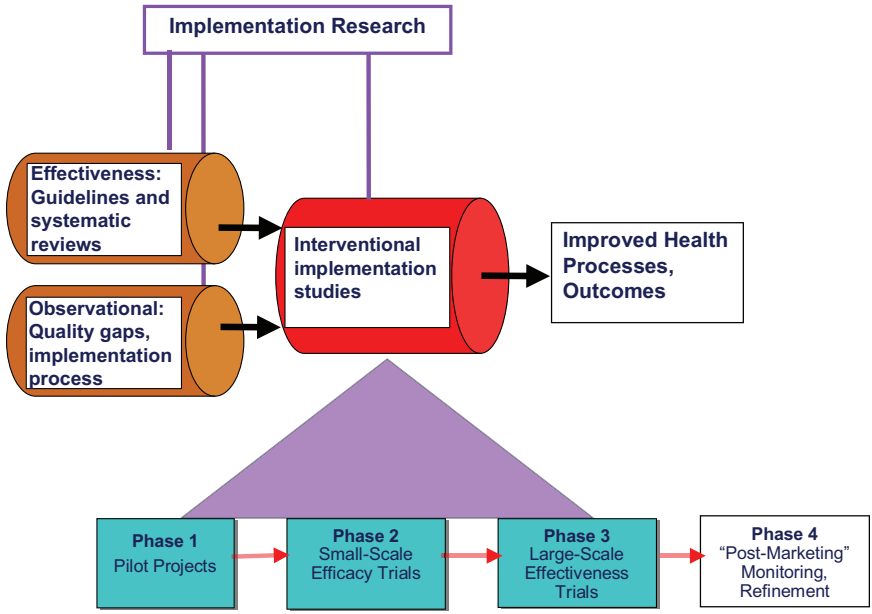

FIGURE A-3 Refined research-implementation pipeline.
SOURCE: Adapted from Stetler et al. 2008.

these outcomes are also targeted by rehabilitation directed toward specific or multiple cognitive domains. The recently funded Defense and Veterans Brain Injury Center (DVBIC) SCORE! trial began enrollment in 2011. The study addresses pervasive TBI comorbidities through inclusion of a comparator arm in which both cognitive and psychological comorbidities are systematically screened for and addressed in a strategy tailored to the individual. This clinically pragmatic approach recognizes that multiple, applicable, efficacious clinical interventions should be tailored to the problems of the individual, both the primary cognitive domain(s) affected and any comorbidities. This approach is analogous to those developed and tested for certain chronic conditions that have a broad range of symptom manifestations.

For example, Alzheimer's disease not only affects memory but also is often accompanied by a wide and varied range of behavior problems and depression in the patient; safety issues; as well as depression, anxiety, and stress in family caregivers. To successfully delay declines in patient health outcomes and to improve caregiver outcomes requires screening for problems, prioritizing goals with the patient and the caregiver, and implementing and following up on care management protocols likely to maximize benefit for that patient–caregiver dyad (Vickrey et al. 2006). In general, U.S. health care is moving toward care delivery strategies for chronic diseases that are preventive; ongoing; include structured, systematic assessments; engage the patient in self-management; and utilize health information technology (IT) to make care delivery more efficient (Wagner et al. 1996). This trend is in contrast to the traditional model of doctor visit–based care, which is more reactive to problems and arose from an era in which acute therapy for problems such as infections and injuries was the standard.

Evidence for the efficacy of CRT for specific domains of cognitive impairment can guide clinical decision making and coverage decisions for individuals with deficits in those domains with similar contexts and clinical profiles as participants in those trials. Yet most individuals with blast-related TBI have other comorbidities not studied in civilian trials. Several studies that research multi-faceted interventions to address multiple comorbidities and broader affected populations are under way (see Appendix C). The findings from these trials will need to be incorporated into future coverage and clinical service decisions to inform subsequent research studies that aim to build on those findings.

RESOURCES FOR COMPARATIVE EFFECTIVENESS RESEARCH APPLICABLE TO ONGOING RESEARCH ON CRT FOR TBI

Prospectively planned analyses of clinically rich data sets are increasingly used to monitor and evaluate the implementation and impact of

clinical and policy interventions in health care. These analyses enable researchers to reassess effectiveness—including both benefits and harms—of interventions as they move into routine care from controlled settings and populations where they have been tested for efficacy. Types of research approaches used for comparative effectiveness and implementation research include systematic reviews, randomized trials, modeling, and observational studies. Observational studies are potentially less expensive to perform than randomized trials. However, observational studies require sufficient clinical variables to enable meaningful analyses, considering disease severity and factors that would influence choice of treatment and outcomes. Likewise, analyses to compare outcomes of different treatment approaches should account for these factors.

The Patient Centered Outcomes Research Institute, a private, nonprofit organization established in 2011, includes a Methodology Committee charged with identifying areas of research to improve the quality of findings from comparative effectiveness studies, particularly observational study designs. An evolving resource that will make observational studies of comparative effectiveness more useful and feasible to conduct is the growth of longitudinal patient registries. Such registries go beyond administrative claims data, which typically lack sufficient clinical data on disease severity. Larger, integrated health care delivery systems are creating registries that link administrative claims data with pharmacy data, laboratory data, electronic medical records, and increasingly, patient-reported data collected in a systematic fashion, to minimize missing data on key variables (Paxton et al. 2010). In the case of CRT in the MHS, a registry could be used to analyze implementation of CRT and the associated outcomes. Such a registry would need to prospectively collect additional data elements, including operationally defined categories or a taxonomy of CRT treatments, as well as the ability to assess (i.e., through analysis of a sample of cases) the extent to which care consistent with CRT is currently delivered by physical therapy, occupational therapy, speech therapy, or other providers. Doing so allows for capture of current patterns and any changes over time via new or modified policy or expanded, evidence-based practices.

The growth in technological capacity for electronic medical records and the national investment in health IT capability are fueling the opportunity to build registries with clinical utility, with few downsides. A registry resource would ideally allow for ongoing investigations of the effectiveness of CRT delivery and coverage policies in the MHS and TRICARE by enabling researchers to access deidentified data (with appropriate approvals) and other resources. This access would help researchers ensure data or a subset of clinically enriched data are prospectively captured and updated. This type of investment will ensure the timely and efficient conduct of

1. Future research on effectiveness and implementation of alternative CRT approaches for members of the military and veterans,
2. Analyses to be used by health care administrators to make decisions about the personnel and resources currently in place and needed in the future to broadly implement CRT interventions identified as of value for certain populations, and
3. Policy analyses on health and cost consequences of existing CRT coverage policies, which will guide future recommendations for changes in coverage for these clinical services as the evidence base and the affected population change over time.

There are many strategies for establishing a registry. Ideally, specific data elements on the delivery of CRT would be built into new or recently created registries and observational studies sponsored by the U.S. Department of Defense (DoD) and U.S. Department of Veterans Affairs (VA), including the congressionally mandated 15-year longitudinal study of TBI outcomes in soldiers being carried out by DVBIC.

POTENTIAL OPPORTUNITIES

Opportunities for advancing knowledge of what works for CRT in TBI and for efficiently translating that knowledge into health care delivery systems and maximizing health outcomes include the following:

- In currently planned DoD and VA registries, purposefully embed the necessary data elements about types of CRT and providers, to prospectively analyze current care patterns and costs, and factors associated with variation (Gliklich and Dreyer 2010).
- Prospectively plan to evaluate current care and any changes in response to policy decisions or new evidence, analogous to the VA's QUERI program and REACH program (Gitlin et al. 2010; Nichols et al. 2011). Outcomes to be assessed in such an evaluation are impact on utilization, benefits, harms, families, and unmet need, as well as quality of care delivered relative to current or usual care patterns.
- Account for heterogeneity of populations and forthcoming advances in disease mechanisms and markers by designing studies of CRT interventions or programs for TBI to include subgroup-level results, as done with comparative effectiveness research on different modes of health care delivery (Kent et al. 2010). This can be accomplished by ongoing surveillance for new evidence, particularly on subgroup effectiveness (Shekelle et al. 2009).
- Create a publicly accessible database of the interventions, including tools (manual, protocols, other resources) for delivering them, fa-

cilitating implementation of new evidence about CRT. This would also enable qualitative analysis of what components appear common to effective interventions, analogous to the Rosalynn Carter Caregiving Institute database of effective caregiver interventions.

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Appendix B

Workshop Agendas

The committee held data-gathering sessions that were open to the public at two of its six meetings. These meetings were held in Washington, DC, and Irvine, California. The open-session agendas of the public meetings are below.

WORKSHOP ONE

Committee on Cognitive Rehabilitation Therapy for
Traumatic Brain Injury
February 7, 2011
Keck Center of the National Academies
500 Fifth Street, N.W., Room 100
Washington, DC

10:00 a.m.–10:10 a.m.	**Welcome and Introductory Remarks** *Ira Shoulson, Georgetown University*
10:10 a.m.–12:00 p.m.	**The Charge to the Committee: A Discussion with the Sponsor** *CAPT Robert DeMartino, TRICARE Management Activity*
1:00 p.m.–1:45 p.m.	**Continuum of Care for TBI in the Department of Defense** *Kathy Helmick, Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury*

1:45 p.m.–2:45 p.m.	**Traumatic Brain Injury: Physical and Clinical Manifestations of Head Trauma** *Eric Nauman, Purdue University* *Tessa Hart, Moss Rehabilitation Research Institute*
2:45 p.m.–3:30 p.m.	**Development of Cognitive Rehabilitation Therapy for TBI** *Keith Cicerone, JFK Johnson Rehabilitation Institute*
3:45 p.m.–4:30 p.m.	**Overview of the Literature** *Martin L. Rohling, University of South Alabama*
4:30 p.m.–5:15 p.m.	**Comorbidities and Confounding Factors of Head Trauma** *Jennifer Vasterling, Boston University*
5:15 p.m.–5:30 p.m.	**Public Comment Period**
5:30 p.m.	**Workshop Adjourns**

WORKSHOP TWO

Committee on Cognitive Rehabilitation Therapy
for Traumatic Brain Injury
March 16, 2011
Beckman Center of the National Academies
100 Academy Way
Irvine, CA

8:30 a.m.–8:40 a.m.	**Welcome and Introduction** *Ira Shoulson, Georgetown University*
8:40 a.m.–10:00 a.m.	**Panel I: Cognitive Rehabilitation Therapy and TBI in Research** *Douglas Cooper, Defense and Veterans Brain Injury Center* *Wayne Gordon, Mount Sinai School of Medicine* *Yelena Bogdanova, Boston University*

10:00 a.m.–11:45 a.m.	**Panel II: Cognitive Rehabilitation Therapy and TBI in Practice** *Mary Kennedy, University of Minnesota* *Lyn Turkstra, University of Wisconsin* *James Malec, Rehabilitation Hospital of Indiana* *Mary Pepping, University of Washington*
1:00 p.m.–1:40 p.m.	**Panel III: Outreach to the Family and Community** *Allison Clark, Baylor College of Medicine* *Ray Dorsey, Johns Hopkins University*
1:40 p.m.–2:15 p.m.	**Keynote: Comparative Effectiveness Research for Neurocognitive Disorders** *Barbara Vickrey, University of California, Los Angeles*
2:15 p.m.–2:30 p.m.	**Public Comment Period**
5:00 p.m.	**Workshop Adjourns**

Appendix C

Recent and Ongoing Clinical Trials: CRT for TBI

The following table includes recent and ongoing clinical trials related to cognitive rehabilitation therapy and traumatic brain injury; these trials may include criteria that go beyond the scope and methods used by the IOM committee in its evaluation of the current evidence. The trials are listed in alphabetical order, with start and end dates ranging from 1996 to 2013. The table was created based on information from ClinicalTrials.gov, a service of the National Institutes of Health (NIH).

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
15 Year Longitudinal Study of TBI Incurred by Members of the Armed Forces in OIF/OEF *Defense and Veterans Brain Injury Center* PI: COL Michael Lewis, M.D.	Phase 1: (Surveillance) DVBIC is collaborating with the Defense Manpower Data Center (DMDC) to assess mortality surveillance of OIF/OEF veterans to determine whether an in-theatre history of TBI increases risk of death among OIF/OEF veterans. DMDC obtains data from a variety of federal sources including information from the Social Security Administration's Death Master File and deceased benefit information from Veterans' Affairs. To date, DMDC has identified approximately 1.5 million service members who have served in OIF/OEF of which over 15,000 are no longer alive as of March 2011. Regarding those deaths, DVBIC is in the process of (a) determining cause of death; and (b) history of TBI. A series of statistical analyses will be performed on the data to identify possible trends within the data in an effort to determine factors that may have preventive benefit. Phase 2: (Previous TBI Diagnosis) is submitting its protocol as an amendment to the Natural History protocol (Phase 3). Phase 2 is designed to collect neurobehavioral information on service members and veterans who are 12 months or more post-TBI diagnosis (dating back to October 2001), as well as trauma controls and healthy controls. Phase 2 includes a second protocol addressing health related quality of life in family caregivers of service members and veterans with TBI. The caregiver protocol will be submitted to OHSP for review last month. Phase 3: (Incident TBI) has received approval for the Natural History protocol from the WRAMC and USUHS IRBs. Recruitment began at WRAMC in May 2011. The study is designed to collect comprehensive pathophysiologic, neurobehavioral, and neuroimaging information on service members newly diagnosed with TBI, trauma controls, and healthy controls. Annual follow-up brief evaluations will be done and intermittently will include a comprehensive examination similar to baseline.
Acute Cognitive and Neurobehavioral Intervention: Efficacy Evaluation *Virginia Commonwealth University; U.S. Department of Education* PI: Jeffrey S. Kreutzer, Ph.D.	**Study Purpose:** To learn more about behavior and everyday functioning after brain injury, and to learn if behavior and functioning gets better with more education about changes after brain injury. **Detailed Description:** To evaluate the efficacy of the First Steps intervention for improving neurobehavioral functioning, functional status, and life satisfaction, and for increasing knowledge about TBI and compensatory strategies. The First Steps program was developed to address the neurobehavioral and emotional concerns of survivors of TBI during the course of inpatient rehabilitation. Program format and content reflects clinical experience and extensive research review. Input from survivors, family members, and rehabilitation staff trained in working with the TBI population has also helped shape the implementation protocol. The foundation of the protocol is a curriculum [Niemeier, J., Kreutzer, J., & Taylor, L. (2005). Acute cognitive and neurobehavioral intervention for individuals with acquired brain injury: Preliminary outcome data. Neuropsychological Rehabilitation, 15(2), 129–146.] The First Steps curriculum consists of 10 lessons and was developed to address the common needs, issues, and concerns of TBI survivors admitted acutely for inpatient rehabilitation.

Sample Description	Study Type	Study Design	Time Frame
Phase I: All OIF/OEF Veteran Service Members since October 2001 Gender: Both Group: Adult **Phase II:** TBI: N = 1,600 Trauma Controls: N = 800 Healthy Controls: N = 800 Gender: Both Group: Adult **Phase III:** Focus Groups: N = 60 Cognitive Interviews: N = 60 Longitudinal Online Questionnaire: N = 300 Gender: Both Group: Adult	Observational	• Primary Purpose: Observational	2007 Start
N = 103 Gender: Both Group: Adult/Senior	Observational	• Observational Model: Cohort • Time Perspective: Prospective	October 2002–October 2008

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Acute Neurobehavioral Program for Improving Functional Status After TBI *Virginia Commonwealth University; Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)* PI: Janet P. Niemeier, Ph.D.	**Study Purpose:** More than 1.4 million people a year in the United States begin confronting life with the medical, cognitive, and psychosocial challenges resulting from traumatic brain injury (TBI). A range of cognitive impairments commonly observed following injury increase caregiver burden as well as per-person lifetime costs for care and support of survivors of TBI, estimated at $600,000 to $1,875,000. Our long-term goal is to lessen these burdens through improving the functional status of patients with TBI by providing an evidence-based, comprehensive, brief, acute-care intervention, First Steps Acute Neurobehavioral and Cognitive Intervention (FANCI). The 10-sesson, manualized FANCI Program will be tested in a controlled, randomized study. Therapeutic components of the FANCI include didactics, cognitive remediation, demonstration, guided self-reflection, rehearsal, and supported practice of skills and strategies. Specific hypotheses are that (1) FANCI will result in more improvement in functional status compared to standard interdisciplinary rehabilitation treatment and (2) FANCI will result in more improvement on measures of neurobehavioral functioning compared to standard rehabilitation care for patients with moderate to severe TBI. We base these hypotheses on the observations that (1) providing information about symptoms, treatment, and coping results in reduced symptom intensity and duration for patients with TBI, and (2) inpatient participants in recent FANCI pilot studies learned > 80% of the FANCI Program curriculum, and (3) the most recent pilot study participants had significantly better functional outcomes at discharge than matched controls. The specific aims of the proposed study are to (1) evaluate the efficacy of FANCI for improving functional status following treatment using the FIM, (2) examine the impact of FANCI on broader outcome measures of general emotional and behavioral functioning and productive activity in the community as measured post-treatment and at 6-month follow-up, (3) examine contributions of participant injury severity and cognitive status at time of treatment to treatment outcome and treatment response, (4) examine contributions of treatment variables of session topic and mastery, caregiver presence, and concurrent therapies on treatment outcome and treatment response for inpatients with TBI. Primary outcome measure is the (FIM). We will secondarily compare scores on the Disability Rating Scale (DRS), Glasgow Outcome Scale-Extended (GOSE), Rehabilitation Intensity of Therapy Scale (RITS), and Frontal Systems Behavior Scale (FRsBe). Our design is a parallel groups, single-blind, randomized, controlled trial. We will enroll 150 (75 treatment, 75 control) participants. Inclusion Criteria: Mod. to Sev. TBI based on time to commands, English speaker, Length of stay ≥ 5 days in acute BI rehabilitation Unit, 18 years of age or older, ≥ 79 on GOAT. **Detailed Description:** N/A

Sample Description	Study Type	Study Design	Time Frame
N = 150 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double Blind (Investigator, Outcomes Assessor) • Primary Purpose: Treatment	March 2008–September 2013

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Amantadine for Treatment of Symptoms of the Post-Traumatic Confusional State *Methodist Rehabilitation Center; U.S. Department of Education* PI: Stuart A. Yablon, M.D.	**Study Purpose:** Patients with traumatic brain injury often experience a period of acute confusion that may include agitation as they recover from their injuries. While this confusion generally resolves with time, patients may pose increased risk of injury to themselves or others during this period. Their behavior may also increase stress for family members and interfere with their ability to benefit from rehabilitation therapies. A number of different medications have been used to treat confusion to decrease agitation, decrease risk of injury, and improve participation in rehabilitation therapies. To this point, there has not been a research or scientific basis for knowing which medication is the best for a specific patient. The overall goal of this study is to conduct a scientific investigation to help determine which medication works best to treat confusion. **Detailed Description:** Patients with TBI who require inpatient rehabilitation are frequently confused at the time of admission for rehabilitation. Our investigations of confusion conducted as part of the TBIMSM have clarified the nature of confusion in early recovery after TBI. Early confusion (PTCS) has been found to be a complex syndrome characterized by disorientation, cognitive impairment, restlessness, decreased level of daytime arousal, sleep disturbance, fluctuation of symptoms, and psychotic-type symptoms. PTCS complicates early management of patients with TBI, and may contribute to increased risk of injury to patients and hospital staff, increased stress among family members and staff, decreased participation in therapies, increased cost of care, and an increased likelihood of being discharged to psychiatric or long-term care settings. These facts indicate the need for effective management of PTCS. Consensus regarding optimal treatment of the cognitive and behavioral symptoms encountered among patients with PTCS does not exist currently. While many agents have been tried to address such symptoms in TBI, few have been investigated systematically. These circumstances indicate the need for appropriate clinical trials to provide guidance to clinicians for medical treatment of PTCS. In response, the NIDRR-Traumatic Brain Injury Model System of Mississippi proposed a randomized, double-blinded, placebo-controlled, parallel group trial for the pharmacological treatment of PTCS. The agent selected for this clinical trial is amantadine, an NMDA and indirect dopamine agonist. This agent will be compared to placebo on response measures of efficacy and safety. *Study hypothesis*: Amantadine will reduce the severity and number of symptoms of PTCS.

Sample Description	Study Type	Study Design	Time Frame
N = 79 Gender: Both Group: Child/Adult/Senior	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) • Primary Purpose: Treatment	April 2003–June 2008

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
An Intervention Program to Reduce to the Risk of Persistent Symptoms After Concussion *University of British Columbia* PI: Noah Silverberg, Ph.D.	**Study Purpose:** This study investigates how well a new therapy program prevents persistent symptoms (e.g., headaches, fatigue, irritability, etc.) after concussion. The program involves examining beliefs about concussion and learning healthy coping strategies, and is completed with the first three months post-injury. **Detailed Description:** Although the majority of patients with mild traumatic brain injury (MTBI) experience complete recovery within three months, a sizeable group continues to report frequent and severe symptoms such as headaches, fatigue, difficulty concentrating, forgetfulness, and irritability, in what is labeled persistent post-concussion syndrome (PCS). Persistent PCS is associated with vocational, recreational, and social disability. Early education and reassurance (treatment as usual) is effective in general, but appears insufficient for this subgroup. Recent research has identified risk factors for persistent PCS, including inaccurate illness beliefs, maladaptive coping behavior, and emotional distress. The present study will evaluate the additive efficacy of a cognitive-behavioral therapy protocol designed to modify these risk factors, over and above treatment as usual. Participants with MTBI will be recruited within 6 weeks of injury. Those identified as being at-risk for persistent PCS based on evidence-based criteria will receive treatment as usual and then be randomly assigned to receive either no further intervention or cognitive-behavioral therapy. We hypothesize that the group receiving cognitive-behavioral therapy will have fewer PCS symptoms and be less disabled at follow-up. We also hypothesize that compensation-seeking status will mitigate this improvement and that illness beliefs, coping behavior, and emotional distress will mediate this improvement. A blinded rater will conduct the baseline and outcome assessments.
Behavioral and Neuroimaging Changes After Cognitive Rehab in Traumatic Brain Injuries (TBI) and Mild Cognitive Impairment (MCI) *Department of Veterans Affairs; Emory University* PI: Benjamin M. Hampstead, Ph.D.	**Study Purpose:** Memory deficits are common after traumatic brain injuries (TBIs) and are characteristic of various forms of dementia, such as Alzheimer's disease and its common precursor mild cognitive impairment (MCI). This project intends to assess the efficacy of cognitive rehabilitation in these patient populations. We will also use neuroimaging (functional magnetic resonance imaging [fMRI]) to assess changes in brain activity that occurs following cognitive rehabilitation. **Detailed Description:** N/A

Sample Description	Study Type	Study Design	Time Frame
N = 65 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Control: Active Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Single Blind (Subject) • Primary Purpose: Prevention	June 2009–April 2011
N = 60 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Control: Active Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Single Blind (Subject) • Primary Purpose: Treatment	July 2008–June 2013

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
CDP-Choline and Working Memory After TBI: A Neuroimaging Study *University of Pittsburgh; National Institutes of Health (NIH); Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)* PI: Patricia M. Arenth, Ph.D.	**Study Purpose:** The purpose of this study is to determine whether an investigational drug, called "CDP-Choline," improves memory in people with traumatic brain injury (TBI). To do this, we are asking for people with traumatic brain injury and people without traumatic brain injury to be a part of this study. We will compare results between each group to see if this investigational drug makes a difference with memory. We will also compare brain imaging results and information collected before and after the taking of the study medication to see if there are any differences. We hypothesize that there will be differences in brain activation patterns between individuals with TBI and healthy controls, as well as differences in performance on memory testing at baseline. We further hypothesize that, after treatment with CDP-Choline, the patterns in neuroimaging findings and cognitive testing results for individuals with TBI will more closely resemble results observed for healthy individuals. We hope that what we learn from this study will be helpful in the future treatment of individuals with head injury. **Detailed Description:** Despite the prevalence of working memory deficits following traumatic brain injury (TBI), the scientific data regarding pharmacological treatment of this problem is limited. As deficits in working memory are known to have a significant impact on functional outcomes for individuals with TBI, further research in this area is essential in order for physicians to be able to treat this problem more effectively. The primary goal of the proposed project is to examine the efficacy of a particular pharmacological agent, CDP-Choline, in the treatment of working memory deficits following traumatic brain injury (TBI). The study sample will consist of 48 subjects: A group of 24 individuals who have sustained moderate to severe TBI, and a group of 24 healthy controls. Each group will be divided into a placebo and treatment group. The project will utilize functional Magnetic Resonance Imaging (fMRI) to investigate the cerebral neurophysiological effects of treatment with CDP-Choline. A working memory task (N-Back) will be employed during fMRI sessions. In addition, the effects of treatment with CDP-Choline on neuropsychological testing performance will also be evaluated, and the correlations between behavioral performance and neuroimaging results will be observed. We will achieve these goals by comparing baseline neuropsychological testing results as well as fMRI results, with a second set of testing and neuroimaging results obtained following 1 month of pharmacological treatment with CDP Choline or placebo. Based on our preliminary studies and the available literature, we expect to see the following: Baseline fMRI results are expected to show that individuals with TBI display altered patterns of cerebral activation during a working memory task, as compared to healthy controls. With CDP-Choline treatment, we expect TBI subjects to display fMRI laterality and dispersion patterns that more closely resemble patterns of healthy controls. In addition, we anticipate improvements in behavioral performance on both the specific working memory task (N-Back), and on traditional neuropsychological tests to be associated with CDP-Choline treatment, with greater magnitude of change on testing results for the TBI group as compared to any changes noted for the control or placebo groups. Finally, we anticipate that specific significant correlations will be observed between neuropsychological testing results and neuroimaging findings, and that the strength of these relationships will be greater for the TBI treatment group, as compared to the placebo or healthy control groups. By conducting the proposed study in this manner, we hope to provide scientific data that will allow for improved treatment, and ultimately improved functional outcomes for individuals who have sustained TBI.

Sample Description	Study Type	Study Design	Time Frame
N = 48 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) • Primary Purpose: Treatment	March 2009–August 2012

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Cognitive Rehabilitation of Blast Traumatic Brain Injury (TBI) *Department of Veterans Affairs* PI: Yelena Bogdanova, Ph.D.	**Study Purpose:** The purpose of this study is to investigate the efficacy of a structured rehabilitation program on cognitive function and quality of life in individuals with blast-induced traumatic brain injury (bTBI). **Detailed Description:** The most common impairments following blast-induced traumatic brain injury (bTBI) are cognitive deficits in the domain of executive functioning, learning and memory, and functional and psychosocial disabilities that are closely related to these cognitive deficits. There are no treatment protocols available to address the multiple cognitive impairments in bTBI, but cognitive rehabilitation has proven efficacious in the treatment of non-blast TBI. The cognitive training modules we plan to evaluate have improved organization and memory function in patients with non-blast TBI, but it is unknown whether their efficacy exceeds that of programs that focus only on education and support. This study is a between group comparison of a cognitive rehabilitation treatment designed specifically to address the most common cognitive complaints in executive and memory function, and an active control group receiving educational intervention geared at personal management of TBI-related symptoms.
Cognitive Therapy to Improve Word Finding *National Institute on Deafness and Other Communication Disorders (NIDCD)* PI: Rhonda B. Friedman, Ph.D.	**Study Purpose:** Adults who sustain brain damage due to stroke, traumatic injury or surgery may develop difficulty finding words. This study compares the effectiveness of two behavior-based programs to improve picture naming ability in these individuals. **Detailed Description:** Difficulty finding words is common in patients with aphasia subsequent to left hemisphere stroke. This study will compare two cognitive therapies for the treatment of acquired word finding difficulties. The therapies use different types of cues. All participants will receive both therapies. Participants in this study will undergo a comprehensive and detailed assessment of language and other cognitive skills. The two treatments will be compared for their efficacy.
Early Rehabilitation of Patients with Posttraumatic Amnesia *University of Aarhus* PI: Jens Christian Sørensen, M.D., Ph.D.	**Study Purpose:** The purpose of this study is to investigate if a systematic intervention with early identifying of patients with posttraumatic amnesia using a reality orientation therapy can reduce the period with posttraumatic amnesia in order to get a better outcome for patients with traumatic brain injury. **Detailed Description:** 1. A systematic review with the latest investigation and treatment of patients with posttraumatic amnesia, 2. Investigate the effect of a systematic nursing program on the length of posttraumatic amnesia, 3. Investigate the effect of a systematic nursing program after 12 month, 4. Describe perspectives for the future within the early rehabilitation of patients with posttraumatic amnesia.

Sample Description	Study Type	Study Design	Time Frame
N = 120 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Open Label • Primary Purpose: Treatment	February 2011–September 2014
N = 40 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Non-Randomized • Control: Uncontrolled • Endpoint Classification: Efficacy Study • Intervention Model: Single Group Assignment • Masking: Open Label • Primary Purpose: Treatment	July 2004–June 2009
N = 62 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Non-Randomized • Control: Active Control • Endpoint Classification: Efficacy Study • Intervention Model: Single Group Assignment • Masking: Open Label • Primary Purpose: Supportive Care	September 2007–September 2010

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Effect of Passive Gait Training on the Cortical Activity in Patients with Severe Traumatic Brain Injury *University of Aarhus; Aarhus County, Denmark* PI: Natallia Lapitskaya, M.D., Ph.D. (c)	**Study Purpose:** The aim of this study is to determine whether passive gait training increases arousal, demonstrated as changes in EEG (electroencephalogram) activity. Hypotheses: (1) Passive gait training increases EEG-frequency in patients with impaired consciousness due to severe traumatic brain injury. (2) Passive gait training increases conductivity speed of the cognitive P300-component of ERP in patients with impaired consciousness due to severe traumatic brain injury. **Detailed Description:** Severe traumatic brain injury, especially after a high energy trauma, is characterized with focal lesions and diffuse axonal injury, which leads to the dysfunction in the cortico-spinal, cortico-cortical connections and reticular activation system. Formatio reticularis plays an important role in arousal. Tactile and proprioceptive stimulation with a view to improving level of consciousness in coma patients is popular in the western world despite insufficient evidence of its effectiveness. Affolter-Bobath-Coombes-concept is the most commonly used tool in the rehabilitation of brain damaged patients. This concept is based on the theory that tactile, proprioceptive and oral stimulation develops new connections in the brain and thereby stimulates consciousness and behavior. Elliot et al shows improvement in level of consciousness due to postural changes from a lying position to a standing posture in 8 of 12 patients using Wessex Head Injury Matrix. Passive movements result in proprioceptive stimulation; the effect of which is close to that achieved by physiological voluntary activity. PET and fMRI studies show that passive movements activate several areas in the motor cortex. In order to increase afferent cortical input, passive gait training in the body weight support robotic gait orthosis could be used in patients with impaired consciousness, inability to cooperate and poor balance. This device gives the possibility to establish therapeutically correct upright body position and passive legs movement simultaneously. To our knowledge there are no studies, which illustrate the effects of passive gait training on cortical activity in patients with impaired consciousness due to severe traumatic brain injury. Our hypothesis is that passive gait training of this group of patients increases arousal, which can be shown in an increased EEG (electroencephalogram)-frequency and increased conductivity speed of the cognitive P300-component of ERP (Event Related Potentials). Comparison(s): EEG- and ERP-activity after a single training session in robotic gait orthosis in patients with severe traumatic brain injury, compared to EEG- and ERP-activity after a single training session in robotic gait orthosis in healthy persons.

Sample Description	Study Type	Study Design	Time Frame
N = 26 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Non-Randomized • Control: Active Control • Endpoint Classification: Efficacy Study • Intervention Model: Single Group Assignment • Masking: Open Label • Primary Purpose: Treatment	August 2006–August 2008

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Efficacy of Pharmacological Treatment of Working Memory Impairment After Traumatic Brain Injury: Evaluation with fMRI *Kessler Foundation; University of Medicine and Dentistry New Jersey; Cephalon* PI: Elie P. Elovic, M.D.	**Study Purpose:** This study is designed to examine the effects of a wake-promoting agent (Modafinil) on working memory (WM) in persons with moderate to severe TBI utilizing a double blinded placebo controlled methodology. Our approach is to evaluate participants with BOLD fMRI and a limited neuropsychological battery to examine WM performance before and after pharmacological intervention. **Detailed Description:** Work from our institution has shown that moderate and severe TBI subjects demonstrate an altered cerebral representation when they attempt to process a verbal WM task. Specifically, our data show a post-TBI pattern of activation that is dispersed and more lateralized to the right hemisphere, as compared to healthy controls. Taken together, we interpret these findings to mean that it is requires more cerebral resources for TBI subjects to process tasks that were previously more automatic. In other words, their processing is less efficient. This is consistent with TBI patients' self-reports of needing to expend greater cognitive effort to perform such tasks, both in the lab and in everyday life. Our preliminary data was the first step in understanding the cerebral substrate of these difficulties. However, simply indicating that individuals with TBI have a WM problem is not enough. The development of targeted interventions to ameliorate these deficits is the next step in the treatment process. The present proposal has important implications for TBI rehabilitation. One of the major goals of cognitive remediation is to help TBI patients learn new information more accurately and efficiently, and to improve their performance in activities of everyday life. Because WM impairments are so prevalent in TBI, the present study can help to shed light on potential treatment alternatives for these potentially devastating problems. In spite of the prevalence and popularity of cognitive remediation strategies and procedures, there remains little empirical support for their efficacy, and virtually no understanding of the underlying neurocognitive processes that facilitate intervention. The ability to develop a potentially efficacious treatment modality, which has a solid foundation, would be immensely beneficial.

Sample Description	Study Type	Study Design	Time Frame
N = 20 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double-Blind • Primary Purpose: Treatment	August 2003–December 2008

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Evaluation of Outcome Measures for Patients Diagnosed with Traumatic Brain Injury *National Institutes of Health Clinical Center (CC); Department of Defense; Center for Neuroscience and Regenerative Medicine* PI: Leighton Chan, M.D., M.P.H.	**Study Purpose:** *Background*: Traumatic brain injury (TBI) is a significant injury in the Armed Forces, but it is also common in the general population. This condition poses significant challenges for both diagnosis and therapy. However, the biological and neurological reasons for TBI remain poorly understood and are in need of more in-depth study. The National Institutes of Health is collaborating with several military medical centers and research units in a multi-year study of TBI in civilian and military patients. In anticipation of these research projects, the Clinical Center's Rehabilitation Medicine Department needs to become familiar with the instruments they will likely need to evaluate this group of subjects. *Objectives*: To evaluate potential test instruments in patients with TBI. To evaluate patient tolerance of an extensive battery of assessments and the time required to complete the assessments. To improve staff competencies on new or novel assessments of the TBI patient population. *Eligibility*: Individuals 18 years of age and older who have been diagnosed with a traumatic brain injury in the past 5 years. Healthy volunteers 18 years of age and older who have had no instances of significant head trauma. *Design*: This study requires approximately 3 days of outpatient or inpatient evaluation. Subjects will undergo cognitive and neuropsychological tests, physical assessments, speech and language evaluation, and balance testing. Tests will be given orally, in writing, and on computers. The testing will be done in blocks of 2 to 3 hours, with rest periods as needed. Subjects may undergo any or all of the following assessments and screening tools, as determined by the researchers: cognitive, quality of life, and functional assessments; speech, language, and swallowing assessments; and physical functional performance and environment assessments (including balance testing). Subjects will remain under the care of their own health care providers while participating in this study. **Detailed Description:** The objective of this study is to evaluate potential test instruments in the traumatic brain injury (TBI) patient population. We will assess outcome measures that test neuropsychological, cognitive, communicative, and physical functional outcomes on up to 60 patients with TBI and 20 healthy volunteers. Our aims are to evaluate the appropriateness of specific tests for TBI as well as to test patient tolerance of an extensive battery of assessments and the time required to complete the assessments. We will also focus on improving staff competencies as they relate to new or novel assessments on the TBI patient population.

Sample Description	Study Type	Study Design	Time Frame
N = 80 Gender: Both Group: Adult/Senior	Observational	Time Perspective: Prospective	October 2009–Unknown

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Evaluation, Pathogenesis, and Outcome of Subjects with or Suspected Traumatic Brain Injury *National Institute of Neurological Disorders and Stroke (NINDS); Center for Neuroscience and Rehabilitation Medicine (CNRM); Department of Defense; Henry Jackson Foundation* PI: Steven Warach, Ph.D.	**Study Purpose:** *Background*: Traumatic brain injury may have a range of effects, from severe and permanent disability to more subtle functional C609 that often go undetected during initial treatment. C598To improve treatments and therapies and to provide a uniform quality of care, researchers are interested in developing more standardized criteria for diagnosing and classifying different types of traumatic brain injury. By identifying imaging and other indicators immediately after the injury and during the initial treatment phrase, researchers hope to better understand the nature and effects of acute traumatic brain injury. *Objectives*: To study the MRI results of individuals who have recently had head injury and suspected traumatic brain injury. To study the natural evolution of traumatic brain injury for up to 3 months after head injury. *Eligibility*: Individuals at least 18 years of age who have been admitted to a hospital with a diagnosed or suspected traumatic brain injury within the past 48 hours. *Design*: Participants will have two 3-hour study visits: an initial visit (within 48 hours of head injury) and a follow-up visit 4 days later. Participants may be asked to have an optional 90-day follow-up. Each visit will involve blood samples, an MRI scan (approximately 30 minutes), and a series of tests to evaluate brain function. At the optional follow-up visit, participants will have blood samples, an MRI scan, and a general traumatic brain injury assessment. This study does not provide treatment and does not replace any current therapies. However, participants who are eligible for other National Institutes of Health studies may be referred to these studies by researchers. **Detailed Description:** *Objective*: To generate natural history data for cohort-based comparisons to serve as the basis for future hypothesis-driven protocols and to contribute to the clinical and physiological understanding of traumatic brain injury (TBI) through the description of manifestations of the injury and the relationship among radiological, hematological, clinical variables and standard functional/cognitive outcome measures. *Study Population*: 300 male and female adult subjects with history of recent head injury with or suspected non-penetrating acute TBI, will be enrolled. Subjects having varying degrees of TBI severity will be recruited from the collaborative programs between NIH and non-NIH hospitals. We anticipate approximately 80% of subjects will be classified as mild TBI, concussion, or no injury, with approximately two thirds of those subjects enrolled being discharged directly from the emergency department. *Design*: This is a prospective cohort study of subjects with known and suspected non-penetrating acute traumatic brain injury. Subjects presenting to the emergency department or trauma service at participating hospitals with a history of recent head injury will be studied during the course of their hospital stay and after discharge using radiological, hematological, clinical and functional/cognitive outcome measures. Subjects will be stratified according to findings into cohorts for comparison. The design is intentionally broad in scope to allow acquisition of initial data for the development of future hypothesis-driven protocols. Research performed under this protocol will not interfere with standard of care and subjects will not be treated with experimental therapies as part of the research study. Data collected under this research study may be shared without personal identifiers with other researchers if subjects approve this option on the informed consent. *Outcome Measures*: A variety of outcome measures will be used including diagnosis, evidence of injury on magnetic resonance imaging (MRI), functional and cognitive impairment, and quality of life (QOL) assessments. The initial research questions will focus on a positive diagnosis of brain injury and monitoring the natural history. Statistical analysis plans will be developed as specific research questions and hypotheses are generated.

Sample Description	Study Type	Study Design	Time Frame
N = 300 Gender: Both Group: Adult/Senior	Observational	Time Perspective: Prospective	May 2010–Unknown

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Feasibility Study of Duloxetine in the Treatment of Depression in Patients with Traumatic Brain Injury (TBI) *Rehabilitation Hospital of Indiana; Eli Lilly and Company* PI: Lance Trexler, Ph.D.	**Study Purpose:** The primary objective of the study is to compare the efficacy of duloxetine 60 mg PO daily with placebo in the prevention of depression associated with mild/moderate traumatic brain injury (TBI) and to enhance cognitive function. Research exploring the use of selective serotonin reuptake inhibitors (SSRIs) in the treatment of post-traumatic depression generally validates this approach (Horsfield et al., 2002). However, the literature suggests that serotonin/norepinephrine reuptake inhibitors (SNRIs) such as duloxetine may be more effective in the treatment of depression. **Detailed Description:** N/A
Improving Executive Functioning After Traumatic Brain Injury (TBI): A Trial of the "Short Term Executive Plus" Program *Mount Sinai School of Medicine; Centers for Disease Control and Prevention* PI: Wayne Gordon, Ph.D.	**Study Purpose:** The purpose of this study is to determine the efficacy of an intensive short term cognitive rehabilitation program aimed towards improving executive functioning in individuals with traumatic brain injury (TBI). **Detailed Description:** Executive dysfunction following brain injury (BI) is commonly observed and has been well documented in the literature (Mateer, 1999; Prigatano, 1999; Levine et al., 2000; Shallice and Burgess, 1991; Cicerone and Giacino, 1992; Goldman-Rakic, 1993; Lezak, 1995; McDonald, 2002; Riegal and Gauggel, 2002; Stuss and Levine, 2003). Level of functioning such as vocational success, community reintegration, and social autonomy are associated with executive functioning abilities following BI (Sohlberg, Mateer, and Stuss, 1993; Mazaux et al. 1997; McDonald, 2002; Stuss and Levine, 2002). However, studies describing the rehabilitation of executive dysfunction have been limited to mostly single case or small group designs (Cicerone et al., 2000). However, there have been three small randomized clinical trials that have had promising results suggesting the need for more study needed in this area. When considering all of the studies it is evident that emphasis has been placed on three areas of intervention: attention remediation, emotional regulation and problem-solving. Consequently, given the pervasive disability found in individuals with BI that is secondary to executive function disorders and the promising, but limited, success of problem-solving-based interventions for executive functions, a randomized controlled trial (RCT) of the efficacy of a short-term, intensive executive function training program (Short-Term Executive Plus) is proposed. The Short-Term Executive Plus (STEP) program will combine treatments and treatment approaches that have proven to be effective in previous studies and will be compared to "wait-list" control group. This design was chosen because no appropriate control intervention exists. In other words there is no "standard" rehabilitation treatment available to these individuals that could serve as an appropriate "control" condition/treatment. As discussed earlier, cognitive remediation is typically delivered in extended full-time day treatment programs or weekly/bi-weekly individual sessions. Using more traditional extended treatments as a control condition would be inappropriate, as persons who can participate in extended, full-time are not the target of the proposed intervention. It is hypothesized that the STEP program will result in significant improvements in executive functioning (and related areas of attention, memory, community participation, and life satisfaction).

Sample Description	Study Type	Study Design	Time Frame
N = 44 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) • Primary Purpose: Treatment	September 1996–September 2012
N = 200 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Crossover • Assignment • Masking: Open Label • Primary Purpose: Treatment	January 2008–August 2012

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Improving Executive Functions After Traumatic Brain Injury (TBI): A Clinical Trial of the "Executive Plus" Program *Mount Sinai School of Medicine; U.S. Department of Education* PI: Wayne A. Gordon, Ph.D.	**Study Purpose:** This is a randomized clinical trial which compares a standard day treatment program for individuals with TBI with the "Executive Plus" program; the latter emphasizes training of attention, emotional self-regulation and problem solving. The goal of the Executive Plus program is to maximize executive functioning, as well as the long-term outcomes of community participation and satisfaction with daily life. **Detailed Description:** This is a randomized clinical trial comparing two approaches to post-TBI comprehensive day treatment. Executive Plus offers systematic treatment of post-TBI executive function deficits, through a focus on problem solving and emotional self-regulation, as well as systematic treatment of post-TBI attention deficits. It relies on modular, contextual, and embedded approaches to treatment. It will be compared to Mount Sinai's currently operating day treatment program. The 26-week programs will run concurrently and potential participants will be randomly assigned to Executive Plus or the standard program, using rolling admissions. Program staffs will be separate. Outcomes will be assessed using measures that focus on functioning within cognitive domains, across domains and in everyday life, and that assess long-term outcomes. Detailed manuals will be developed to guide the implementation of each program's operation.
Improving Work Outcomes for Veterans with Traumatic Brain Injury *Department of Defense* PI: Elizabeth W. Twamley, Ph.D.	**Study Purpose:** The 12-month study will investigate a cognitive training augmentation of supported employment to improve cognitive performance and work outcomes, which are expected to result in improved quality of life and community integration for veterans with mild to moderate traumatic brain injuries. The primary hypothesis is that compared to veterans who receive enhanced supported employment, those who receive supported employment plus cognitive training will work more weeks during the 12 months. **Detailed Description:** N/A
Life Improvement Following Traumatic Brain Injury *University of Washington; National Institutes of Health (NIH); U.S. Department of Education* PIs: Jesse R. Fann, M.D., M.P.H., Charles H. Bombardier, Ph.D.	**Study Purpose:** Major Depressive Disorder (MDD) is the most prevalent psychiatric disorder in persons with traumatic brain injury (TBI) and is most common during the first several years after injury. MDD following TBI is associated with poor behavioral, health, and functional outcomes. While neurological factors contribute somewhat to the development of MDD in this population, there is evidence that numerous psychological, social and vocational factors also contribute. The investigators are conducting a three arm trial of Cognitive Behavioral Therapy (CBT) to treat Major Depression Disorder (MDD) that emerges within the first 10 years after complicated mild to severe traumatic brain injury (TBI). The overall objective of the study is to develop a 12-session telephone-based and in-person CBT program for people with TBI (CBT-TBI), and to evaluate its feasibility, acceptability, and effectiveness. **Detailed Description:** N/A

Sample Description	Study Type	Study Design	Time Frame
N = 77 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Control: Active Control • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Single Blind (Outcomes Assessor) • Primary Purpose: Treatment	October 2005–November 2010
N = 64 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Control: Active Control • Intervention Model: Parallel Assignment • Masking: Single Blind (Outcomes Assessor) • Primary Purpose: Treatment	September 2008–August 2011
N = 90 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Endpoint Classification: Efficacy Study • Intervention Model: Parallel Assignment • Masking: Single Blind (Outcomes Assessor) • Primary Purpose: Treatment	September 2007–August 2012

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Methylphenidate (Ritalin) and Memory/ Attention in Traumatic Brain Injury (TBI) *Dartmouth-Hitchcock Medical Center; National Institutes of Health (NIH)* PI: Thomas W. McAllister, M.D.	**Study Purpose:** Traumatic brain injury (TBI) is a significant public health problem, with 1.5–2.0 million Americans injured each year. Cognitive deficits, particularly in the domains of memory and attention are frequently the source of lingering disability after TBI and a source of enormous distress to the injured individuals and their family/caregivers. To date, interventions to ameliorate chronic cognitive deficits have been directed at either pharmacological interventions or cognitive rehabilitation. We propose to (1) To compare the efficacy of three interventions: memory and attention training (MAAT), methylphenidate, and memory/ attention training in combination with methylphenidate and (2) use functional MRI (fMRI) to characterize changes in activation of the neural circuitry of memory and attention due to MAAT alone, methylphenidate alone, and MAAT in combination with methylphenidate. This is a two by two design with medication (methylphenidate/placebo) and cognitive therapy (Memory and Attention Training [MAAT] or an attention control intervention) as possible interventions. Using a randomized, placebo-controlled, double-blind design, 200 individuals with persistent cognitive deficits 6–12 months after MTBI will be randomized to receive a six week trial of either (1) MAAT and placebo, (2) MAAT and methylphenidate (0.3 mg/kg BID), (3) attention control intervention and methylphenidate (0.3 mg/kg BID), or (4) attention control intervention and placebo. Symptom distress, attention and memory performance, and activation patterns of the neural circuitry of attention and memory while undergoing fMRI will be characterized at baseline, and after the four treatment conditions. This study will provide important information on three interventions for the most disabling sequelae of an enormous public health problem. Further, it will help to clarify underlying neural mechanisms and suggest additional treatment possibilities. **Detailed Description:** *What is known*: There are two interventions of promising efficacy in ameliorating deficits in attention and memory after MTBI: (i) memory and attention training/rehabilitation, and (ii) catecholaminergic augmentation (particularly with methylphenidate, which augments both dopaminergic and adrenergic systems). fMRI and other functional imaging strategies are providing valuable insights into the underlying neural mechanisms of the cognitive enhancing effects of methylphenidate in some neuropsychiatric populations (individuals with ADHD), and the effects of cognitive rehabilitation efforts in some domains (e.g., speech and language in individuals after stroke). *What is not known*: To date there are no studies that apply a psychopharmacological strategy of augmenting neurotransmitter systems known to modulate memory/attention (dopaminergic and adrenergic systems) in combination with a cognitive rehabilitation intervention known to improve memory/ attention (memory/attention training) in individuals with MTBI. We are aware of no published studies that use fMRI to assess the neural mechanisms of memory/attention improvement from the use of catecholaminergic agents or memory/attention training in individuals with MTBI. It is important to determine the efficacy of combined memory/attention training and methylphenidate. It is equally important to begin to understand the neural mechanisms underlying effective treatment as it may help to inform the development of the next generation of interventions and perhaps lead to individually tailored treatment interventions. This proposal will start to address these gaps in our knowledge.

Sample Description	Study Type	Study Design	Time Frame
N = 160 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Efficacy Study • Intervention Model: Factorial Assignment • Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) • Primary Purpose: Treatment	February 2007–December 2012

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Mindfulness-Based Cognitive Therapy Intervention to Treat Depression in Individuals with a Traumatic Brain Injury *Lakehead University; Ontario Neurotrauma Foundation* PI: Michel Bédard, Ph.D.	**Study Purpose:** The purpose of this study is to determine whether mindfulness-based cognitive therapy is effective in reducing depression symptoms in individuals who have experienced a traumatic brain injury. The investigators hypothesize that participants who are given the 10-week intervention will have fewer depression symptoms than the participants in the control group, and this improvement will be maintained at the 3-month follow-up assessment. **Detailed Description:** Major depression is a significant chronic problem for people with traumatic brain injury (TBI), and its treatment is difficult. A promising approach to treat depression is mindfulness-based cognitive therapy (MBCT), a relatively new therapeutic approach rooted in mindfulness-based stress-reduction (MBSR) and cognitive behavioral therapy (CBT). This multi-site, randomized, controlled trial of a MBCT intervention will examine the value of this intervention in improving quality of life and decreasing depression in people with TBI. MBCT may represent a time-limited, cost-effective group intervention through which clinicians would have an opportunity to address some of the most debilitating aspects of TBI.
PC-Based Cognitive Rehabilitation for Traumatic Brain Injury (TBI) *Department of Veterans Affairs* PI: David L. Woods, Ph.D.	**Study Purpose:** The investigators will evaluate whether it is possible to improve memory and attention in patients who have suffered traumatic brain injury through the use of at-home computer training. Patients will be issued a computer and will train for three months on tasks that become more challenging as the subjects performance improves. The investigators will evaluate whether the training strengthened mental abilities in general, but evaluating mental abilities in the laboratory before and after testing. **Detailed Description:** Here we propose two randomized clinical trials to determine if at-home PC-based adaptive training can improve cognitive function in chronic TBI patients. Both trials will use protocols designed to drive beneficial neuroplastic changes using paradigms similar to those that have shown promising results in smaller scale studies. The first experiment will investigate the effects of training of short-term verbal and spatial memory. Thirty-six patients with chronic mild, moderate and severe TBI will be evaluated with an extensive battery of neuropsychological tests (NPTs) and subjective rating scale measures at study entry. NPT and rating scale data will be compared to those obtained from 100 matched control subjects to characterize the cognitive deficits following mild, moderate and severe TBI. Patients will then be randomly assigned to immediate training (IT) or delayed training (DT) groups in a longitudinal crossover design. IT patients will begin training for 20 min/day on each of three different memory tasks for a period of three months. Training data will be automatically uploaded to monitor daily compliance and learning rate. NPT and rating scale assessments will be obtained midway through the study. Comparisons of changes in trained (IT) and untrained (DT) groups will be used to evaluate training efficacy. Then, during the second phase of the study, the DT group will undergo identical training. Repeat testing at the end of the study will quantify the effects of training on the DT group, and evaluate retention of training benefit in the IT group. The second experiment will evaluate the effects of training on attention and executive function using a similar randomized trial with a separate group of 36 chronic TBI patents. A comparison of the magnitude of training-related improvements in the two experiments will be used to evaluate specific and non-specific factors that contribute to training benefit and identify the patient characteristics that are most critical for successful cognitive rehabilitation.

Sample Description	Study Type	Study Design	Time Frame
N = 120 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Endpoint Classification: Efficacy Study • Intervention Model: Crossover Assignment • Masking: Open Label • Primary Purpose: Treatment	March 2009–April 2010
N = 100 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Endpoint Classification: Efficacy Study • Intervention Model: Crossover Assignment • Masking: Open Label • Primary Purpose: Treatment	July 2009–December 2012

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Recombinant Human Growth Hormone During Rehabilitation From Traumatic Brain Injury *University of Texas Southwestern Medical Center; Baylor University* PI: Ramon R. Diaz-Arrastia, M.D., Ph.D.	**Study Purpose:** Growth Hormone (GH) deficiency, defined by insufficient GH response to a variety of stimulating compounds, is found in 20-35% of adults who suffer traumatic brain injuries (TBIs) requiring inpatient rehabilitation1. However, there is no accepted gold standard for diagnosing GH deficiency in this population. Further, the major effector molecule of the somatotropic axis, Insulin-Like Growth Factor-1 (IGF-1) has recently been recognized as an important neurotrophic agent. Since most repair and regeneration after TBI occurs within the first few months after injury, absolute or relative deficiencies of GH and IGF-1 in the subacute period after TBI are potentially important factors why some patients fail to make a good functional recovery. The proposed study is a randomized, double-blind, placebo-controlled trial of recombinant human Growth Hormone (rhGH), starting at 1 month post TBI, continuing for 6 months. This study has one primary hypothesis, that treatment with rhGH in the subacute period after TBI results in improved functional outcome 6 months after injury. As secondary hypotheses, we will investigate what is the optimal method to diagnose GH deficiency in TBI survivors and study the relationship between GH deficiency and insufficiency and functional recovery. **Detailed Description:** N/A
Rehabilitation of Traumatic Brain Injury in Active Duty Military Personnel and Veterans *The Defense and Veterans Brain Injury Center; James A. Haley Veterans Administration Hospital; Hunter Holmes McGuire Veteran Affairs Medical Center; Minneapolis Veterans Affairs Medical Center; VA Palo Alto Health Care System; Department of Veterans Affairs* PIs: Deborah L. Warden, M.D., Elaine Date, M.D., Steven Scott, D.O., Barbara Sigford, M.D., Ph.D., William Walker, M.D.	**Study Purpose:** Context: Traumatic brain injury (TBI) is a common condition associated with significant long-term cognitive, behavioral, and functional morbidities. There are minimal controlled efficacy data of various acute rehabilitation intervention approaches. Objective: To determine the relative efficacy of two different acute TBI rehabilitation approaches—cognitive-didactic versus functional-experiential. Secondarily to determine relative efficacy for different patient subpopulations based on baseline cognitive functioning. **Detailed Description:** A randomly assigned, intent-to-treat model of two different comprehensive treatment programs conducted between July 19 1996 and May 16, 2003 in 360 adult participants with moderate to severe TBI treated in four participating Veterans Administration TBI rehabilitation centers. All patients admitted to the Commission for Accreditation of Rehabilitation Facilities (CARF) accredited acute inpatient rehabilitation brain injury programs at four participating Veterans Administration Medical Centers (VAMCs) (Minneapolis, Palo Alto, Richmond, and Tampa) during the study enrollment period were screened for eligibility. The design was a randomized-controlled trial with two treatment arms (cognitive-didactic and functional-experiential), both embedded within an interdisciplinary TBI rehabilitation program. All treatment was hospital based. The interactive nature of the experimental conditions precluded subject blinding. Since each participating site serves a wide geographic area, the protocol permitted post-hospital outcome assessments by structured telephonic interview, to minimize drop out. Participants completed baseline assessment then received by random assignment one of the two standardized protocol rehabilitation programs (summarized below and described in detail elsewhere). Participants received 1.5 to 2.5 hours daily of protocol-specific therapy plus another 2 to 2.5 hours daily of occupational and physical therapy. Independent teams of therapists functioned at each site to deliver the separate treatments and by necessity were not blinded to treatment. Protocol monitoring site visits, biweekly conference calls, and biannual investigator meetings were conducted to ensure uniformity of protocol treatment over time.

Sample Description	Study Type	Study Design	Time Frame
N = 164 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Safety/Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double • Blind (Subject, Caregiver, Investigator, Outcomes Assessor) • Primary Purpose: Treatment	September 2008–September 2012
N = 360 Gender: Both Group: Adult/Senior	Interventional	• Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: Single Blind (Outcomes Assessor) • Primary Purpose: Supportive Care	July 1996–May 2003

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Resuscitative Endocrinology: Single-Dose Clinical Uses for Estrogen-Traumatic Brain Injury *University of Texas Southwestern Medical Center* PI: Jane G. Wigginton, M.D.	**Study Purpose:** Each year in the United States alone, a third of a million persons are hospitalized for traumatic brain injury (TBI), of whom approximately one-quarter die. Most are less than 30 years of age. Not only are the health care costs staggering for both initial care and rehabilitation, but the societal loss in terms of economic impact reaches into the billions of dollars annually in the United States alone. Despite advances in neurosurgical interventions and intensive care management, many survivors do not fully recover. A significant cause of this mortality and morbidity is thought due to potentially preventable secondary injury, namely oxidant injury, inflammation, and apoptosis in the penumbra (the area of brain surrounding the primary lesion, which is at-risk, but potentially salvageable), beginning in the first few hours after the severe traumatic event. Despite the current bleak outlook for many of these patients, a series of animal investigations have uncovered a promising solution to the problem of the secondary injury seen in severe TBI and other similar processes, namely the early administration of estrogen, a strong anti-oxidant, anti-inflammatory and anti-apoptotic compound. Based on these encouraging results from animal studies, the investigators hypothesize that early administration of IV Premarin® in patients with severe TBI will safely reduce secondary brain injury, improve neurological outcomes, and improve survival. **Detailed Description:** N/A

Sample Description	Study Type	Study Design	Time Frame
N = 50 Gender: Male Group: Adult	Interventional	• Allocation: Randomized • Control: Placebo Control • Endpoint Classification: Safety/Efficacy Study • Intervention Model: Parallel Assignment • Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor) • Primary Purpose: Treatment	July 2009–Unknown

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
Telerehabilitation for Operation Iraqi Freedom/ Operation Enduring Freedom (OIF/OEF) Returnees with Combat-Related Telerehab for Traumatic Brain Injury *Department of Veterans Affairs* PI: Kris Siddharthan, Ph.D.	**Study Purpose:** The scientific objective of this program is to meet the rehabilitation needs of combat wounded veterans with mild to moderate Traumatic Brain Injury (TBI) via telerehabilitation and determine the effect of this modality of care on patients' physical health and outcomes including function and community participation. We will also evaluate the benefits and limitations of rehabilitation using telehealth from the veteran and caregiver perspectives and evaluate the impact of rehabilitation via telehealth on Veterans Administration (VA) healthcare facility use. **Detailed Description:** Rational: TBI can cause life-long impairments in physical, cognitive, behavioral and social function that are usually more disabling than the residual physical deficits. Recovery can continue many years after initial trauma. Little is known about optimal methodologies to treat the vast and complicated secondary manifestations of combat-related TBI. Applicability: The goal of this rehabilitation program is eventually to optimally define telerehabilitation services for all veterans with polytrauma, including accurate and efficient screening instruments, educational material for patients and families, family support, and family counseling to enhance care coordination and to maximize functional outcomes and quality of life. Patient population: The program will help wounded veterans with a diagnosis of TBI from combat operations in Iraq and Afghanistan. Many veterans reside in rural and underserved areas. Although access to health care for rural patients remains a critical challenge, telerehabilitation may represent a viable means for the delivery of therapeutic services to such patients, particularly those served by the VA. The program has implications for civilian populations as well including those injured in automobile or industrial accidents and similar in illness to the cohort of veterans we intend to follow. Clinical applications, benefits and risks: The goals of the rehabilitation project will be to enhance the wounded veteran's capacity to process and interpret information and to improve his ability to function in all aspects of family and community life. It will involve a combination of restorative training which focuses on improving a specific cognitive function and compensatory training which educates veterans on adapting to the presence of a cognitive deficit that may or may not be curable using singular one to one interventions as well as integrated interdisciplinary approaches to target multiple conditions. We see no risks involved in this clinical intervention. Projected time to achieve a consumer-related outcome: The results of the telerehabilitation project should immediately be available for dissemination throughout the VA. The VA has already committed itself to a nationwide rollout of similar telerehabilitation projects for wounded veterans. Hence, the findings should have immediate application in VA care for returnees from combat.

Sample Description	Study Type	Study Design	Time Frame
N = 85 Gender: Both Group: Adult	Interventional	• Control: Uncontrolled • Endpoint Classification: Efficacy Study • Intervention Model: Single Group Assignment • Masking: Open Label • Primary Purpose: Treatment	July 2008–May 2012

Study Title, Sponsor, and Principle Investigator	Study Purpose and Detailed Description
The Study of Cognitive Rehabilitation Effectiveness for Mild Traumatic Brain Injury (SCORE) *Brooke Army Medical Center; The Defense and Veterans Brain Injury Center; Henry M. Jackson Foundation for the Advancement of Military Medicine* PI: Douglas B. Cooper, Ph.D.	**Study Purpose:** The objective of this trial is to evaluate the effectiveness of cognitive rehabilitation in OIF/OEF service members with a history of mild traumatic brain injury and persistent (3–24 months post-injury) cognitive complaints. This is a prospective, randomized, control treatment trial of cognitive rehabilitation for OEF/OIF Service Members with a history of mild traumatic brain injury and persistent (3–24 months post-injury) cognitive complaints. Subjects will be recruited from consecutive patient referrals to the TBI Service at SAMMC-North. Patients who meet eligibility criteria and consent to participate in the treatment trial will be randomly assigned to one of four, 6-week treatment arms of the study. Subjects will be evaluated prior to the start of treatment and 3, 6, 12, and 18 weeks following the initiation of the study. The total number of patients to be studied is 160 (maximum), which is approximately 20 patients per month. **Detailed Description:** This is a prospective, randomized, control treatment trial of cognitive rehabilitation for OEF/OIF Service Members with a history of mild traumatic brain injury (mTBI) and persistent (3–24 months post-injury) cognitive complaints. Subjects will be recruited from consecutive patient referrals to the TBI Service at SAMMC-North. Patients who meet eligibility criteria and consent to participate in the treatment trial will be randomly assigned to one of four, 6-week treatment arms of the study: 1. Psychoeducational control group; 2. Non-therapist directed, computerized cognitive rehabilitation; 3. Therapist-directed individualized cognitive rehabilitation; and 4. Integrated interdisciplinary cognitive rehabilitation combined with cognitive-behavioral psychotherapy. (Components of the treatment arms are described in detail in section 4.6; Research Design and Methods.) All subjects enrolled in the study will receive the standard of care in management of chronic post-concussive symptoms, consistent with the VA/DoD Clinical Practice Guidelines for the Management of Concussion/mild TBI (Barth et al., 2009), regardless of treatment assignment. The standard of care includes provision of patient education materials (adapted from existing studies to address more persistent rather than acute symptom management), regular scheduled follow-up with a medical provider every 3 weeks, and symptom-based treatment of post-concussive complaints (e.g., medication trials for headache and co-occurring psychiatric disorders, physical therapy for vestibular complaints, case management, and supportive counseling with social work for soldiers assigned to the Warriors-in-Transition Battalion). Study participants who are assigned to treatment arms 2, 3, or 4 will additionally receive manualized cognitive rehabilitation therapies during the 6-week treatment phase of the study. Cognitive rehabilitation treatment intensity (i.e., number of hours of treatment per week) will be matched for individuals assigned to treatment arms 2, 3, or 4. Participants assigned to the control treatment group (treatment arm 1) will be offered individualized cognitive rehabilitation therapy if their cognitive complaints do not abate following the completion of the 6-week treatment trial. Study participants will be evaluated prior to the initiation of treatment, as well as at 3-weeks, 6-weeks, 12-weeks, and 18-weeks following the start of treatment. Study evaluators will be blind to treatment assignment. Pre-treatment baseline assessments and peri-/post-treatment outcome assessments will include demographic information, injury-related variables, self-report inventories, performance on neuropsychological testing, and functional status (e.g., work status; healthcare utilization). Detailed descriptions of the data to be collected including primary and secondary outcome measures, as well as covariate measures can be found in section 4.8: Instrumentation.

Sample Description	Study Type	Study Design	Time Frame
N = 160 Gender: Both Group: Adult	Interventional	• Allocation: Randomized • Endpoint Classification: Efficacy Study • Intervention Model: Factorial Assignment • Masking: Double Blind (Subject, Outcomes Assessor) • Primary Purpose: Treatment	June 2011–August 2014

Appendix D

Biosketches of Committee Members and Staff

Ira Shoulson, M.D. (*Chair*) (IOM), is professor of neurology, pharmacology, and human science and director of the Program for Regulatory Science and Medicine at Georgetown University—new full-time academic positions effective January 1, 2011. Previously, Dr. Shoulson was the Louis C. Lasagna Professor of Experimental Therapeutics and professor of neurology, pharmacology and medicine at the University of Rochester School of Medicine & Dentistry in Rochester, New York. He received his M.D. degree (1971) and postdoctoral training in medicine (1971–1973) and neurology (1975–1977) at the University of Rochester and in experimental therapeutics at the National Institutes of Health (1973–1975). Dr. Shoulson founded the Parkinson Study Group (www.parkinson-strudy-group.org) in 1985 and the Huntington Study Group (www.huntington-study-group.org) in 1994—international academic consortia devoted to research and development of treatments for Parkinson's disease, Huntington's disease, and related neurodegenerative and neurogenetic disorders. He has served as principal investigator of the National Institutes of Health–sponsored trials "Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism," the "Prospective Huntington At Risk Observational Study," and more than 25 other controlled multi-center studies. He was formerly a member of the National Institute of Neurological Disorders and Stroke Council and president of the American Society for Experimental NeuroTherapeutics. He is currently associate editor of *Archives of Neurology* and a member of the Institute of Medicine of the National Academies. He has authored more than 280 scientific reports.

Rebecca A. Betensky, Ph.D., is professor of biostatistics at the Harvard School of Public Health and a biostatistician at Massachusetts General Hospital (MGH). She directs the statistical core of the Alzheimer's Disease Research Center at MGH and she is co-leader of the Biostatistics Program at the Dana-Farber/Harvard Cancer Center. She graduated from Stanford University with a Ph.D. in 1992. Her current methodological research interests are in the areas of latent class modeling for genomic data and survival analysis under complex sampling and with auxiliary information. Dr. Betensky's research involves the use of penalization, either in a frequentist or Bayesian setting, to enable model fitting with the high dimensional data. This research is motivated by problems that Dr. Betensky encounters in her collaborations in neuro-oncology and neurologic diseases.

Peter Como, Ph.D., joined the U.S. Food and Drug Administration (FDA) in 2009 as a lead reviewer and neuropsychologist in the Division of Ophthalmic, Neurological and Ear, Nose and Throat Devices, Neurodiagnostic and Neurotherapeutic Devices Branch. He obtained his doctorate in clinical psychology/neuropsychology from the University of Delaware. Prior to joining the FDA, Dr. Como was an associate professor of neurology, psychiatry, and brain and cognitive science at the University of Rochester Medical Center for 25 years. He served in a clinical capacity as a neuropsychologist in the Movement and Inherited Neurological Disorders Unit in the Department of Neurology. Dr. Como was also a principal investigator in several clinical research studies (observational and clinical drug trials) in Huntington's disease, Parkinson's disease, and Tourette syndrome. Dr. Como has been invited to speak at major national and international meetings with respect to his expertise in neuropsychology, clinical trials, and neurological movement disorders. Dr. Como was part of the clinical investigative team who presented to an FDA advisory panel, which ultimately led to the approval of tetrabenazine for the treatment of chorea, associated with Huntington's disease, in 2008.

Ray Dorsey, M.D., is an associate professor of neurology at The Johns Hopkins University where he directs the movement disorders division and neurology telemedicine. His research focuses on developing new treatments and improving the way health care is delivered, including the use of telemedicine, for neurological disorders. He previously was an assistant professor of neurology at the University of Rochester and an associate for the consulting firm, McKinsey & Company. He attended medical and business school at the University of Pennsylvania.

Charles E. Drebing, Ph.D., is the acting mental health service line manager at the Bedford Veterans Administration (VA) Medical Center, and the as-

sociate director for the New England Mental Illness Research, Education & Clinical Center. Since joining the staff of the VA in 1992, he has been involved with a range of studies examining interventions for psychiatric rehabilitation settings, as well as studies of health services utilization within the VA. The majority of his research has been focused on understanding and enhancing rehabilitation interventions designed to help veterans with comorbid substance abuse and psychiatric disorders return to full lives in the community. He has conducted a range of studies examining existing VA vocational rehabilitation services, how they are used by veterans, what factors predict their success or failure, and how their outcomes can be enhanced. His research includes studies of contingency management interventions designed to enhance vocational rehabilitation and transitional housing programs, studies of motivational interviewing interventions designed to enhance vocational rehabilitation, studies of a supported self-employment treatment model, and studies of a harm reduction intervention for problem gambling. He has also examined the role of families and social support in health care utilization, including studies of family supports and problem recognition, treatment entry, and treatment outcome. He has published over 50 articles, including a book for family members of adults with problem gambling, and several chapters on psychiatric interventions. His most current research work includes studies of supported employment for veterans with posttraumatic stress disorder, examination of peer support and peer-provided supported education, new contingency management applications, and pathways-to-care studies of common VA rehabilitation interventions.

Alan I. Faden, M.D., received his medical degree from the University of Chicago and neurology training at the University of California at San Francisco. He is the David S. Brown Professor in Trauma, and professor of anesthesiology, anatomy and neurobiology, neurosurgery, and neurology at the University of Maryland School of Medicine. He also serves as director of the Shock, Trauma and Anesthesiology Research Organized Research Center and the Charles "McC" Matthias National Study Center for Trauma and Emergency Medical Systems at the University of Maryland, Baltimore. In addition to providing oversight for clinical research related to trauma and critical care, Dr. Faden directs an active preclinical research program in neurotrauma, supported by multiple grants from the National Institutes of Health. He has published 325 peer-reviewed papers. Dr. Faden was previously professor of neuroscience, neurology, and pharmacology at Georgetown University, where he served as dean for research and scientific director of the medical center, associate dean for biomedical sciences for the graduate school, and director of the Georgetown Institute for Cognitive and Computational Sciences. Prior to Georgetown he was professor and vice chair of neurology at the University of California, San Francisco, where he

also held positions as chief of neurology at the San Francisco Veterans Administration Medical Center and director of the Center for Neural Injury. Dr. Faden is editor-in-chief of *Neurotherapeutics*. He served as president of the American Society for Experimental NeuroTherapeutics, inaugural president of the National Neurotrauma Society, and as president of the San Francisco Neurological Society.

Robert T. Fraser, Ph.D., is a professor in the University of Washington's Department of Rehabilitation Medicine, joint with the Departments of Neurological Surgery and Neurology and a consultant with Associates in Rehabilitation and Neuropsychology, Seattle, Washington. He was recently appointed to the U.S. Social Security Administration to advise on the revision to the disability eligibility process. He is an active counseling and rehabilitation psychologist, a certified rehabilitation counselor, and a certified life care planner who directs neurological vocational services within rehabilitation medicine. Within neurological rehabilitation, he has specialized in epilepsy, brain injury, and multiple sclerosis. Dr. Fraser has received master's degrees in rehabilitation counseling (University of Southern California) and public administration (Seattle University). His doctorate is in rehabilitation psychology from the University of Wisconsin-Madison, with a dissertation focused on the use of task analysis in the national classification and utilization of state agency vocational rehabilitation personnel.

Tamar Heller, Ph.D., is head of the Department of Disability and Human Development, University of Illinois at Chicago and director of its University Center of Excellence in Developmental Disabilities for the State of Illinois. She also directs the Rehabilitation Research and Training Center on Aging with Developmental Disabilities: Lifespan Health and Function and projects on family support and health promotion interventions for individuals with disabilities. One of these projects is the Special Olympics Research Collaborating Center. She is past president of the board of the Association of University Centers on Disabilities. In 2005 she was Senator Obama's delegate to the White House Conference on Aging. As a co-founder of the national Sibling Leadership Network, she is a member of its executive board.

Richard Keefe, Ph.D., is professor of psychiatry and behavioral sciences at Duke University Medical Center in Durham, North Carolina. He received his B.A. from Princeton University and his Ph.D. in clinical psychology from New York University. His research is primarily devoted to understanding cognitive dysfunction and its treatment in patients with schizophrenia and related disorders, including those at high risk for schizophrenia. Dr. Keefe has had a leadership role for cognitive methods in several large National Institute of Mental Health studies including the *Clinical Antipsychotic Tri-*

als in Intervention Effectiveness, Measurement and Treatment Research to Improve Cognition in Schizophrenia, Treatment Units for Research on Neurocognition and Schizophrenia, and *Treatment and Evaluation Network for Trials in Schizophrenia* projects. He has published more than 150 scientific papers, and has authored two books. He serves on the editorial boards of several journals, including *Schizophrenia Research*, *Schizophrenia Bulletin*, and *Clinical Innovations in Neuroscience*, and is an associate editor of *Psychological Medicine*. He is president-elect of the International Society for Central Nervous System Clinical Trials and Methodology, and on the scientific board of National Alliance on Mental Illness and the Brain and Behavior Research Foundation. He is the founder and chief executive officer of NeuroCog Trials, Inc. He is also a co-principal investigator and director of the Neurocognitive Core for the Translational and Clinical Research Schizophrenia project at the Institute of Mental Health in Singapore.

Mary R. T. Kennedy, Ph.D., is an associate professor in the Speech-Language-Hearing Science Department at the University of Minnesota, Twin Cities. She has over 30 years of clinical and research experience working with individuals with cognitive and communication disorders as a result of traumatic brain injury (TBI). Dr. Kennedy has published and presented widely on these topics in both peer-reviewed scientific journals and publications aimed at translating evidence into practice. Her research has been funded by grants on the executive functions, language, and metacognition of survivors of TBI and the academic impact of these impairments. Her current projects involve translating research evidence into practical assessment and instruction techniques that support individuals with TBI they transition back to college. Dr. Kennedy chairs the Academy of Neurological Communication Disorders & Sciences committee that systematically reviews research evidence and develops practice guidelines on managing cognitive and communication disorders after TBI.

Harvey Levin, Ph.D., is professor at the Baylor College of Medicine, in the Departments of Physical Medicine and Rehabilitation, Pediatrics, Neurosurgery, and Psychiatry and Behavioral Sciences. Dr. Levin is also director of the Center of Excellence for Traumatic Brain Injury at the Michael E. De Bakey Veterans Affairs Medical Center in Houston, Texas. He obtained his M.A. in clinical psychology and Ph.D. in clinical psychology/neuropsychology at the University of Iowa in 1972. Following his graduate work, he interned at the Illinois Masonic Medical Center in Chicago, as well as the University of Iowa Hospital in Iowa City where he completed a postdoctoral fellowship in clinical neuropsychology. He is board certified in clinical neuropsychology, and is a Texas licensed psychologist. His subspecialty is neuropsychology, and his clinical interests are in brain injury, epilepsy, and stroke. He conducts research at Baylor College in cognitive neuropsychology.

Cynthia D. Mulrow, M.D. (IOM), is clinical professor of medicine at the University of Texas Health Science Center at San Antonio and senior deputy editor of the *Annals of Internal Medicine*. Dr. Mulrow's expertise is in clinical methodology, information synthesis, and clinical guidelines. She is a member of the American Society for Clinical Investigation and the Institute of Medicine (IOM) and currently serves on the IOM Board on Health Care Services. She was previously director of the San Antonio Veterans Administration Cochrane Center, program director of the Robert Wood Johnson Foundation's Generalists Physician Scholars Program, and director of the San Antonio Evidence-based Practice Center. Dr. Mulrow has served on several editorial boards, including the *British Medical Journal* and the *American Journal of Medicine*. She was a member of the U.S. Preventive Services Task Force and has served on guideline development panels for the RAND Corporation and U.S. Agency for Healthcare Research and Quality. She currently participates in multiple groups that develop reporting standards for medical research including the Consolidated Standards of Reporting Trials Group (reporting standards for trials), the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Group (reporting standards for systematic reviews), and the Strengthening the Reporting of Observational Studies in Epidemiology Group (reporting standards for observational studies).

Hilaire Thompson, Ph.D., R.N., FAAN, is an assistant professor in the School of Nursing at the University of Washington and a core faculty of the Harborview Injury Prevention and Research Center. Dr. Thompson's research has focused on improving outcomes from traumatic brain injury (TBI). In particular, her efforts have focused on understanding and improving the delivery of health care services to persons with TBI and the use of translational approaches to manage and reduce symptoms following injury. She currently serves as the Clinical Practice Guideline Series editor for the American Association of Neuroscience Nurses. Dr. Thompson earned her Ph.D. in nursing from the University of Pennsylvania in 2003, after completing her M.S. and post-M.S. Certificate in adult medical-surgical nursing and as an adult acute care nurse practitioner, respectively, from Virginia Commonwealth University. She also received her B.S.N. from Catholic University of America in 1992 and an M.S. in clinical epidemiology from the University of Washington in 2008.

John Whyte, M.D., Ph.D., is a physiatrist and experimental psychologist specializing in traumatic brain injury rehabilitation. He was the founding director of the Moss Rehabilitation Research Institute, begun in 1992, and continues in this position. His research focuses on cognitive impairment and cognitive rehabilitation after brain injury as well as the special methodo-

logic challenges posed by rehabilitation research. Dr. Whyte has received research funding from the National Institutes of Health (NIH), the National Institute on Disability and Rehabilitation Research, the Department of the Army, and a number of private foundations. He is the past president of the Association of Academic Physiatrists, former chair of the National Center for Medical Rehabilitation Research's Advisory Board, and past principal investigator and program director (now associate program director) of the Rehabilitation Medicine Scientist Training Program, a NIH-funded program to train physiatric researchers.

CONSULTANTS

Jennifer J. Vasterling, Ph.D., obtained her doctorate in psychology from Vanderbilt University in 1988, subsequently completing pre- and postdoctoral training in clinical neuropsychology at the Boston Veterans Affairs Medical Center. She currently serves as the chief of psychology at the Veterans Administration (VA) Boston Healthcare System and as a clinical investigator within the Behavioral Sciences Division of the VA National Center for Post Traumatic Stress Disorder. Dr. Vasterling is a professor of psychiatry at Boston University School of Medicine and a lecturer in psychiatry at Harvard Medical School. Prior to her current positions, Dr. Vasterling served as the associate director for research for the VA South Central (VISN 16) Mental, Illness, Research, Education, and Clinical Center, staff psychologist at the New Orleans Veterans Affairs Medical Center, and as a clinical professor of psychiatry and neurology at Tulane University School of Medicine. Dr. Vasterling's research has centered on furthering understanding of the neurocognitive and emotional changes that accompany war-zone deployment and posttraumatic stress responses. Her recent work includes leadership of the Neurocognition Deployment Health Study, a prospective study examining short- and long-term neuropsychological and emotional outcomes of military deployment to Iraq.

Barbara G. Vickrey, M.D., M.P.H., is professor and vice chair of the Department of Neurology at the University of California, Los Angeles (UCLA), where she directs the Health Services Research Program in Neurology. She is also associate director for research at the Greater Los Angeles Veterans Administration Parkinson Disease Center and an affiliated investigator at the RAND Corporation. Dr. Vickrey's research focuses on translating evidence from clinical trials into routine medical practice and improved patient health outcomes. She led a multisite randomized trial that demonstrated substantially improved quality and better patient and caregiver outcomes from a coordinated care approach to dementia care delivery. Her research has led to enhanced clinical trials for epilepsy and multiple

sclerosis by developing widely used instruments to quantify how these patients view their health-related quality of life. Currently, Dr. Vickrey leads an American Heart Association Outcomes Research Center investigating methods to address racial and ethnic disparities in stroke and training postdoctoral fellows in this field of investigation. She received her M.D. from Duke University School of Medicine and her M.P.H. from UCLA School of Public Health. In 1998, she received the Alice S. Hersh Young Investigator Award from AcademyHealth.

INSTITUTE OF MEDICINE STAFF

Rebecca N. Koehler, Ph.D., is a program officer and study director at the Institute of Medicine of the National Academies. She most recently worked as a postdoctoral fellow from 2007 to 2010 at the U.S. Military Human Immunodeficiency Virus (HIV) Research Program, where she initiated and carried out research projects exploring human genetic factors influencing HIV infection and clinical disease course. These studies were influential in uncovering specific alleles contributing to protection from HIV in East African populations. Dr. Koehler earned her Ph.D. at Georgetown University in biology, with a concentration in molecular and cellular biology. Her doctoral work focused on the transcriptional regulation of the *ADE* genes in the genetic model system yeast. Prior to graduate school Dr. Koehler participated in the Jesuit Volunteer Corps for one year in Los Angeles, serving as a case manager at the Saint Joseph Homeless Service Center. She is a graduate of the University of Notre Dame with a bachelor of science in biology and a minor in art history.

Erin E. Wilhelm, M.P.H., was an associate program officer at the Institute of Medicine (IOM) of the National Academies, with the Board on the Health of Select Populations. Previously, Ms. Wilhelm served as the research associate on two studies evaluating disability criteria, related to cardiovascular diseases and HIV/AIDS. In October 2010, she coordinated a three-day workshop for TRICARE at the IOM, bringing together experts on quality management systems and scopes of practice for behavioral health professionals in the Military Health System. Prior to joining the IOM in 2009, Ms. Wilhelm served as a guest researcher at Fogarty International Center of the National Institutes of Health (NIH), where she contributed to a literature review and portfolio analysis for the Trans-NIH Working Group on Climate Change and Health. Among other roles, she has also served as a publications editor for the Corporate Executive Board, a best practice research firm in Washington, DC, and a staff writer for the *St. Petersburg Times* in Tampa, Florida. Ms. Wilhelm holds a Master of Public Health in global health from

The George Washington University and a dual Bachelor of Arts in broadcast journalism and political science from the University of South Florida.

Alicia Jaramillo-Underwood was a program assistant at the Institute of Medicine (IOM) until August 2011 when she joined the National Academies' Division of Behavioral and Social Sciences and Education. Prior to joining the IOM, she graduated from Georgetown University in May 2010 with a B.A. degree in psychology. In the interim from graduation and joining the staff, Alicia spent 6 months in Heidelberg, Germany, as a volunteer with the American Red Cross. From 2009 to 2010 Alicia was a research assistant at Georgetown University's Department of Psychology, conducting interviews for a cross-cultural study on emotions. In the summers of 2007 and 2008, she volunteered at the American Red Cross as an instructor, as well as in the pharmacy at Prince William County Hospital, in Manassas, Virginia. Alicia has taught English, traveled to Tamaulipas, Mexico, on a medical mission, and has volunteered in other capacities as well, including briefly for the neurosurgery department at Georgetown University Hospital.

Jon Q. Sanders is a veteran program associate with the Board on the Health of Select Populations at the Institute of Medicine (IOM). He received his B.A. degree in anthropology with a minor in geosciences from Trinity University and recently completed the program management certification at George Mason University. In his 10 years with the National Academies Mr. Sanders has worked on a variety of projects on topics ranging from childhood obesity to national security, and most recently on a multiple award-winning project on lesbian, gay, bisexual and transgender health. He is coauthor of *Sitting Down at the Table: Mediation and Resolution of Water Conflicts* (2001). His research interests include public health, emergency management, and environmental decision making.

Frederick (Rick) Erdtmann, M.D., M.P.H., is currently director of the Board on the Health of Select Populations and the Medical Follow-Up Agency at the Institute of Medicine (IOM). Prior to joining the IOM he was a career military physician in the U.S. Army. While in the military, he served as chief of several large departments of preventive medicine at U.S. installations at home and overseas. He also was commander of the military community hospital at Ft. Carson, Colorado, and later served as hospital commander for the Walter Reed Army Medical Center. He had several assignments at the Army Surgeon General's Office, working on military health care policies. He received his undergraduate degree from Bucknell University and an M.P.H. from the University of California, Berkeley. He is a graduate of Temple University Medical School and is board certified in the specialty of preventive medicine.