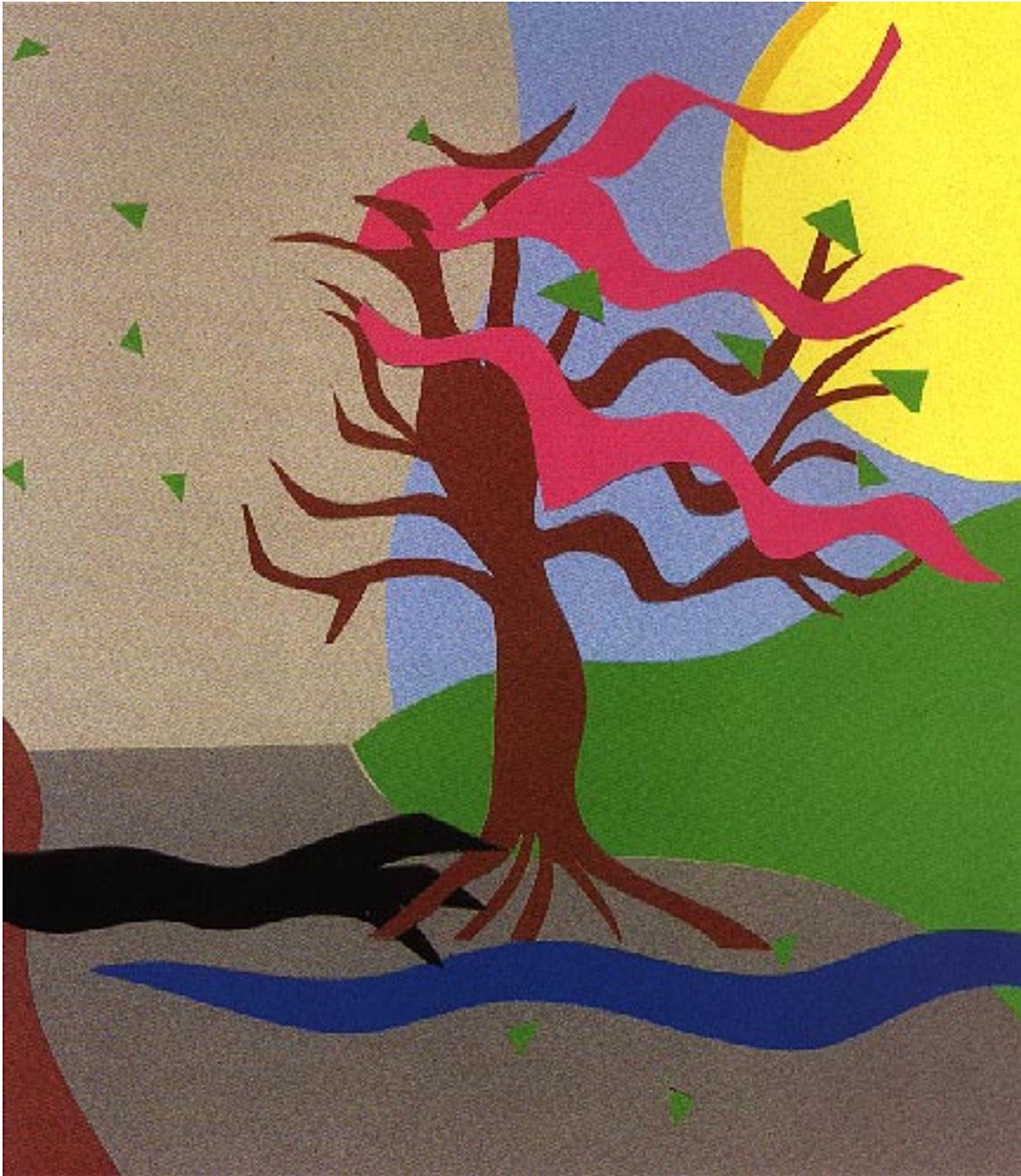


NIH Consensus Development Conference



Rehabilitation of Persons With Traumatic Brain Injury

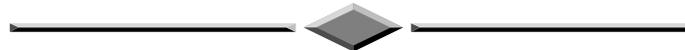
Program and Abstracts

Office of the Director
National Institutes of Health

**NIH Consensus Development
Conference on
Rehabilitation of Persons With
Traumatic Brain Injury**



**October 26-28, 1998
Natcher Conference Center Auditorium
National Institutes of Health
Bethesda, Maryland**



Sponsored by:

◆ National Institute of Child Health and Human Development ◆ Office of Medical Applications of Research ◆

Cosponsored by:

◆ National Institute on Deafness and Other Communication Disorders ◆ National Institute of Mental Health ◆ National Institute of Neurological Disorders and Stroke ◆ National Institute of Nursing Research ◆ Office of Alternative Medicine ◆ Office of Research on Women's Health ◆ Agency for Health Care Policy and Research ◆ Centers for Disease Control and Prevention ◆



National Institutes of Health

Continuing Medical Education

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Introduction

Traumatic brain injury (TBI), defined as brain damage caused by externally inflicted trauma to the head, may result in significant impairment of an individual's functioning—physical, cognitive, and psychosocial. In the United States, an estimated 1.5 to 2 million people incur TBI each year, principally as a result of automobile crashes, sports accidents, falls, and acts of violence. The number of people surviving TBI has increased significantly in recent years because of faster and more effective emergency care, quicker and safer transportation to specialized treatment facilities, and advances in acute medical management. TBI strikes people across the age range and is the leading cause of disability among children and young adults.

Each year, approximately 70,000 to 90,000 individuals incur a TBI so severe that they are left with irreversible, debilitating losses of functioning. The result is frequently a dramatic change in the individual's life-course, profoundly disorganizing effects on the family, and huge medical and related expenses over a lifetime. Less severe injuries may result in functional problems that are visible only in particular circumstances.

Although TBI may result in chronic physical impairments, the more problematic difficulties concern the individual's cognition, emotional functioning, and behavior in connection with interpersonal relationships, school, or work. Cognitive remediation, behavior modification, psychopharmacologic management, and individual and family education and counseling are the primary methods of treatment in rehabilitation settings. Those settings may include a rehabilitation hospital or a department in a general hospital and, subsequently, a variety of day treatment or residential programs.

The Traumatic Brain Injury Act of 1996 instructed the Secretary of Health and Human Services, acting through the Director of the National Center for Medical Rehabilitation Research within the National Institute of Child Health and Human Development, to conduct "a national consensus conference on managing traumatic brain injury and related rehabilitation concerns." The National Institutes of Health (NIH) has organized this 2½-day conference to evaluate the scientific data concerning rehabilitation practices for persons with TBI. Particular emphasis will be placed on practices related to the cognitive, behavioral, and psychosocial difficulties that may be associated with TBI, both severe and mild.

The conference will bring together national and international experts in the fields of relevant medical research and health care as well as representatives from the public.

On the second day of the conference, 1½ hours have been allocated for 5- to 10-minute formal oral presentations by individuals presenting statements regarding the conference issues on behalf of interested organizations. In addition, if time allows during this 1½-hour session, persons wishing to present their own individual statements may do so after the organizational presentations.

After 1½ days of presentations and audience discussion, an independent, non-Federal consensus panel chaired by Dr. Kristjan Ragnarsson, Professor and Chair, Department of Rehabilitation Medicine, Mount Sinai School of Medicine, will weigh the scientific evidence and write a draft statement that will be presented to the audience on the third day. The statement will take into account the panel's review of the scientific literature prepared during the preceding year. The consensus statement will address the following key questions:

- What is the epidemiology of traumatic brain injury in the United States, and what are its implications for rehabilitation?
- What are the consequences of traumatic brain injury in terms of pathophysiology, impairments, functional limitations, disabilities, societal limitations, and economic impact?
- What is known about mechanisms underlying functional recovery following TBI, and what are the implications for rehabilitation?
- What are the common therapeutic interventions for the cognitive and behavioral sequelae of TBI, what is their scientific basis, and how effective are they?
- What are common models of comprehensive, coordinated, multidisciplinary rehabilitation for people with TBI, what is their scientific basis, and what is known about their short- and long-term outcomes?
- Based on the answers to these questions, what can be recommended regarding rehabilitation practices for people with TBI?
- What research is needed to guide the rehabilitation of people with TBI?

On the final day of the meeting, the conference chairperson, Dr. Ragnarsson, will read the draft statement to the conference- audience and invite comments and questions. A press conference will follow to allow the panel and chairperson to respond to questions from media representatives.

General Information

Conference sessions will be held in the Natcher Conference Center, National Institutes of Health, Bethesda, Maryland. Sessions will run from 8:30 a.m. to 5:30 p.m. on Monday, from 8 a.m. to 1 p.m. on Tuesday, and from 9 a.m. to 2 p.m. on Wednesday. The telephone number for the message center is (301) 496-9966. The fax number is (301) 480-5982.

Cafeteria

The cafeteria in the Natcher Conference Center is located one floor above the auditorium on the main floor of the building. It is open from 7 a.m. to 2 p.m., serving breakfast and lunch.

Continuing Medical Education

The purpose of this Consensus Development Conference is to review the current state of knowledge regarding the rehabilitation of persons with traumatic brain injury and identify directions for future research.

The conference will (1) present in open, public sessions state-of-the-art information about the rehabilitation of persons with traumatic brain injury, (2) prepare a statement in response to the seven specific questions, and (3) inform the biomedical research and clinical practice communities and the general public of the conclusions and recommendations of the panel.

In accordance with Accreditation Council for Continuing Medical Education (ACCME) requirements regarding conflict of interest, each speaker presenting at this conference has been asked to submit documentation outlining any real or potential conflict of interest.

The NIH/FAES is accredited by the ACCME to sponsor continuing medical education for physicians.

The NIH/FAES designates this educational activity for a maximum of 14 hours in category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he or she actually spent in the educational activity.

Sponsors

The primary sponsors of this meeting are the National Institute of Child Health and Human Development and the NIH Office of Medical Applications of Research. The conference is cosponsored by the National Institute on Deafness and Other Communication Disorders, the National Institute of Mental Health, the National Institute of Neurological Disorders and Stroke, the National Institute of Nursing Research, the Office of Alternative Medicine, and the Office of Research on Women's Health of the National Institutes of Health; the Agency for Health Care Policy and Research; and the Centers for Disease Control and Prevention.

Agenda

Monday, October 26, 1998

- 8:30 a.m. Opening Remarks
Duane Alexander, M.D., Director, National Institute of Child Health and Human Development
- 8:35 a.m. Remarks
Representative James C. Greenwood, U.S. House of Representatives
(invited)
- 8:45 a.m. Charge to Panel
John H. Ferguson, M.D., Director, Office of Medical Applications of Research
- 8:50 a.m. Conference Overview and Panel Activities
Kristjan T. Ragnarsson, M.D., Mt. Sinai Medical Center

I. Overview

- 9:00 a.m. Rehabilitation of Individuals With Traumatic Brain Injury:
Status of the Art and Science
John Whyte, M.D., Ph.D., Moss Rehabilitation Research Institute

II. Epidemiology of TBI

- 9:20 a.m. Panel Overview
Janet R. Daling, Ph.D., Fred Hutchinson Cancer Research Center
- 9:30 a.m. Challenges in Determining the Epidemiology of Traumatic Brain Injury:
Issues Affecting Incidence, Prevalence, and Risk Factor Identification or
Measurement
Jess F. Kraus, Ph.D., U.C.L.A. School of Public Health
- 9:50 a.m. Trends in Traumatic Brain Injury-Related Hospitalizations—
United States, 1980–1995
David J. Thurman, M.D., M.P.H., Centers for Disease Control and
Prevention

Monday, October 26, 1998 (continued)

III. Consequences of Traumatic Brain Injury

- 10:00 a.m. Discussion
- 10:20 a.m. Panel Overview
Kit N. Simpson, Dr.P.H., M.P.H., University of North Carolina at Chapel Hill and Chiron Diagnostics
- 10:30 a.m. Neurocognitive/Behavioral Outcomes in Children and Adults
Harvey S. Levin, Ph.D., Baylor College of Medicine
- 10:55 a.m. Functional Consequences and Outcome Measurements
Mitchell Rosenthal, Ph.D., Rehabilitation Institute of Michigan and Wayne State University
- 11:10 a.m. Consequences of Traumatic Brain Injury for the Family
Jeffrey S. Kreutzer, Ph.D., ABPP, Medical College of Virginia
- 11:30 a.m. Consequences of Traumatic Brain Injury for Functioning in the Community
John D. Corrigan, Ph.D., Ohio State University
- 11:45 a.m. Economics of Traumatic Brain Injury Rehabilitation: Observations on Progress and Recommended Directions
Mark V. Johnston, Ph.D., Kessler Rehabilitation Research and Education Corporation
- 12:00 p.m. Discussion
- 12:45 p.m. Lunch

IV. Mechanisms Underlying Recovery From Traumatic Brain Injury

- 1:45 p.m. Panel Overview
Steven L. Small, M.D., Ph.D., University of Maryland School of Medicine
- 1:55 p.m. Receptor-Based Mechanisms of Functional Recovery
Tracy K. McIntosh, Ph.D., University of Pennsylvania Medical Center

Monday, October 26, 1998 (continued)

- 2:10 p.m. Cellular Mechanisms of Recovery
John T. Povlishock, Ph.D., Medical College of Virginia
- 2:25 p.m. Neuroplasticity, Experience, and Mechanisms of Brain Information Storage
William T. Greenough, Ph.D., Beckman Institute and University of Illinois
- 2:40 p.m. The Cognitive and Behavioral Mechanisms Underlying Recovery From Traumatic Brain Injury at Different Stages After Injury
Donald T. Stuss, Ph.D., Rotman Research Institute, University of Toronto
- 2:55 p.m. Discussion

V. Common Cognitive Rehabilitation Interventions

- 3:30 p.m. Panel Overview
Elliot J. Roth, M.D., Northwestern University Medical School and Rehabilitation Hospital of Chicago
- 3:40 p.m. Agency for Health Care Policy and Research Evidence-Based Practice Report
Randall M. Chesnut, M.D., Oregon Health Sciences University
- 4:00 p.m. Cognitive Rehabilitation: An Impairment-Oriented Approach Embedded in a Holistic Perspective
George P. Prigatano, Ph.D., Barrow Neurological Institute
- 4:15 p.m. A Contextualized and Routine-Based Approach to Cognitive and Behavioral Rehabilitation: A Historical Perspective
Mark Ylvisaker, Ph.D., College of St. Rose
- 4:30 p.m. Cognitive Rehabilitation: Research Approaches
Ronald M. Ruff, Ph.D., University of California, San Francisco
- 4:50 p.m. Discussion
- 5:30 p.m. Recess

Tuesday, October 27, 1998

VI. Overview of Traumatic Brain Injury Rehabilitation Models

- 8:00 a.m. Panel Overview
Jerry C. Parker, Ph.D., University of Missouri–Columbia, School of Medicine
- 8:10 a.m. Institute of Medicine Model of Disability
Diana D. Cardenas, M.D., University of Washington
- 8:25 a.m. Models of Head Injury Care
D. Nathan Cope, M.D., Paradigm Health Corporation
- 8:45 a.m. Access to Brain Injury Rehabilitation and Other Post-Acute Services
Gerben DeJong, Ph.D., National Rehabilitation Hospital Research Center
- 9:05 a.m. The Consumer Perspective on Existing Models of Rehabilitation:
The Rehabilitation of Persons With Traumatic Brain Injuries
Theresa M. Rankin, Brain Injury Association
- 9:20 a.m. Discussion

VII. Issues in Traumatic Brain Injury Research Methodology

- 10:00 a.m. Quality of Life and Life Satisfaction Studies
Allen W. Heinemann, Ph.D., ABPP, Northwestern University School of Medicine
- 10:15 a.m. Ethical Considerations in Research Design Involving Persons With
Traumatic Brain Injury
John Banja, Ph.D., Emory University School of Medicine
- 10:30 a.m. Methodologic Issues in Study Design: New Research Paradigms From
Other Fields
Kit N. Simpson, Dr.P.H., M.P.H., University of North Carolina at Chapel
Hill and Chiron Diagnostics
- 10:45 a.m. Approaches to Resolving the Dilemma
Kenneth J. Ottenbacher, Ph.D., University of Texas at Galveston
- 11:00 a.m. Discussion
- 11:30 a.m. Public Presentations
- 1:00 p.m. Recess

Wednesday, October 28, 1998

- 9:00 a.m. Presentation of Consensus Statement
- 9:30 a.m. Public Discussion
- 11:00 a.m. Panel Meets in Executive Session
- 1:00 p.m. Press Conference
- 2:00 p.m. Adjournment

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Abstracts

The following are abstracts of presentations to the NIH Consensus Development Conference on Rehabilitation of Persons With Traumatic Brain Injury. They are designed for the use of panelists and participants in the conference and as a reference document for anyone interested in the conference deliberations. We are grateful to the authors, who have summarized their materials and made them available in a timely fashion. Abstracts for the following presentations do not appear:

Economics of Traumatic Brain Injury Rehabilitation: Observations on Progress and Recommended Directions—Mark V. Johnston, M.D.

Methodological Issues in Study Design: New Research Paradigms From Other Fields—Kit N. Simpson, Dr.P.H., M.P.H.

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Rehabilitation of Individuals With Traumatic Brain Injury: Status of the Art and Science

John Whyte, M.D., Ph.D.

Traumatic brain injury (TBI) is a problem of enormous public health consequence. Large numbers of individuals of all ages sustain TBIs each year. Significant morbidity and mortality are associated with moderate and severe injuries. Mild injuries, although producing far less morbidity, are still a serious problem because of their extremely high prevalence. Because of the high incidence in childhood and young adulthood and the long-term impact on employment, TBI-related disability has enormous economic and social consequences across the lifespan (Max, MacKenzie, Rice, 1991; Lehmkuhl, Hall, Mann, et al., 1993; Haffey, Abrams, 1991). Although the outcome of moderate and severe TBI is reasonably well characterized over the first few years post-injury, very little is known about the long-term consequences of mild TBI or about the consequences of aging with a more severe TBI. In particular, there is concern that significant numbers of children requiring special educational and social services, and adults in the mental health and penal systems, may have a history of TBI that is relevant to their ongoing problems.

Much of the damage sustained in TBI is immediate (referred to as primary injury), including diffuse axonal injury, cortical contusions, and disruption of small blood vessels. However, recent research has provided some optimism that even these forms of pathology have a temporal evolution that might be amenable to intervention (Povlishock, Christman, 1995). Secondary injury, including development of edema, expanding hematomas, hemodynamic instability, and hydrocephalus, can exacerbate brain damage and is clearly subject to intervention (Whyte, Hart, Laborde, et al., 1998). While improvements in trauma care and neurosurgical management have led to increased survival and improved outcomes, significant functional deficits exist for many persons who have experienced TBI.

The goals of rehabilitation in TBI are extremely broad because of the enormous range of outcomes that are possible in TBI. Variations in injury severity require services for individuals with mild TBI, where one helps to control persisting symptoms, such as dizziness, headache, and difficulty concentrating (Ruff, Levin, Marshall, 1986), and for individuals in a vegetative state, where one attempts to optimize bodily integrity and the odds of cognitive recovery (Whyte, Laborde, DiPasquale, in press). Differences in the nature and location of the neuropathology also lead to varied needs, since patients can present with virtually any constellation of cognitive, motor, and behavioral impairments. Finally, an individual's social context shapes rehabilitation needs. Those with little social support must reach much higher levels of independence to survive outside a formal service system than those with well-developed social networks and financial resources.

The duration of service need is also extremely variable. Those with relatively mild injuries may require a brief period of rehabilitation and then may return essentially to their

premorbid status. Others, however, will have severe, lifelong deficits that require a shift from a medical treatment model to a psychosocial and environmental support model over time (Whyte, Hart, Laborde, et al., 1998). As needs become less traditionally medical, funding sources for meeting those needs become increasingly scarce.

Despite this heterogeneity in rehabilitation needs, there are certain commonalities. Shortly after a moderate or severe TBI, a variety of medical problems are common, including seizure disorders, hydrocephalus, and heterotopic ossification, as well as the myriad complications of associated trauma. Physical function is frequently compromised by combinations of weakness or paralysis, spasticity and contractures, ataxia, and slowness of movement. However, cognitive and behavioral deficits, as opposed to motor impairments, account for the greatest share of long-term disability, financial dependence, and family distress. Among these, difficulties in attention and concentration (Whyte, Polansky, Fleming, et al., 1995), memory (Levin, Benton, Grossman, 1982; Schacter, Crovitz, 1977), executive skills (Hart, Jacobs, 1993), and social skills (Brooks, 1984) are particularly problematic. These problems collectively result in very high levels of unemployment and social isolation.

The largest amount of research has been conducted on the middle band of TBI patients, namely those with significant impairments but a clear ability to improve. Less progress has been made on the two extremes of the severity spectrum. Individuals in the vegetative state, or the newly described minimally conscious state, experience diminishing odds of significant recovery as time passes. Numerous treatment strategies, including pharmacologic intervention (Di Rocco, Maira, Meglio, et al., 1974; Horiguchi, Inami, Shoda, 1990; Ross, Stewart, 1981), coma stimulation therapy (Zasler, Kreutzer, Taylor, 1991; Wilson, McMillan, 1993), and deep brain stimulation (Tsubokawa, Yamamoto, Katayama, et al., 1990), have been recommended, but none of these has been definitively tested for efficacy. Individuals with persistent symptoms after mild head injuries present a diagnostic dilemma. Few objective tools are capable of documenting organic sources of their symptoms, and significant controversy remains about how to diagnose mild TBI, much less how to treat it (Zasler, 1996).

Much progress has been made in brain injury research over the last two decades. Advances in neurosurgical research and animal models of TBI have allowed the development of more rational acute interventions designed to minimize secondary injury and have changed the patterns of practice in such areas as hyperventilation, steroid use, management of intracranial pressure, and prevention of seizures (Whyte, Hart, Laborde, et al., 1998). Advances in the neurosciences have also taught us much about biological and psychological plasticity and how particular tasks are managed by the intact brain. More sophisticated tools have been developed for measuring the severity of TBI (e.g., the Glasgow Coma Scale and the Galveston Orientation and Amnesia Test) and for objectively documenting the functional outcomes that result (e.g., the Disability Rating Scale, Functional Independence Measure, and Glasgow Outcome Scale). Much has been learned about the types of outcomes experienced by individuals with TBI, and a great deal of this information comes from the NIDRR-funded TBI Model Systems, which have characterized the inpatient rehabilitation population along a number of dimensions in a longitudinal fashion. Finally, progress has been made in the development of a conceptual model of disablement that stresses the complex interactions among pathology, impairment, disability,

and handicap (to use the WHO classification system) (World Health Organization, 1980) and points to the importance of the interaction between individuals and their environments in determining their real-world successes and failures.

Far less research is available on the efficacy of specific treatments or rehabilitation treatment systems in addressing the range of problems faced by individuals with TBI and their families. Consequently, it may be useful to focus primarily on the factors that limit our ability to answer these critical questions. Most important is the nature of rehabilitation research on all disabilities. The outcomes that are of greatest importance to injured individuals, their families, and their communities are located at the disability and handicap levels, whereas many of the causes of these outcomes are at the levels of pathology and impairment. The correspondence among these levels is highly complex, making it difficult to identify the cause(s) of particular functional problems or to predict the outcome of treatment directed at improving the individual's competence (Whyte, 1997). This problem is particularly intense in TBI because of the large number of interacting impairments that may occur in an individual.

A related practical problem is the question of how to focus treatment or service efforts. At one extreme, one can treat a long list of specific impairments in the hope that the sum total of this work will translate into high-quality global outcomes (an approach directed at the injured individual). At the other extreme, one can accept an individual with a current constellation of disabilities and handicaps and examine how social and environmental supports can be woven in relation to the individual's strengths and weaknesses to improve the outcome (an approach directed at the environment) (Whyte, 1997). In practice, most rehabilitation services engage in a combination of these approaches, but the combination is built largely by trial and error and tradition and therefore is resistant to rigorous study.

Finally, much of the research has been largely empirical. Thus, when a treatment is effective, one learns only that it is useful but not how it might be improved or augmented. When a treatment is found to be ineffective, one learns nothing. There is a great need for development of more precise theories about the interrelationships among pathology, impairment, disability, and handicap; about the nature of the intervention process and how it exerts its effects; and about the design and delivery of service systems. At present, theory exists primarily within specific topic domains (e.g., memory), with little connection to the overall person or treatment system.

In addition to these overarching dilemmas, there are specific research obstacles facing each of the common cognitive and behavioral problems. Attempts to improve attention and concentration have been limited by the state of research on this topic. There remains considerable controversy about how to subdivide the domain of attention and how to measure its components (Whyte, Polansky, Cavallucci, et al., 1996). There is even some question about whether it is possible to measure aspects of attention in any pure form that will predict attentional performance across a broad range of tasks or whether attention is an emergent property of tasks themselves and must be studied (and rehabilitated) in the context of those tasks. Moreover, the theoretical advances in attention that have emerged recently from cognitive neuroscience and related domains focus almost exclusively on how attention normally works or

how it becomes deranged by brain damage and very little on how it can be changed by interventions.

In the area of memory, we have learned a great deal over the last 20 years. We have learned that certain memory systems are preserved even in dense amnesia and that they may support some types of learning (Ewert, Levin, Watson, et al., 1989). We have also learned that repetitive memory exercises are ineffective in improving memory, though they may effectively teach the specific information that is repeatedly exposed (Glisky, Schacter, 1986). Various forms of memory aids, such as notebooks and computers, have been shown to be effective in individual cases. The bulk of progress in applied memory research has taken place in constrained laboratory environments. Thus, little is yet known about whether one can build an effective rehabilitation program around the preserved memory systems or who can be an effective user of what kind of memory aids.

Executive skills refer to the higher order regulatory capacities that are uniquely human and depend heavily on frontal lobe systems (Shallice, Burgess, 1991; Varney, Menefee, 1993). This loose term refers to capacities such as reasoning, problem-solving, self-monitoring, goal-setting and prioritizing, and so on. As the name suggests, it is these skills that determine whether one can be an “executive” (whether at work, or merely in one’s own life), who manages changing demands and priorities, or one who must work on an “assembly line,” where tasks are completely routine and predictable. Since real world environments are never fully routine, training individuals in the specifics needed to manage their lives is never fully sufficient. Executive skill deficits are, at the same time, one of the largest sources of disability and one of the most challenging to treat (Hart, Jacobs, 1993; Sohlberg, Mateer, Stuss, 1993). Basic research on executive skills is among the least developed areas of cognitive psychology. (Indeed, whereas conferences are held on attention, memory, and language, they are sometimes held on frontal lobe function, signifying that we are not entirely sure about how to name the functions they support.) As with the other areas, there is an additional knowledge gap between how executive skills are normally performed and how impaired executive skills can be rehabilitated. There is some preliminary evidence for the efficacy of certain medications (McDowell, Whyte, D’Esposito, in press), but evidence about training-based approaches is virtually nonexistent.

Social skill deficits are a prominent reason for unemployment, social isolation, lack of intimate relationships, and family stress. Their roots are probably multifactorial and variable from individual to individual, including problems with temper control, disinhibition of normal impulses, lack of self-awareness, and the collective impact of the range of cognitive impairments. There has been some limited research on pharmacologic treatment of severe behavioral disturbances (Silver, Yudofsky, Hales, 1994) and on social skills training (Brotherton, Thomas, Wisotzek, et al., 1988), but much more work is needed.

These research challenges have important implications for the organization and funding of rehabilitation research. Large groups of researchers are typically needed for the interdisciplinary collaborations that are required to study a domain spanning cells and sociology. Large subject samples are also needed either to allow selection of homogeneous samples out of the sea of heterogeneity or to cope with the measurement “noise” related to that heterogeneity.

The bulk of rehabilitation interventions are training or device based. This requires the development of treatment protocols or algorithms for individual treatments, or structural descriptions of service systems that can operationalize the active ingredients of treatment for study. The enormous selection biases associated with the types of treatments that individuals naturally receive and the types of service systems they naturally reside in must be coped with. To pursue randomized study designs, for example, will require enormous resources because much or all of the treatment milieu will need to be supported by research funds rather than clinical reimbursement, unlike, for example, randomized medication trials.

Despite these challenges, brain injury rehabilitation is a rapidly developing field. The descriptive research and outcomes measurement tools that were developed over the past two decades give us the foundation for defining the problems in need of future study and measuring the impact of our interventions. The field has reached a level of maturity and sophistication that is now allowing rapid movement into clinical trials, spurred at least in part by Federal efforts such as this consensus conference.

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Challenges in Determining the Epidemiology of Traumatic Brain Injury: Issues Affecting Incidence, Prevalence, and Risk Factor Identification or Measurement

Jess F. Kraus, Ph.D.

Traumatic brain injury (TBI) is one of the world's most serious unresolved public health problems, and although the quantity and quality of epidemiologic research is expanding, many unresolved issues hinder a complete understanding of TBI's natural history and hence prevention at the primary, secondary, and tertiary levels. Current basic epidemiological information, while insightful, is not definitive. This presentation examines issues associated with incidence, prevalence, and risk factor delineation.

Incidence, namely the occurrence of newly diagnosed brain injury in populations, is crucial and in some respects is the key element in the natural history of the problem. Prevention cannot proceed and the impact of intervention cannot be assessed without it. Incidence depends on a valid and consistently used definition, yet early studies either failed to define or included ill-defined entities such as "head" injury. The result was a group of incidence cases, many of which were misclassified as to presence of intracranial trauma. Accurate and complete enumeration of cases for rate (or case group) determinations was and continues to be beset with case-finding uncertainty coming from the variety of diagnoses (and hospital-assigned ICD codes) that constitute brain injury. This problem will continue even with the introduction of the 10th revision of the ICD, which has new rubrics, some of which are secondary outcomes as opposed to the description of the primary lesion.

Prevalence is a difficult concept in the epidemiologic nomenclature of TBI. It is a measure of those who are newly identified with TBI as well as those with physical, cognitive, or memory impairment from an earlier injury. How one defines (and identifies) such cases using extant data sources is problematic. This issue will become more acute (along with incidence definitions) as the 10th revision rubrics and codes come into play.

The current population burden (prevalence) of TBI is unknown largely because many persons with permanent disability reside outside institutional settings. Hospital discharge data often are used to estimate the prevalence and incidence of TBI, but problems with multiple admissions, repeat injury, and diagnostic hierarchy will continue to lead to misclassification and to compromise accuracy.

Risk factors are characteristics or attributes of people or environments that enhance the likelihood of a brain injury. Risk factors describe the character and probability of a specific outcome following the event. Although some risk factors for TBI (as well as other events) are well established, such as alcohol consumption and risk of crash or age and probability of a poor TBI outcome, they have been studied superficially or in the incorrect context. For example, the

pathophysiologic role of alcohol in secondary complications or gender in short-, intermediate-, or long-term outcomes raises intriguing questions that should be addressed.

Other epidemiological issues addressed in this presentation include severity and its measure(s), the vagaries of some external cause classes, new limitations on access to sources of data, and outcome definitions and measures.

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Trends in Traumatic Brain Injury-Related Hospitalizations—United States, 1980–1995

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Surveillance of traumatic brain injury (TBI) in the United States shows a recent decline in TBI-related hospitalizations and fatalities (Centers for Disease Control and Prevention, in press; Sosin, Sniezek, Waxweiller, 1995). To describe long-term trends in TBI-related hospitalization in the United States, the authors analyzed data from the National Hospital Discharge Survey collected from 1980 through 1995 (National Center for Health Statistics, 1997). During this interval, the annual rates of hospitalization related to TBI decreased an estimated 48 percent, from 195 to 101 per 100,000 population. When the levels of TBI severity were taken into account, it was found that the decline in hospitalization rate occurred primarily among persons with TBI who were classified as least severe.

These findings suggest that in addition to successes in injury prevention, changes in hospital practices may be a major factor in the decline of reported rates of TBI. These hospital practices appear increasingly to exclude persons with less severe TBI from hospital admission and to shift their care to outpatient settings. Because data addressing the adequacy of such outpatient care of TBI are lacking, further study of this issue is needed.

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Neurocognitive/Behavioral Outcomes in Children and Adults

Harvey S. Levin, Ph.D.

Conceptual Framework

Heterogeneity in the pattern of diffuse and focal cerebral insults and their interaction with host factors such as age and comorbidities (e.g., substance abuse) contributes to the enormous interindividual variation in cognitive and behavioral sequelae (Kelly, Johnson, Knoller, et al., 1997). Although the term neurobehavioral outcome implies an end point, recovery is a dynamic process, particularly during the 6 to 12 months after restoration of consciousness (Levin, Benton, Grossman, 1982). Extracerebral injury contributes to the morbidity of TBI and can have a major impact on the outcome of mild injury (Dacey, Dikmen, Temkin, et al., 1991). Consistent with experimental models of early brain insult, the post-injury environment interacts with TBI severity in its effect on neurobehavioral outcome (Taylor, Drotar, Wade, et al., 1995).

Cognitive Outcome of TBI in Adults

Severe TBI. Following recovery of consciousness, patients with TBI pass through posttraumatic amnesia (PTA), characterized by anterograde and frequently retrograde amnesia associated with confusion that persists for at least 1 month in two-thirds of cases (Ellenberg, Levin, Saydjari, 1996). Cognitive function during PTA is highly variable and difficult to evaluate. In contrast with persons with markedly impaired explicit memory, most patients with TBI are capable of implicit learning during PTA (Ewert, Levin, Watson, et al., 1989). However, a third of patients with severe TBI remain untestable on standard neuropsychological tests for at least 3 to 6 months because of profound cognitive and behavioral disturbance (Scheibel, Levin, Clifton, in press). Cognitive recovery gradients are steep during the first 6 months post-injury and typically become more gradual over the ensuing 6 months (Levin, Benton, Grossman, 1982). Of the patients with severe TBI who are testable during the period between 6 and 12 months post-injury, explicit memory deficit on multitrial recall tests is the most common cognitive deficit. Serial testing indicates improved explicit memory beyond 1 year in a subgroup, whereas a plateau or late decline occurs in other survivors (Ruff, Young, Levin, et al., 1991). Corresponding deficits in everyday memory generally parallel the findings on memory tests (Wilson, Cockburn, Baddeley, 1985). Attention deficit is reflected by slowed information processing and compromised divided attention on dual tasks (McDowell, Whyte, D'Esposito, 1997). Diminished motor speed on tasks, such as the grooved pegboard, is also a frequent sequel related to global outcome (Clifton, Kreutzer, Choi, et al., 1993). Although scores on psychometric measures of intellectual ability improve to the normal range in most survivors of severe TBI (Mandleberg, Brooks, 1975), deficits on tests of executive function (i.e., problem-solving involving shifts in strategy, anticipating the consequences of actions, and monitoring performance) can persist (Goldstein, Levin, 1991; Stuss, Ely, Hugenholtz, et al., 1985).

Communication deficit at the level of processing discourse and pragmatics is a common sequel, whereas classical aphasia is initially present in 5 to 10 percent of cases (Mentis, Prutting, 1987). Similarly, marked visuospatial deficits associated with unilateral neglect arise from posterior lesions that are relatively infrequent but contribute to disability (Levin, Benton, Grossman, 1982).

Behavioral disturbance after severe TBI has been documented by interviews with a significant other (Livingston, Brooks, Bond, 1985) and the survivor of TBI (Jorge, Robinson, Arndt, et al., 1993) and clinical ratings based on a structured interview (Levin, High, Goethe, et al., 1987). Frequently reported behavioral sequelae include depression, irritability, disinhibition, decreased initiative, and increased dependence. Unawareness of neurobehavioral deficits has been documented by disparities between the patient's self-ratings and ratings obtained from a family member (Livingston, Brooks, Bond, 1985), the clinician's ratings (Levin, High, Goethe, et al., 1987), and the patient's performance on cognitive tests (Sherer, Boake, Levin, et al., 1988). In contrast with the pattern of cognitive recovery, behavioral disturbance tends to persist or even worsen over time (Livingston, Brooks, Bond, 1985).

Mild-to-moderate TBI. Elucidating the neurobehavioral sequelae of mild-to-moderate TBI has been facilitated by refining the definitions of these less serious injuries. Mild impairment of consciousness (i.e., GCS score of 13 to 15) associated with an acute brain lesion results in cognitive deficits that are similar to the sequelae of a moderate TBI (Williams, Levin, Eisenberg, 1990), thus suggesting that this group be classified as "high risk" mild (Hsiang, Yeung, Yu, et al., 1997) or moderate TBI (Williams, Levin, Eisenberg, 1990). Within the group of patients with GCS scores in the 13 to 15 range, morbidity is increased in patients whose GCS is 13 to 14, whereas good recovery is attained with a GCS score of 15 in more than 90 percent of the patients (Hsiang, Yeung, Yu, 1997). Cognitive deficit is apparent during the first week post-injury and generally resolves in the ensuing 1 to 3 months (Gronwall, Wrightson, 1974). Preexisting conditions such as previous TBI (Gronwall, Wrightson, 1975) and alcohol abuse (Kelly, Johnson, Knoller, et al., 1997) interact with mild TBI, producing more persistent cognitive deficits. Cognitive deficit after moderate TBI is more persistent than after uncomplicated mild TBI, particularly residual memory deficit (Rimel, Giordani, Barth, et al., 1982). Neurobehavioral sequelae of mild TBI, which include postconcussional symptoms such as headaches, dizziness, and fatigability, frequently persist after cognitive recovery (Gronwall, Wrightson, 1974). Similar symptoms more frequently persist after moderate TBI and are associated with disability (Rimel, Giordani, Barth, et al., 1982). Depression is the most common psychiatric complication of mild-to-moderate TBI, particularly in women older than 25 years and in patients with past emotional problems (Fenton, McClelland, Montgomery, et al., 1993).

Neurobehavioral Outcome of TBI in Children

Severe TBI. In contrast with recovery to a pre-injury baseline in adults, severe TBI in young children adversely affects cognitive development (Anderson, Moore, 1995). In comparison with severe TBI in children older than 10 years and in adolescents, comparable injuries in young children produce more severe impairment of intellectual function (Anderson,

Moore, 1995) and visuomotor skills (Thompson, Francis, Stuebing, et al., 1994). Executive function (e.g., problem-solving, planning), metacognitive, attention, and declarative memory deficits have been reported in both cross-sectional and longitudinal designs (Anderson, Moore, 1995; Thompson, Francis, Stuebing, et al., 1994; Levin, Culhane, Mendelsohn, et al., 1993; Yeates, Blumenstein, Patterson, et al., 1995). Discourse-processing deficits persist, as reflected by inclusion of fewer propositions in story retells, disruption of the story structure, and omission of gist information (Chapman, Culhane, Levin, et al., 1992). Behavioral sequelae include attention deficit/hyperactivity disorder, oppositional behavior, and depression (Max, Robin, Lindgren, et al., 1997). The risk of developing a new psychiatric disorder increases with time following severe TBI (Max, Robin, Lindgren, et al., 1997). Early prefrontal injury has been implicated in disruption of moral development and empathy, contributing to intractable behavioral disorder (Price, Daffner, Stowe, et al., 1990).

Mild-to-moderate TBI. Because pre-injury learning disability and behavioral disturbance are more common in children sustaining TBI than in the general pediatric population (Max, Robin, Lindgren, et al., 1997), it is essential to include a comparison group, such as children with orthopedic injuries, in outcome studies. Satz and colleagues (1997) concluded that controlled studies provide no compelling evidence for persistent cognitive or behavioral sequelae attributable to mild TBI in children. Although few studies have focused on moderate TBI in children, the long-term neurobehavioral recovery appears to approximate more closely the outcome of mild injuries than that of severe TBI (Levin, Culhane, Mendelsohn, et al., 1993).

Directions for research. Development of measures derived from cognitive psychology could further elucidate the sequelae of TBI and identify potential interventions for rehabilitation. Functional brain imaging combined with cognitive studies is needed to characterize the mechanisms of neurobehavioral sequelae. Standard procedures for assessing cognitive and behavioral functioning in everyday activities are necessary to extrapolate findings from the laboratory or clinic and to study patients with severe TBI who are unable to cooperate with neuropsychological testing. Longitudinal designs from a developmental perspective are needed to characterize neurobehavioral recovery in older adults and the implications for adult life of TBI in childhood.

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Functional Consequences and Outcome Measurements

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The functional consequences of traumatic brain injury (TBI) are determined by multiple factors, including location and extent of brain damage; course of recovery; comorbid conditions and medical complications; preexisting history of neurologic, psychiatric, and psychosocial dysfunction; and characteristics of the posthospitalization environment. Although all persons with TBI have unique presentations, resulting impairments are often categorized in the following manner: medical complications, for example, seizure disorder, heterotopic ossification, sensory impairments; neuropsychological sequelae, for example, deficits in short-term memory, poor problem-solving, disinhibited or other inappropriate social behavior; problems in mobility and self-care, such as impaired ambulation and need for physical assistance and verbal cueing to perform basic activities of daily living; problems in community integration, such as reduced capacity to resume educational or work pursuits; inability to drive or use public transportation; and diminished capacity to resume a role as a spouse, parent, or sibling.

In recent years, the development of measures to assess the functional impact of illness or injury has been guided by the World Health Organization Classification of Impairments, Disabilities and Handicaps (World Health Organization, 1990). This system categorizes the consequences of injury or illness into impairments, disabilities, and handicaps. Specific measures, such as the Glasgow Outcome Scale (Jennett, Bond, 1975), Disability Rating Scale (Rappaport, Hall, Hopkins, et al., 1982), Rancho Los Amigos Levels of Cognitive Functioning Scale (Hagen, Malkmus, Durham, 1972), Functional Assessment Measure (Hall, Mann, High, et al., 1996), Community Integration Questionnaire (Willer, Rosenthal, Kreutzer, et al., 1993), Patient Competency Rating Scale (Prigatano, Altman, 1990), Mayo-Portland Adaptability Inventory (Malec, Thompson, 1994), Neurobehavioral Functioning Inventory (Kreutzer, Marwitz, Seel, et al., 1996), and Supervision Rating Scale (Boake, 1996), have been specifically designed to measure the functional consequences of TBI. In addition, more generic disability measures such as the Functional Independence Measure (FIM) (Keith, Granger, Hamilton, et al., 1987) are also commonly used in the acute rehabilitation setting.

Functional outcome measurement is useful in a variety of contexts: as a criterion for assessing the predictive validity of injury severity measures (e.g., duration of consciousness, length of posttraumatic amnesia); as an index of change to gauge the effectiveness of acute or postacute rehabilitation programming; as a basis for judging the effectiveness of clinical drug or therapy trials; and as a tool to determine the cost-effectiveness of specific interventions. As Hall (in press) and others have noted, a number of key issues should guide the selection of functional outcome measures in TBI rehabilitation: psychometric properties (standardization, reliability, and validity), sensitivity to change, age range, level of reading comprehension required, brevity and ease of administration (in-person, phone, mail), and comprehensiveness. Several of these issues will be reviewed in detail.

Given the dynamic nature of rehabilitation following TBI, sensitivity to change is a fundamental characteristic. The Glasgow Outcome Scale, although still considered the “gold standard” of functional outcome measurement in the neurosurgical community, has been supplanted in most rehabilitation settings by the Disability Rating Scale (DRS) and the FIM, which represent a significantly broader range of disability. A longitudinal, multicenter study of 267 patients, based on the NIDRR TBI Model Systems of Care (with an average Glasgow Coma Scale of 8.4 [severe injury] at emergency room admission), demonstrated that patients with TBI in acute rehabilitation progress from an average DRS of 13 (severe disability [at rehabilitation admission]) to a DRS rating of 6 (moderate disability [at rehabilitation discharge]) and a DRS of 3 (partial disability [at 1 year post-injury]). This decrease in level of disability is confirmed by ratings on the FIM (N = 261), showing a gain from rehabilitation admission of 3.14 (moderate assistance) to 5.7 (supervision needed) at rehabilitation discharge and 6.32 (modified independence) at 1 year post-injury (Harrison-Felix, Newton, Hall, et al., 1996). After 1 year, however, neither the DRS nor the FIM shows much change, reflecting a ceiling effect (Hagen, Malkmus, Durham, 1972).

There is considerably less uniformity in postacute TBI rehabilitation as to the measure or set of measures that best assess level of functional outcome. Measures of psychosocial functioning and capacity to function independently, such as the Patient Competency Rating Scale, Mayo-Portland Adaptability Inventory, Supervision Rating Scale, and Neurobehavioral Functioning Inventory, are examples of scales that have demonstrated reliability and validity and are often useful in postacute TBI rehabilitation programs and research studies.

Within the past several years, the measurement of quality of life has become a more frequent component in measuring functional outcome in persons with disabilities. In the case of TBI, important but univariate measures, such as return to work or independent living, are important markers of rehabilitation success. However, these indicators are not sufficient to characterize quality of life following a catastrophic injury with significant physical, cognitive, and behavioral sequelae. The Community Integration Questionnaire (CIQ) (Willer, Rosenthal, Kreutzer, et al., 1993) was developed to address quality of life following TBI. The scale was factored into three subscales: home integration, social integration, and productivity. It was found to differentiate between a “normative” sample, that is, a group of chronic, very severely brain-injured community-dwelling residents (6.8, mean years post-injury; 31.2 days, mean length of coma), and patients followed up at 1 year postdischarge from the TBI Model Systems programs (1.4, mean years post-injury; 4.2 days, mean length of coma). In reviewing the extant literature on the CIQ, Dijkers (1997) found a number of key methodological issues requiring attention: limited scope and content validity, lack of consistency in metric, lack of adequate normative data, effects of age and gender, independence of dimensions or factor scores, and cultural sensitivity. Dijkers and colleagues have collected pilot data on a new version of the CIQ (CIQ-2) to address some of the limitations enumerated in Dijkers’ review article. Other measures of subjective well-being and health status, such as the Satisfaction with Life Scale (Diener, Emmons, Larsen, et al., 1985) and the SF-36 (Ware, Sherbourne, 1992), respectively, have shown promise for many other health conditions and are now being reported in the TBI research literature.

From a consumer viewpoint, functional outcome measurement (especially quality of life) is extremely important, yet concerns have been raised throughout the past decade that all too often assessment of functional outcome is based on staff or family ratings rather than on data derived directly from the person with a disability. Most researchers have assumed, perhaps erroneously, that persons with cognitive impairment are unreliable and inaccurate in rating their own behavior, particularly in more subjective areas. Several recent studies, however, suggest that this “conventional wisdom” may be without strong foundation. Studies conducted by Sander and colleagues (1997) have shown that persons with TBI and their families show high levels of concordance in their ratings on the CIQ and other measures of postacute functioning.

Given the enormous pressure on rehabilitation programs to demonstrate cost-effectiveness, there is a need to further refine functional outcome measurement to accurately reflect change over time, show sensitivity to the effects of all levels of injury severity across the lifespan, reflect the added value of rehabilitation in achieving meaningful outcomes, assess quality of life, and describe levels of client and family satisfaction with rehabilitation intervention.

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Consequences of Traumatic Brain Injury for the Family

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Recent analysis of the national Model Systems database (Harrison-Felix, Newton, Hall, et al., 1996) reveals that rehabilitation lengths of stay are decreasing and 9 of every 10 brain injury patients are discharged to home. Earlier discharges necessitate a greater in-hospital focus on physical and functional goals with fewer opportunities to address family members' emotional needs. Shorter hospital stays leave family members less time to recover from the emotional shock triggered by the initial injury. Furthermore, briefer rehabilitation stays allow less time for neurobehavioral recovery and discharge planning.

Despite staff members' best efforts to educate and prepare family members, many report feeling overwhelmed and ill-equipped to provide for the complex and changing long-term needs of the individual who sustained the brain injury (Gillen, Tennen, Affleck, et al., 1998; Hall, Karzmark, Stevens, et al., 1994; Jacobs, 1988). Traumatic brain injury typically affects the entire family system, disrupting relationships, communication, and sharing of responsibilities (Lezak, 1978; Kozloff, 1987; Kreutzer, Sander, Fernandez, 1997; Maitz, Sachs, 1995). At least since 1972, researchers have endeavored to study families after brain injury. Their research has focused on four primary areas: (a) family members' coping and psychological well-being, (b) family members' needs, (c) family functioning, and (d) changes in relationship status.

Family Members' Coping and Psychological Well-Being

The emotional distress of individual family members, particularly parents and spouses, has been documented, with depression and anxiety most frequently reported (Mauss-Clum, Ryan, 1981; Kreutzer, Gervasio, Camplair, 1994a; Waaland, Kreutzer, 1988). Increased use of tranquilizers, alcohol, and mental health counseling have been offered as indications of severe emotional distress (Livingston, 1987; Brooks, 1984).

Years ago, Panting and Merry (1972) suggested that spouses were more vulnerable than parents to emotional distress. Their assertion was supported by a series of investigations (Mauss-Clum, Ryan, 1981; Kreutzer, Gervasio, Camplair, 1994a; Gervasio, Kreutzer, 1997). For example, Mauss-Clum and Ryan documented the overwhelming consequences for wives. A majority of patients' wives reported problems with frustration, irritability, annoyance, depression, social isolation, anger, decreased time for self, and financial insecurity. Research also indicates that family functioning and personal well-being are correlated with the severity of neurobehavioral sequelae (Kreutzer, Gervasio, Camplair, 1994b).

Family Members' Needs

Mauss-Clum and Ryan (1981) were among the first to empirically investigate family needs following brain injury. Later studies by Mathis (1984) and Campbell (1988) addressed family members' needs soon after injury. To address concerns relating to reliability and validity, Kreutzer, Serio, Witol, and colleagues (1994c, 1995, 1996, 1997) developed the Family Needs Questionnaire (FNQ). The FNQ, composed of six empirically distinct scales (Serio, Kreutzer, Witol, 1997), allows family members to rate the perceived importance of each need and the extent to which each need has been met. A series of studies regarding family members' post-injury needs with the FNQ indicated that needs for information and support were ranked as most important but least often met (Kreutzer, Serio, Bergquist, 1994c; Witol, Sander, Kreutzer, 1996; Serio, Kreutzer, Gervasio, 1995). Serio, Kreutzer, and Gervasio (1995) found that the extent to which family members' needs are met is related to the quality of patients' neurobehavioral and neuropsychological functioning.

Family Functioning

Though overall family functioning is known to be affected by brain injury, few studies have examined the family unit. The Family Assessment Device (FAD) (Epstein, Baldwin, Bishop, et al., 1983) has been used by researchers to characterize changes in overall family functioning. Initially, the measure was developed to characterize psychiatric populations; more recently, the measure has been applied to neurological populations. Zarski, DePompei, and Zook (1988) helped establish the measure's validity with the brain injury population. The FAD comprises six scales complemented by a global scale, General Functioning. In a study of families after brain injury, Kreutzer and colleagues (1994b) found that families were most affected by adverse changes in communication and ability to provide reciprocal emotional support.

Changes in Relationship Status

Researchers have begun to investigate the effects of brain injury on relationships. Peters and colleagues (1992), using the dyadic adjustment scale, raised concerns about emotional expression and responsiveness, dyadic satisfaction, and cohesion, relating the severity of marital problems to injury severity. A few other investigators have focused on the stability of marital relationships. For example, Wood and Yurdakul (1997) studied a sample of 131 couples after brain injury. Only 42 percent of couples were able to sustain their relationship for more than 5 years after injury. Analysis revealed that the likelihood of maintaining a relationship was related to injury severity and length of relationship before injury.

Methodological Issues, Research Limitations, and Future Directions

Reliance on cross-sectional, single center methodologies. Most studies have examined selected participants in a single setting and collected information at a single point in time.

Proposed solution: Generalization of findings could be improved by employing longitudinal designs and selecting participants from geographically and ethnically diverse settings.

Use of assessment tools with uncertain reliability and validity. A number of researchers have developed their own assessment strategies without examining or demonstrating their psychometric properties. **Proposed solution:** Develop brain injury relevant, reliable, and valid instruments; incorporate reliable and valid measures used for other populations (e.g., stroke, psychiatric, and other medical disorders).

Failure to fully consider the influence of pre-existing psychosocial factors, comorbidities, and family members' characteristics on outcomes. **Proposed solution:** On a sufficiently large sample, collect data that may serve as a useful covariate or outcome predictor; information regarding outcome variations relating to ethnicity and minority status is particularly lacking.

Failure to consider the outcomes of family members other than primary caregivers. Information regarding patients' dependent children is especially lacking. **Proposed solution:** Investigate outcomes for more than one immediate family member.

Lack of validated family intervention protocols. Most research has focused on family members' post-injury status; there is a dearth of information regarding the efficacy of interventions to enhance the functioning of individual family members, the family unit, and spousal relationships. **Proposed solution:** Conduct a series of randomized multicenter trials evaluating treatment alternatives.

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Consequences of Traumatic Brain Injury for Functioning in the Community

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Corrigan (1994) proposed a quality of life framework for conceptualizing community integration following traumatic brain injury (TBI). The framework comprises six dimensions: health concerns, finances, residence and immediate community, productivity, intimate and other interpersonal relations, and self-direction.

Although each person's pre-injury circumstances, injury-related characteristics, and post-injury situation are highly unique, there are common barriers that arise because of similarities among the population of persons injured, typical ways in which the brain is affected, and frequently encountered impediments in society. Because other presenters will be addressing health, finances, and family issues, those dimensions, or aspects of dimensions, will not be addressed here.

Place of residence is a pressing concern for adults seeking to reestablish independence after TBI. It appears that a relatively small proportion of individuals are living in institutions at 1 year post-injury: 11 percent of the TBI Model Systems cohort (Harrison-Felix, Newton, Hall, et al., 1996), 2.4 percent of Coloradans hospitalized because of TBI (Whiteneck, Brooks, 1998). Though infrequent, placement of a young person in a long-term care facility is one of the most costly negative outcomes that can occur after TBI (General Accounting Office, 1998). A more frequent concern with regard to residence is the ability of adult children who are living with parents to live more independently; 35 percent of Model Systems subjects lived with parents at 1 year post-injury (Harrison-Felix, Newton, Hall, et al., 1996). Brzuzy and Corrigan (1996) found that adults living with parents were somewhat younger, more recently post-injury, less educated, more likely to have been living with parents pre-injury, and had higher current incomes. Perhaps most striking from this study was the finding that 98 percent of those living alone had lived with parents an average of 3 years before moving out on their own. While the availability of affordable housing is one aspect of this problem (Foley, Lehmkuhl, 1994), a significant barrier is presented by the lack of support services when a person wishes to live on his or her own. Wright (1993) predicted that in the next 20 years, government agencies will experience unprecedented demands for assistance in living independently as family caregivers age.

When gainful employment is sought, outcomes are poor. Dikmen and colleagues (1994) found that among patients with severe brain injuries who had been employed before their injuries, only 37 percent were employed 2 years later. Among Coloradans hospitalized because of TBI, 14.7 percent failed to return to work by 1 year post-injury (Whiteneck, Brooks, 1998). Employment outcomes in the TBI Model Systems data set indicated that among persons working before injury, less than 40 percent were employed at any of the annual followups 1 to 4 years

post-injury (Sander, Kreutzer, Rosenthal, et al., 1996). Brooks and colleagues (1987) used a cross-sectional design to study persons with closed head injuries who were 2 to 7 years post-injury. While 86 percent of their subjects had been employed before injury, only 29 percent were employed at followup. Tashjian and Hayward (1993) found that timing of referral to the State-Federal vocational rehabilitation system was significantly delayed for persons with traumatic brain injuries, averaging 7 years post-injury among 2,700 cases reviewed. The decision about when to start vocational rehabilitation may be one of the most important made in the post-acute setting; however, it is one of the least studied.

The rate of return to school is quite high because of the Federal requirement for a public education regardless of disability for persons younger than age 22 who have not received a high school diploma. Among Coloradoans hospitalized because of TBI, only 2.6 percent failed to return to school 1 year post-injury (Whiteneck, Brooks, 1998). Despite the accessibility of primary and secondary education, the quality of transitional activities and supporting services varies greatly from school district to school district (DiScala, Osberg, Savage, 1997). Parents and advocates often experience resistance due to lack of funds to address individual needs, as well as lack of knowledge or support among instructional, administrative, or other professional staff. The tools needed for effective support exist; however, utilization of this knowledge does not appear to be widespread (DePompei, Blosser, 1991; DePompei, Blosser, 1997).

As time proceeds post-injury, an individual's social network constricts, and the intensity of time spent with family increases as other social contacts are lost (Jacobs, 1988; Kozloff, 1987; Brzuzy, Speziale, 1997). This constriction is not optimal for the individual or the family, and both end up feeling isolated (Morton, Wehman, 1995; Wallace, Bogner, Corrigan, et al., 1998). Social support is consistently found to correlate with life satisfaction (Diener, Larsen, 1993; Fuhrer, Rintala, Hart, et al., 1992). Among Coloradoans 1 year after hospitalization for TBI, 37.6 percent scored below criterion on the Social Integration scale of the Craig Handicap Assessment and Reporting Technique (CHART) (Whiteneck, Charlifue, Gerhart, et al., 1992), the largest proportion for any of the six CHART dimensions (Whiteneck, Brooks, 1998). Problems initiating and maintaining intimate relationships present a significant barrier to many young adults who experience TBI.

Life satisfaction appears to be dynamic in the first few years following brain injury, perhaps declining before improving 4 to 5 years post-injury (Corrigan, Smith-Knapp, Granger, 1998). Perceived control over the important aspects of one's life has shown the highest correlation with life satisfaction in other disability groups (Fuhrer, Rintala, Hart, et al., 1992; Schultz, Decker, 1985). Adults want to have options and the freedom to choose among them. Choices made toward optimizing quality of life after TBI are limited by lack of options, lack of information, and lack of assistance in access to or coordination of services. Available options may also be limited by discrimination. Fuhrer and colleagues (1992) have suggested that perceived control is an important psychological variable that may mediate the relationship between actual loss of function and life dissatisfaction due to that loss.

Community integration will be optimal when existing service delivery systems can collaborate to maximize personal options. Although each person's life, lifestyle, and situation

are unique, systems of support have to be in place to allow individualized answers. The systems that affect a person's choices are multiple and varied, formal and informal; they include the person's family, the local community, advocacy organizations, health care (including medical rehabilitation), vocational rehabilitation, public and private education, entitlement programs, social service agencies, and public transportation. In most cases, the service delivery systems are large and persons with brain injury are infrequent users so that their unique needs may be easily neglected or their access severely limited. Still, finding methods to increase the successful negotiation of existing systems of human service should be a high priority for addressing long-term functioning in the community.

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Receptor-Based Mechanisms of Functional Recovery

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Delayed or secondary neuronal damage following traumatic injury to the central nervous system (CNS) may result from an upregulation, release, or induction of a number of potentially damaging and/or reparative endogenous neurochemical factors. Recent studies have attempted to integrate the temporal pattern of activation of these injury factors in an attempt to draw a coherent profile of the response of the nervous system to trauma. Recent evidence from clinically relevant experimental models of traumatic brain injury (TBI) suggests that widespread and diffuse neuronal damage and loss may be progressive and prolonged for months to years after the initial insult in selectively vulnerable brain regions of the cortex, hippocampus, thalamus, striatum, and subcortical nuclei. The development of new neuropathological and molecular techniques has generated new insights into the cellular and molecular sequelae of TBI. This presentation reviews the literature suggesting that neurochemically induced receptor activation of receptors on nerve cells results in alterations in intracellular calcium with resulting changes in gene expression, activation of intracellular proteases (calpains), alteration in neurotrophic factor expression profiles, and activation of cell death genes (apoptosis) that may play a role in mediating delayed cell death after trauma. A working knowledge of these molecular and cellular alterations will guide the development of novel therapeutic strategies that will be important for future guidelines regarding the rehabilitation and treatment of people with TBI.

Calcium and Calcium Channels

For more than two decades, it has been argued that alterations in brain calcium homeostasis and membrane receptors/channels associated with calcium entry into cells are associated with regional brain swelling (edema), vasospasm, and delayed cell death following traumatic CNS injury. Several studies, using preclinical models of TBI, have reported that profound global alterations in calcium persist for several days following trauma (Fineman, Hovda, Smith, et al., 1993; Nilsson, Gazelius, Carlson, et al., 1996; Nilsson, Laursen, Hillered, et al., 1996). The role of voltage-sensitive calcium channels (VSCC) in mediating cellular damage and dysfunction associated with brain trauma can be indirectly inferred from studies employing calcium channel antagonists such as (S)-emopamil that have been shown to attenuate neurological motor and cognitive dysfunction and improve regional cerebral blood flow to injured brain regions following experimental TBI (Okiyama, Smith, Thomas, et al., 1992).

Glutamate Receptors and Calcium-Mediated Damage

The release of excitatory amino acid neurotransmitters glutamate and aspartate can activate specific receptors that are coupled to a sodium/calcium ion channel, thereby causing

increased influx of these cations into the nerve cell. Both experimental and clinical studies have now documented that glutamate is massively released for a prolonged period following TBI (Bullock, Fujisawa, 1992; Faden, Demediuk, Panter, et al., 1989; Globus, Alonso, Dietrich, et al., 1995; Katayama, Becker, Tamura, et al., 1990). Moreover, more than 30 preclinical studies have been published that demonstrate the efficacy of competitive and noncompetitive glutamate receptor antagonists, as well as presynaptic blockers of glutamate release in the treatment of experimental TBI (McIntosh, Juhler, Wieloch, 1998; Hayes, Jenkins, Lyeth, et al., 1988).

Calcium-Mediated Cytoskeletal Proteolysis

The intracellular enzyme calpain, which is irreversibly activated when calcium levels increase above a certain threshold, can proteolyze a wide range of cytoskeletal proteins involved with the architectural support of the nerve cell, thereby destroying the internal architecture of the cell. Calpain activation following brain trauma has been reported (Liu, Salminen, He, et al., 1994), and calpain-induced degradation of the cytoskeletal proteins spectrin and microtubule-associated protein 2 (MAP-2) has been demonstrated to occur for weeks following experimental TBI (Newcomb, Kampfl, Posmantur, et al., 1997; Saatman, Coyne-Bozyczko, Marcy, et al., 1996; Hicks, Smith, McIntosh, 1995; Lewen, Li, Olsson, et al., 1997; Posmantur, Hayes, Dixon, et al., 1994; Posmantur, Kampfl, Taft, et al., 1996; Posmantur, Kampfl, Liu, et al., 1996; Povlishock, Christman, 1995). Therapeutic strategies to block or antagonize the proteolytic effects of calpain on the cytoarchitecture of the cell have demonstrated significant improvement in both posttraumatic motor and cognitive dysfunction associated with experimental TBI (Saatman, Murai, Bartus, et al., 1996; Posmantur, Kampfl, Siman, et al., 1997).

Apoptosis and Programmed Cell Death Pathways in TBI

It has been hypothesized that the diffuse and progressive cell death observed following brain trauma may be related to the induction of programmed cell death (PCD) that involves the initiation and active expression of new genes and proteins. During development of the nervous system, PCD and its morphological hallmark apoptosis represent the primary mechanism of cell death. Rather surprisingly, new evidence suggests that traumatic injury to the CNS will reactivate these developmental programs that, unfortunately, result in cell death. Several studies have now documented the progressive regional and temporal pattern of apoptotic cell death in experimental models of TBI (Rink, Fung, Trojanowski, et al., 1995; Colicos, Dixon, Dash, 1996; Conti, Raghupathi, Lee, et al., in press). Therapeutic strategies focusing on trophic factor replacement have resulted in encouraging preclinical data demonstrating a reduction of cell death and improvement in neurobehavioral function. Further work must be directed at unraveling and understanding the complex molecular and cellular cascades following brain trauma to stimulate new therapeutic advances to aid in the rehabilitation and recovery of function of persons with brain injuries.

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Cellular Mechanisms of Recovery

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In the study of the cellular mechanisms of recovery from traumatic brain injury (TBI), most researchers have relied on lesioning and/or ablation models to remove various areas of the brain to evaluate either local circuit or downstream target reorganization. Although such experimental paradigms have provided insight into the potential recovery associated with focal lesions in TBI, such as contusion and/or hematoma formation, they provide little insight into either the damaging consequences or recovery associated with some of the more diffuse or generalized changes occurring in the TBI that may be major players in long-term morbidity. Such changes include diffuse axonal injury with subsequent diffuse deafferentation and traumatically induced neuroexcitation that can lead to abnormal agonist-receptor interactions (reviewed by Dr. McIntosh). As will be explicated in this presentation, diffuse axonal injury involves the process of widespread, delayed axotomy that translates into target deafferentation within 24 to 48 hours of injury. Importantly, this delayed axotomy and deafferentation frequently occur concomitant with neuroexcitatory-mediated events that can further complicate the pathobiology of TBI, particularly in relation to the ensuing recovery process.

Traumatically Induced Axonal Injury

As recently as 15 years ago, it was assumed that the tensile forces of TBI were so severe as to mechanically tear axons throughout the brain and cause an expulsion of their axoplasmic mass to form large reactive axonal swellings. More contemporary studies in animals and humans, however, have shown that this is not the case (Povlishock, Jenkins, 1995; Maxwell, Povlishock, Graham, 1997; Povlishock, Marmarou, McIntosh, et al., 1997; Pettus, Povlishock, 1996; Okonkwo, Pettus, Moroi, et al., 1998). Rather severe TBI evokes discrete, focal changes in the axolemma's permeability, allowing for the local influx of calcium. This triggers the subaxolemmal activation of calpain-mediated spectrin proteolysis, which, over time, further modifies the axolemmal properties to allow for continuing calcium influx. This then leads to a perturbation of the intra-axonal cytoskeleton with neurofilament and microtubular modification that impairs axoplasmic transport over a 6- to 24-hour period, thereby contributing to axonal swelling and detachment. The detached axonal segment undergoes Wallerian degeneration, with the concomitant degeneration of those synaptic terminals originating from the injured axon (Erb, Povlishock, 1991). Because this axonal swelling and disconnection is a delayed post-injury process, hope exists for therapeutic intervention. Recent experimental studies in this area have provided considerable promise by showing that early as well as delayed moderate hypothermia (32 °C) can block the progression of the axonal swelling and disconnection by stabilizing the axolemma and blunting the progression of the calpain-mediated spectrin proteolysis (Koizumi, Povlishock, in press). In addition, the use of cyclosporin A, which blocks the mitochondrial permeability transition pore, also appears to afford considerable axonal protection (Okonkwo,

Povlishock, in press). In this case, cyclosporin A has been demonstrated to protect mitochondria in the injured axons, thereby providing the energy necessary to maintain membrane pumps and restore the disordered axolemmal permeability change. Although in our estimation both therapeutic approaches are provocative, they do require more extensive preclinical evaluation before these strategies can be taken into the clinical setting.

The Consequences of Traumatically Induced Axonal Injury

As noted previously, traumatically induced delayed axonal injury results in axonal disconnection and the loss of the synaptic terminals originating from the damaged axons. In the case of mild to moderate TBI, this delayed axotomy and deafferentation, which occur within 24 to 48 hours of injury, set the stage for adaptive recovery. In the case of mild to moderate TBI, the diffuse axonal injury translates into diffuse terminal loss (Erb, Povlishock, 1991). In this situation, the diffuse deafferentation occurs in relation to many unaltered/intact fibers that subsequently sprout to reoccupy, over several months, the previously deafferented domains (Erb, Povlishock, 1991). In mild to moderate TBI, this deafferentation followed by synaptic sprouting appears adaptive because in most cases the same neurotransmitter population returns to the previously deafferented site (Erb, Povlishock, 1991). This process of terminal loss and recovery is entirely consistent with morbidity and subsequent recovery typically seen following mild TBI in humans, suggesting that those events seen in experimental animals are operant in humans. Although these events explain the morbidity and recovery associated with mild injury, they do not explain the more limited and/or maladaptive recovery associated with severe TBI. Admittedly, severe injury is typically associated with secondary insults such as hypoxia and/or hypotension that can complicate morbidity and recovery. Yet, there is now increased recognition that the diffuse deafferentation occurring with severe injury is also most likely superimposed on synaptic target sites that have already been modified by the traumatically induced neuroexcitation, suggesting another confounding factor.

The Interaction of Traumatically Induced Neuroexcitation and Deafferentation in the Process of Posttraumatic Recovery

As noted above, there is a strong suggestion that TBI may involve both the induction of neuroexcitation and target deafferentation that together translate into a less-than-optimal recovery. Although this suspicion is based on human clinical studies, the precise confirmation of this premise, particularly in animal models, has remained elusive because it is difficult to dissect out the interaction of these events in a complex disease state such as TBI. To obviate this problem, we have attempted to recreate this scenario in vivo using a paradigm of isolated traumatically induced neuroexcitation followed by controlled deafferentation (Phillips, Lyeth, Hamm, et al., 1994). In this experimental paradigm, animals are subjected to TBI capable of evoking neuroexcitation without significant diffuse axonal injury, followed 24 hours later by select lesioning of entorhinal projectional systems that target the dentate gyrus of the hippocampus. These procedures are followed by anatomical, behavioral, and electrophysiological studies to assess the subsequent neuroplastic responses occurring within the hippocampal dentate gyrus. Unlike the above-described adaptive neuroplastic responses seen in

mild TBI, the combination of neuroexcitation followed by deafferentation results in unanticipated synaptic rearrangement within the dentate gyrus. In this situation, the major dentate synaptic input moves from the outer and inter molecular layers now to be confined to the middle molecular layer (Phillips, Lyeth, Hamm, et al., 1994). This synaptic rearrangement is associated with change in the dentate granule cell dendritic trees in terms of their orientation and number. Furthermore, these changes are associated with profound and enduring behavioral morbidity reflected in impaired spatial memory assessed via the use of the Morris water maze (Phillips, Lyeth, Hamm, et al., 1997). These same animals also demonstrate parallel electrophysiological deficits reflecting a persistent impairment in long-term potentiation (LTP) of the evoked population postsynaptic potentials (Reeves, Zhu, Povlishock, et al., 1997). Interestingly, these anatomical, behavioral, and functional changes were effectively blunted through the use of various glutamate receptor antagonists when given at the time of entorhinal lesioning/target deafferentation (Phillips, Lyeth, Hamm, et al., in press). When given pre-TBI, these same agents did protect spatial memory; however, this protection did not persist beyond 15 days post-injury (Phillips, Lyeth, Hamm, et al., 1997). Only when the glutamate receptor antagonists were given at the time of deafferentation was spatial memory retained over a prolonged posttraumatic period (Phillips, Lyeth, Hamm, et al., in press). These findings speak to the complexity of the issues involved in the recovery phases of TBI and suggest that future therapeutic approaches must include early as well as delayed interventions targeting specific TBI-generated pathologies. Also, our recent finding that dopamine agonism may exert similar protection, presumably through interaction with N-methyl D-aspartate receptors, speaks to the likelihood that future therapeutic studies will likely involve polypharmacia at specific times post-injury.

Summary and Recommendations

The above passages speak to the complexity of the initial pathology and recovery associated with traumatic brain injury. Recent work suggests the potential for therapeutic intervention to influence either the initial morbidity or recovery associated with TBI. Although considerable progress has been made, much remains to be done.

Recommendations:

1. The precise pathobiology of traumatically induced axonal injury and the maladaptive neuroplastic responses evoked by the combination of traumatically induced neuroexcitation and axonally linked deafferentation must be confirmed in higher order, gyrencephalic animals.
2. The temporal sequence of the progression of the above-described axonal and deafferentation-mediated responses observed primarily in rodents must be evaluated in higher order animals to determine whether their temporal progression is the same or more elongated. Furthermore, within the given temporal framework seen in higher order animals, there will be the need to repeat the above-described therapeutic studies to determine whether they have similar efficacy.

3. Lastly, there is a need to continue detailed investigative studies on the pathobiology of the axotomy and subsequent deafferentation/neuroexcitation-mediated changes. Such studies are necessary for understanding the precise mechanisms involved in the above-described pathologies. Such information is integral to designing more focused therapeutic interventions in order to more favorably impact outcome.

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Neuroplasticity, Experience, and Mechanisms of Brain Information Storage

William T. Greenough, Ph.D.

The developing brain appears to use two basic mechanisms for the storage of information. Relatively early in development, many brain regions *overproduce synapses* (e.g., Cragg, 1975; Huttenlocher, Dabholkar, 1997). Subsequently, experience directs *pruning* and *selective stabilization* of a subset from this population to generate neural organization, a process Black and Greenough (1986) termed “experience-expectant” brain information storage. This process takes advantage of information readily available in the normal experience of all members of a species, such as the availability of patterned binocular visual experience in the development of the visual system (e.g., LeVay, Wiesel, Hubel, 1980). Even parts of very long pathways connecting distant regions of the nervous system may be entirely withdrawn in some cases (Stanfield, O’Leary, 1985). In at least some cases, the presence of these “extra” connections allows for responses to brain damage that are not possible in later life; that is, connections that would normally be lost can be preserved and can subserve functions that would otherwise be lost as a result of damage (e.g., Hicks, D’Amato, 1975).

The second mechanism, “experience-dependent” brain information storage (Black, Greenough, 1986), persists from development into adulthood and probably subserves much of the effect of therapeutic intervention directed at brain damage, as well as what we call learning and memory. In contrast with experience-expectant processes, there is no evident anticipatory buildup of synapses in experience-dependent information storage; rather, *new synapses are generated* in response to experiences that provide opportunities for *learning*. The classic example of this is the increase in dendritic field size and in the number of synapses per neuron that occurs in various brain regions, such as the visual cortex, of rats reared in, or placed as adults in, a complex (sometimes termed “enriched”) environment, compared with rats housed individually or in small groups in standard cages (Volkmar, Greenough, 1972; Turner, Greenough, 1985). Such animals also exhibit increased amounts of astrocyte per neuron, which is more closely associated with synapses (Jones, Greenough, 1996) and increased brain vascularization, the latter falling off with increasing age of the animals when first placed in the environment. It is assumed that these brain changes are related to the superior performance exhibited by these animals in various learning tasks (e.g., Juraska, Henderson, Muller, 1984).

The synaptic increases appear to be driven specifically by learning, whereas vascular increases appear to be driven by activity. Black and colleagues (1990) found that animals that learned motor skills but were involved in a minimum of physical activity added synapses to the cerebellar paramedian lobule while exhibiting no changes in the density of vascularization, whereas animals that exercised vigorously but learned little exhibited increased vascular density but no synapse addition. Astrocytic increases appeared to be associated with the addition of synapses. Both the synaptic effects and the enhanced behavioral performance persisted for

4 weeks (the only interval examined) in the absence of continued training, whereas the astrocytic effects declined.

These processes appear to mediate functional recovery or compensation in model systems involving brain damage. For example, when the forelimb region of somatosensory-motor cortex is damaged unilaterally in rats, there is an increase in dendritic field size and the number of synapses per neuron in the intact contralateral forelimb cortex which is dependent upon the use of the forelimb governed by the intact cortex (Jones, Kleim, Greenough, 1996). Behaviorally, there is increased dependence on the forelimb governed by the intact cortex (Jones, Schallert, 1994). It should be noted that therapy directed at the damaged hemisphere that begins too soon following damage can actually exacerbate the damage (Kozlowski, James, Schallert, 1996). A second example of therapeutic intervention involves a model of human fetal alcohol exposure, in which rats are exposed postnatally to “binge-like” alcohol treatment that results in the loss of cerebellar Purkinje and granule neurons and severe motor deficits. Exposure of these animals, as adults, to a motor skill learning paradigm increased the number of synapses on the remaining Purkinje neurons and therapeutically enhanced performance on a number of tests of motor ability. These findings provide insight into the mechanisms underlying effects of therapeutic intervention and encourage broader efforts to develop rehabilitative procedures appropriate to different types of brain damage and different aspects of the recovery process (e.g., compensatory change vs. restoration of function).

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The Cognitive and Behavioral Mechanisms Underlying Recovery From Traumatic Brain Injury at Different Stages After Injury

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Recovery from traumatic brain injury (TBI) is affected by different mechanisms. It is essential to unveil the factors that result in variance in outcome. The discovery of these factors will assist diagnostic, prognostic, and rehabilitation efforts.

Three areas are reviewed that may shed light on how to dissociate the causes of differential outcome. In the acute stage of recovery, there is a *cognitive recovery cascade*, which refers to different cognitive mechanisms recovering at different stages. These are likely related to different pathophysiological mechanisms. Recovery of ongoing memory can be predicted with greater accuracy in the acute stage (termination of posttraumatic amnesia [PTA]) if a *multivariate approach* is used that considers multiple determinants of outcome. After TBI, patients are variable in performance of certain tasks. This *variability of performance* may be not only a factor affecting the study of mechanisms but also an avenue to one or more important mechanisms.

Cognitive Recovery Cascade

Hospitalized patients with different levels of severity of injury were prospectively followed from date of injury to recovery of memory over a period of 24 hours. During this period, a number of simple tests of attention, orientation, and memory were administered until perfect performance was achieved on each of the tests. The tests varied in levels of complexity.

In the patients with mild TBI (Glasgow Coma Score [GCS], 13 to 15), there was a distinct pattern of recovery of cognitive functions. Simple attention recovered first. The memory tasks recovered in the following order: orientation, recognition, and spontaneous recall. All the administered attentional tasks recovered before the patients were able to recall three words over 24 hours.

In the patients with severe TBI (GCS < 9), the pattern was similar, but the differences among the various cognitive measures were not always as clearly significant.

This type of cognitive dissociation may provide a window on potential differential pathophysiological mechanisms underlying recovery. For example, in patients with mild TBI, the pathology would likely be less severe diffuse axonal and perhaps brain stem injury, usually without focal pathology (Jane, Steward, Gennarelli, 1985; Oppenheimer, 1968; Povlishock, Becker, Cheng, et al., 1983). Such an injury would result primarily in an attentional deficit,

without a true amnesia. In the more severely damaged patients, the commonly observed temporal and frontal lobe damage could result in both attentional problems and true amnesia.

Perhaps most important, cognitive dissociations may be used to direct timed pharmacological interventions (Arnsten, Smith, in press).

Multivariate Approach to Prediction of Recovery

Improvement in accuracy of prediction of recovery from PTA would significantly enhance clinical care. Identifying the role of specific predictors provides a framework to investigate the pathophysiological basis of recovery. In a prospective study of TBI recovery, the author used a multivariate approach that started with a designated measure of recovery, in this case, the ability to recover three words after a 24-hour delay. The technique, called the Classification and Regression Tree (Breiman, Friedman, Olshen, et al., 1984), allows potential predictor variables to be used repetitively. As a consequence, the use of the relevant variance in a measure is maximized.

This analysis revealed multiple subgroups in the time to recovery of continuous memory. This differentiation of subgroups facilitated prediction in the acute recovery period. Age, duration of loss of consciousness, and the GCS at 6 hours provide the most discrimination information. The more refined subgroups have two advantages above and beyond the improved accuracy for short-term prediction of outcome. First, these might allow a finer distinction for prediction of longer term outcome. Second, the subgroups could be an additional aid to improving understanding of the pathophysiological mechanisms of recovery, at least in the short term.

Variability of Performance

In a study of TBI patients, in an attempt to show reliability of research findings by testing patients 2 weeks in a row, the author stumbled on a most interesting result. On a measure of focused attention, patients showed remarkably different performance between the two test sessions (Stuss, Stetham, Hugenholtz, et al., 1989). Curiously, this was not a practice or learning effect. The patients had performed the task appropriately the first week (albeit more slowly than did matched controls) but were impaired the second week. In essence, the results were not reliable.

At the same time, analysis was made of the results of a prospective study of individuals who had suffered concussion (Hugenholtz, Stuss, Stetham, et al., 1988). The same reaction time paradigm was used and the test was repeated five times over 3 months. The variability of performance was again evident, but less severe. In essence, this was replication of apparent unreliability. This evidence, on reflection, was consistent with the author's clinical experience. Patients with TBI often had the skills to complete a job yet somehow were often dismissed after a short period. They were not consistent in completing tasks or in how they did tasks.

A finer investigation of stability of performance indicated that the patients were not just variable in all things they did (Stuss, Pogue, Buckle, et al., 1994). Their performance was stable on most automatic tasks. The important factor appeared to be the sustaining of top-down control processes. Task demands are a major factor causing variability of performance (Shammi, Bosman, Stuss, 1998). A further cross-sectional study comparing patients with severe TBI at 5- and 10-year followup revealed that at 10 years the variability had decreased, although the speed of response had not (Hetherington, Stuss, Finlayson, 1996).

The discovery of variability of performance in TBI subjects raises several questions: What is the mechanism for this? Is it possible that there are several mechanisms, perhaps underlying different types of variable performance? How does this affect performance on other cognitive tests, and what are the implications for neuropsychological testing?

In conclusion, the review of these three areas highlights the differences in timing and expression of different cognitive and behavioral disturbances after traumatic brain injury and provides a potential framework for correlation with the pathophysiological mechanisms. Perhaps more important, these data have significant clinical implications.

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Agency for Health Care Policy and Research Evidence-Based Practice Report

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Traumatic brain injury (TBI) is the number one cause of morbidity and mortality in adults younger than 45 years of age. For persons with TBI, the process of recovery begins at the time of injury and lasts the rest of their lives. Acute care has made marked advances recently in improving not only the rate of survival but also the level of function of persons with TBI. As such, the need for TBI rehabilitation is increasing steadily. In addition, the scope and complexity of TBI rehabilitation is also expanding.

Methods

The purpose of this study was to produce an evidence-based analysis of TBI rehabilitation. It was performed under contract between the Agency for Health Care Policy and Research (AHCPR) and the Oregon Health Science University's Evidence-Based Practice Center (OHSU EPC). In order to convert the question of TBI rehabilitation into a form amenable to proper, thorough evidence-based analysis, the focus of this work was directed toward five distinct TBI rehabilitation questions designed to address issues spanning the entire course of recovery.

The five questions specifically addressed in this work were:

1. Should interdisciplinary rehabilitation begin during acute hospitalization for TBI?
2. Does the intensity of inpatient interdisciplinary rehabilitation affect long-term outcomes?
3. Does the application of cognitive rehabilitation enhance outcomes for persons who sustain TBI?
4. Does the application of supportive employment enhance outcomes for persons with TBI?
5. Does the provision of long-term care coordination enhance the general functional status of persons with TBI?

Regarding the literature review, a MEDLINE search was undertaken (1976 to 1997), supplemented by searches in HealthSTAR (1995 to 1997), CINAHL (1982 to 1997), and PsychINFO (1984 to 1997). This produced a total of 3,098 references to be considered for

inclusion. Of these, 569 applied to questions one and two, 600 applied to question three, 392 applied to question four, and 975 applied to question five. Each abstract was reviewed and rejected only if it was clearly inappropriate. The inclusion criteria were explicit and fairly broad. If the abstract suggested that the article was eligible, or if it did not contain sufficient information to determine eligibility, the full text of the article was retrieved for review. We retrieved 87 abstracts pertaining to questions one and two, 114 articles pertaining to question three, 93 articles pertaining to question four, and 69 articles pertaining to question five passed the eligibility screening. An additional 67 articles were recommended for inclusion by experts for review of reference lists of review articles. This resulted in a list of 363 articles for retrieval from the library for review and abstraction.

Subcommittees were formed to review all of the eligible articles relevant to each individual question. All articles were reviewed by all members of the subcommittees and ranked according to scientific and statistical validity using a 3-point rating scale. Class I included only well-designed randomized control trials (RCTs). Class II included RCTs with design flaws, well-done prospective quasi-experimental or longitudinal studies, and case-control studies. Class III reports included case reports, uncontrolled case series, and expert or consensus opinion. These classifications were used to determine key articles for each of the research questions which were then reviewed in depth by all members of the subcommittees. At several stages of analysis, the progress of each subcommittee was reported to the entire OHSU EPC committee, a national committee of experts, and other resource groups (including the Aspen Neurobehavioral Conference [see below]). In June 1998, a preliminary draft of the entire analytic process was submitted for review by the AHCPR and 25 peer reviewers, including officials of relevant professional organizations, national TBI rehabilitation experts, and authors of key articles on each topic. Peer reviewers' comments were then collected and considered in detail in forming the final document, which was submitted to the AHCPR in July 1998.

During the course of analysis of the literature, it became apparent that fundamental problems of research design are highly common and extremely detrimental to TBI rehabilitation studies. A special effort was made to address these problems. A group of experts from disciplines spanning the spectrum of TBI rehabilitation was convened at the fourth annual Aspen Neurobehavioral Conference held in Aspen, Colorado, in April 1998. This group specifically addressed problems inherent in current TBI rehabilitation research design and formulated a set of specific recommendations for addressing these issues.

Results

Question 1. Should interdisciplinary rehabilitation begin during acute (“trauma center”) hospitalization for traumatic brain injury?

A single, small observational study evaluated this question using retrospective analysis. They compared formalized, physiatrist-driven multidisciplinary rehabilitation versus “nonformalized” rehabilitation performed during the acute stay at the trauma hospital (Mackay, Bernstein, Chapman, et al., 1992). Their dependent variables were a combination of physiologic

and cognitive outcome measures. They concluded that formalized, multidisciplinary, physiatrist-driven rehabilitation should be considered as soon as possible following trauma center admission. Unfortunately, the lack of multivariate compensation for confounding variables weakens the strength of this study as does the lack of long-term followup. The overall level of evidence is class III and deals only with adult patients with severe brain injury (Glasgow Coma Scale 3-8).

Question 2. Does the intensity of inpatient interdisciplinary rehabilitation affect long-term outcomes?

Since this question assumes efficacy of direct inpatient TBI rehabilitation in general, this issue was addressed first. Only one controlled study assesses the effectiveness of acute inpatient TBI rehabilitation. This quasi-experimental study used an unmatched control group without formal inpatient rehabilitation compared with a group at a specialized inpatient brain injury program that received formal, physiatrist-driven, multidisciplinary rehabilitation (Aronow, 1995). Both physiologic- and psychosocial-dependent variables were measured. This study suggested that direct transfer to a formal inpatient rehabilitation setting was associated with improved outcome and decreased cost of care. Unfortunately, the two patient cohorts differed significantly along a number of variables, and their overall prediction model did not possess much power. This class III study, however, is the only controlled study of the efficacy of early inpatient TBI rehabilitation and does provide some degree of support.

The question of how early acute inpatient TBI rehabilitation achieves its positive results is unanswered. There have been attempts to address this issue by assessing the correlation between intensity of treatment and outcome, where intensity is measured as hours of individual or grouped therapeutic modalities. Three studies address this, one class II (Heinemann, Hamilton, Linacre, et al., 1995) and two class III (Blackerby, 1990; Spivack, Spettell, Ellis, et al., 1992). The class II study used prospectively collected data but suffered from an unspecified definition of TBI, no control for severity of injury, and lack of long-term followup. Overall, it did not support an interaction between treatment intensity and outcome except for a relationship between intensity of psychological services (generally delivered as cognitive therapy) and cognitive Functional Independence Measure (FIM) scale scores as measured at discharge from inpatient rehabilitation.

The two class III studies both used retrospective databases and were weakened by unspecified definitions of TBI, lack of multivariate control for confounding variables, and absence of long-term followup. In addition, the Blackerby study was confounded by programmatic changes that strongly interacted with intensity of therapy. None of these studies provided convincing evidence of a correlation between intensity of therapy and improvement attributable to inpatient rehabilitation.

A major problem with this area of study is the definition of intensity of therapy in terms of hours of delivered treatment. It is quite possible that time alone is not the proper axis along which to define intensity. Unfortunately, this issue cannot be resolved using the present data

since the above studies were prone to missing a significant relationship should one exist (a Type II error), because of their methodological weaknesses.

From a clinical aspect, the evidence does not support equating different TBI rehabilitation delivery systems on the basis of equivalent times of patient exposure to various therapeutic modalities. For example, this analysis would not support predicting that patient benefit would be equivalent if an equal time spectrum of rehabilitation therapies was delivered at a rehabilitation center as compared with a skilled nursing facility. More detailed analysis of factors involved in predicting response to rehabilitation modalities must be considered in approaching such questions.

Additionally, mandating a minimum number of hours of applied therapy for all persons with TBI is not supported by the present state of scientific knowledge. The issue of how much of which interventions optimizes recovery in a given type of patient remains inadequately studied. It is certainly reasonable to avoid situations in which patients do not receive potentially beneficial treatment. Based on the above studies, however, defining a minimal rehabilitation program in terms of time of applied therapy is not likely to optimize either therapists' time or patients' recovery. It is probable that specific basic programs would have to be related to individual patient groups. Developing such algorithms requires future research.

Question 3. Does the application of cognitive rehabilitation enhance outcomes for persons who sustain TBI?

In terms of the relationship between cognitive rehabilitation and health outcomes, there are five RCTs (Helffenstein, Wechsler, 1982; Neistadt, 1992; Novack, Caldwell, Gage, et al., 1996; Ruff, Niemann, 1990; Schmitter-Edgecombe, Fahy, Whelan, et al., 1995). Two studies examined compensatory cognitive rehabilitation (CCR), one examined restorative cognitive rehabilitation (RCR), and two used a combination of CCR and RCR. Only the Schmitter-Edgecombe study included long-term outcome (6 months). The rest of the studies had short or no followup testing. Two of the studies (Helffenstein, Wechsler, 1982; Schmitter-Edgecombe, Fahy, Whelan, et al., 1995) showed there was some effect of cognitive rehabilitation. The strongest evidence for a positive result came from the use of physical adaptive devices to reduce everyday memory failures, although the long-term durability of this effect is questionable. Furthermore, some data suggest that CCR consisting of interpersonal process recall might produce some improvements on anxiety and self-concept scales (Helffenstein, Wechsler, 1982). Other studies did not show a strong correlation between cognitive rehabilitation and health outcomes. These studies were confounded, however, by apparent spontaneous recovery and by the unclear definition of appropriate control groups.

There was also one observational class II study that directly measured health outcomes (Wilson, Evans, Emslie, et al., 1997). This study used a case-control (a-b-a) design to test the ability of individually adapted reminder devices (Neuropage) to enhance memory. A significant decrease in everyday memory failures was associated with use of the device.

When indirect measures of improvement were used, there was no direct evidence from randomized trials for the effect of cognitive rehabilitation on employment. Both RCTs and

comparative studies provide support for an association between cognitive rehabilitation and intermediate measures of cognitive function. Two class I trials suggest that the restorative technique of practice with and without the use of a computer may improve short-term recall on laboratory tests of memory (Kerner, 1985; Twum, Parente, 1994). There is some evidence from comparative studies that certain cognitive rehabilitation methods improve performance on neuropsychological tests and other laboratory data-based methods of evaluating cognitive function (Gray, Robertson, Pentland, et al., 1992; Thomas-Stonell, Johnson, Schuller, et al., 1994; Wood, Fussey, 1987). Unfortunately, there are no studies meeting the criteria for this review that support an association between laboratory-based measures of cognitive function and health outcomes such as functional independence, activities of daily living, or measures of everyday memory.

Overall, very few controlled studies of cognitive rehabilitation have examined direct effects on health outcomes or employment. Of the six studies that directly addressed health outcome, three showed positive effects, supporting cognitive rehabilitation particularly when it involves compensatory devices. This was supported by one class II case-control study. In general, however, studies in this field remain hampered by myriad methodological problems and a lack of long-term health outcome results.

Question 4. Does the application of supportive employment enhance outcomes for persons with TBI?

There is one class II prospective, controlled, observational study (Haffey, Abrams, 1991) and one class III study (Wehman, Kreutzer, West, et al., 1989; Wehman, Sherron, Kregel, et al., 1993; Wehman, West, Fry, et al., 1989; Wehman, Kreutzer, West, et al., 1990) on supported employment in the literature. These two studies use different experimental designs and different models of supportive employment. The class II study suffers severely from a highly biased allocation of clients to the study groups. The class III study was a case-control investigation with the inherent limitations of such a study design. Both studies did provide evidence that supported employment could improve the rehabilitational outcome of persons with TBI. Supportive employment appears to be a promising way to increase the vocational success of persons with TBI, but the present literature does not give definitive proof of its effectiveness and does not adequately clarify why it works or provide guidance to the best applications of the method. Data on durability is also lacking. Because of the limitations inherent in these studies, they must be interpreted cautiously in the absence of replication.

Question 5. Does the provision of long-term care coordination enhance the general functional status of persons with TBI?

One RCT addresses this question, although the randomization was of hospital systems, not patients (Greenwood, McMillan, Brooks, et al., 1994). This study evaluated the efficacy of a medical model of case management, defined as clinical needs assessment during acute hospital care, formulation of proactive rehabilitation plans, and facilitation of rehabilitation cooperation and involvement among patients, families, and professionals. It studied persons with severe TBI

and evaluated functional status at 24 months as the primary outcome. They found no significant differences between the treatment and control groups.

There are two class III studies in this population. One is a completed study (Ashley, Persel, Lehr, et al., 1994), the other a report on preliminary results at 1 year (Malec, Buffington, Moessner, et al., 1995). The Ashley study focused on persons with moderate disability and looked at models in which the key aspects were the authority to approve disability payments and rehabilitation service claims as a function of insurance coverage. This study had an 8- to 9-month followup and suggested that case management improved vocational status and was associated with a single case manager.

The preliminary report (Malec, Buffington, Moessner, et al., 1995) presented 1-year followup on a combination of mild to severe injuries. They evaluated a combination of nurse and vocational case manager model that included early assessment and rehabilitation planning during acute hospital care. This method of management was similar to the Greenwood study. This study also found an association between case management and improved vocational status similar to that found in the Ashley study.

Overall, the significant differences between these studies prevent adequate comparison. The one randomized control trial showed no overall benefit attributable to that particular model of case management. This may have been due to a number of uncontrolled confounding variables (such as the amount and type of rehabilitation received by clients); alternatively, that particular case management program might be ineffective. The other two studies did show some efficacy for single and multiple case managers/insurance approaches, but these studies suffer from design limitation and are only class III investigations. Clearly, further investigation into the efficacy of case management and improving outcome from TBI is needed to evaluate differing case management models in well-controlled studies.

Future Research

Randomized trials of timing and intensity of early (trauma center) and acute inpatient rehabilitation would be useful. Because the patient characteristics that affect outcome also affect the type and level of rehabilitation services delivered, it may be unlikely that any observational study can provide decisive evidence about effectiveness. Moreover, assigning patients to different levels of intensity or to early versus conventional initiation of rehabilitation in a prospective trial may be ethically acceptable since these different levels present a range of current practice rather than a deviation from it.

Population-based studies of all patients with TBI, including those who do not enter inpatient rehabilitation facilities, are imperative. Important questions about the effectiveness of rehabilitation and its component disciplines require the development of regional or national registries with standardized data collection and identification and followup of all patients with head injury.

Research designs for future studies of cognitive therapy should incorporate health outcomes of importance to persons with TBI and their families. Commonly used measures should be more strongly linked to health outcomes. Future studies should address the effect of spontaneous recovery and systematized recovery for entering cognitive rehabilitation and differentiate between the effects of general stimulation and specific technique. Careful construction of adequate control groups is also imperative.

The greatest overall need for the evaluation of supportive employment programs is a series of trials with adequate controls and unbiased allocation of clients to the conditions compared.

Future research should focus on improving the outcome measures used to examine the results of case management in TBI rehabilitation. In addition to patient functionality outcomes, studies should also address family functionality. Since much of case management communication is directed toward helping family members learn what to expect and where to obtain services, relevant outcomes would include family use of community and rehabilitation services and indicators of family assertiveness about care expectations. Although case management may only indirectly affect a patient's functional outcome, such as level of disability, vocational status, and living status, it is possible that case management can directly affect family knowledge of TBI rehabilitation needs and services, level of psychosocial anxiety, and family competency in coping with TBI.

A Need for Common Currency in TBI Rehabilitation

A number of common and very confounding issues run through the field of TBI rehabilitation. It is vitally important to remember that TBI recovery is a long-term process for each person. Each therapeutic manipulation changes the course of that recovery and will influence the need for and response to subsequent interventions. This means that a person with TBI cannot be simply "picked up" at any point during recovery without an accurate understanding of the course. This requires a specific, precise, and universally accepted language to describe the patient characteristics throughout the continuum that begins with injury and, indeed, is also highly influenced by pre-injury characteristics.

The same continuum needs to be addressed with respect to outcome. This is particularly important because variables that act as outcome measures to persons performing interventions early in recovery will subsequently become input variables (cohort descriptors or confounding variables) in studies of interventions taking place at later stages. Additionally, there is growing evidence that the sets of variables that serve as strong predictors of outcome evolve markedly as the course of recovery develops in outcome measures change. As an example, although the response to acute care of a person with TBI will influence that person's subsequent response to cognitive therapy, the set of predictors relevant to outcomes from these treatments will be quite different.

One major shortcoming in the area of TBI rehabilitation is the inability to compare studies. This arises because of insufficient description of study cohorts, lack of any uniformity in

choices of outcome measures, and inadequate characterization of rehabilitative interventions. Not only are most studies not comparable with each other, but most individual investigations would be extremely difficult to replicate with any probability of reproducing similar results.

A uniform conclusion at the Aspen Neurobehavioral Conference was that a necessary and optimal method of addressing these issues is to construct a consensus-based set of pragmatic definitions, forming a uniform data set that has the capability of spanning the continuum of recovery from TBI. This language needs to address severity of injury, disability, impairment, and handicap, and it also needs to codify a basic set of outcome measures that can be used as milestones and that would be useful in measuring outcome as well as progress. Finally, it is critical that a language describing interventions be developed so that the true nature of the independent variables in various studies can be understood.

Given the current state of this body of research, we surely lack the ability to construct the optimal language in any of these areas at this time. Because of the critical need for us to exit the current Tower of Babel, however, a consensus-based construction of an ad hoc uniform data set that can be immediately employed and improved over time is immediately needed.

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Cognitive Rehabilitation: An Impairment-Oriented Approach Embedded in a Holistic Perspective

George P. Prigatano, Ph.D.

Holistic approaches to neuropsychological rehabilitation consist of five interrelated activities (Prigatano, in press), one of which is cognitive rehabilitation. Cognitive rehabilitation aimed at directly remediating an impairment of brain function remains controversial. Ben-Yishay and Diller (1993) concluded that it would be premature to draw definitive conclusions regarding its validity and use for rehabilitation purposes on the basis of current evidence. In a review of cognitive remediation after cerebrovascular accidents (CVAs), Plisken and colleagues (1996) concluded that the overall scientific evidence is at best nonconclusive and at worst negative, despite reports of positive results.

Efforts to remediate cognitive impairments have included drill and practice exercises of the function that appears impaired (Prigatano, Glisky, Klonoff, 1996), teaching strategies to circumvent a theoretically identified component of a cognitive process considered to produce the impairment (Luria, 1948/1963), and a broadband approach that attempts to stimulate a wide variety of theoretically defined brain functions (i.e., arousal, alertness, attention, memory, and mental energy) in an effort to facilitate either the rate of recovery or the overall level of recovery (Prigatano, Fordyce, Zeiner, et al., 1986). The final analysis frequently shows only modest improvements on certain psychometric tests or tasks after direct retraining of a cognitive impairment. Clinically, the impact of an impairment-oriented approach on daily functioning appears minimal.

Problems With Current Research on Cognitive Rehabilitation: Impairment Approaches

Four major problems must be addressed in order to determine whether cognitive rehabilitation aimed at remediating an impairment will prove effective.

1. The impaired function is often not clearly defined. Ponsford and Kinsella (1988) attempted to retrain attention directly in traumatically brain-injured (TBI) patients since this function is reportedly affected negatively. Their results proved discouraging. Later, however, they redefined the problem as reflecting a disorder of speed-of-information processing (Ponsford, Kinsella, 1992).

2. The rules that govern a normal higher cerebral functional relationship are not known. By the term “function rule,” we mean that a function f is a correspondence or relationship that pairs each member of a given set with exactly one member of another set (Lynch, Olmstead, 1998). A set can be defined as numbers, geometric configurations, or neural networks responsible for emergent complex psychological functions. It is probable that direct remediation

of a cognitive impairment may prove most effective in those circumstances in which the function rule is only slightly disturbed or indirectly rendered inoperable. When damage to the brain substantially alters the functional relationship (i.e., function rule), adaptation, rather than retraining, seems the most useful approach (see Figure 13 from Prigatano, in press).

If the impaired function can be defined and the variables that contribute to the function rule clarified, two other problems need to be addressed.

3. Evidence that the brain of a given patient has the potential for cortical plasticity for the function that is being retrained is needed.

4. Technology to deliver retraining activities in a manner that is cost-efficient and effective is also needed. Merzenich and colleagues (1996a) and Tallal and colleagues (1996) provided an interesting prototype of how technology can be used with children with language-based learning impairments. The function that seemed to be disturbed was identified as the encoding of phonemic aspects of sound. The children were then delivered auditory stimuli in a manner that required finer and finer temporal discriminations. The tasks were engaging to the children rather than frustrating. The interventions produced greater improvements in different speech and language functions than did traditional speech and language therapies.

Quality of Data Available

Research studies on the effects of direct retraining of cognitive impairments can be categorized into three broad types. The first includes retrospective clinical assessments of primarily neuropsychological and personality test scores before and after holistic milieu-oriented rehabilitation programs (Prigatano, Fordyce, Zeiner, et al., 1984; Prigatano, Klonoff, O'Brien, et al., 1994). These studies are not randomized prospective investigations, and their reported positive findings must be interpreted as only suggestive (not definitive) of their effectiveness.

The second group of studies can be classified as primarily multiple individual case designs in which baseline/interventions/postintervention assessments are made. As noted, these studies often report modest improvements on certain target cognitive impairments.

The third type of study is the traditionally randomized group design in which subjects receive a specific treatment, no treatment, or pseudotreatment and are compared with controls (e.g., Gray, Robertson, Pentland, et al., 1992). These studies tend to report modest improvements on complex tasks.

There are, however, studies that show that specific skill retraining (i.e., learning to operate a computer, improving phonemic perceptions, etc.) is possible in humans after brain insults. These studies support the possibility of cortical plasticity throughout the lifespan for certain skills that are not necessarily global functions (Merzenich, Jenkins, Johnston, et al., 1996a).

A Clinical and Research Perspective

The nature of higher cerebral functions is not purely cognitive (Prigatano, in press). They often seem to integrate both thinking and feelings. Remediation programs must be stimulating, not frustrating. They need to build on the natural interests and strengths of patients while attempting to remediate an underlying impairment. When emotional and motivational disturbances become the focus of rehabilitation as well as cognitive impairments, improved psychosocial outcomes have been reported (Prigatano, Fordyce, Zeiner, et al., 1984; Ben-Yishay, Rattok, Lakin, et al., 1985; Christensen, Pinner, Pedersen, et al., 1992; Rattok, Ben-Yishay, Ezrachi, et al., 1992; Prigatano, Klonoff, O'Brien, et al., 1994).

In the course of clinical practice, three broadly defined higher cerebral functions seem amenable to direct retraining, although they are difficult to measure. The first category concerns patients' overall energy to sustain mental effort on cognitive tasks. Patients engaged in day-treatment programs are able to improve their overall cognitive energy with such interventions. The measurement of this complicated function is worth further investigation. Second, a number of patients with severe TBI lack insight into their neuropsychological impairments. They simply do not experience the impairments in a manner similar to those around them. Clinically, efforts at trying to improve self-awareness appear to have been effective in some patients. When this type of treatment is successful, patients often make more appropriate choices and avoid substantial psychosocial difficulties.

Finally, speed-of-information processing is often compromised after severe TBI. Cognitive remediation tasks that attempt to improve the processing speed associated with various functions may have important consequences. For example, speed of finger tapping is related to the achievement of rehabilitation goals not only for patients with postacute TBI but also for individuals who have suffered acute cerebrovascular accidents (Prigatano, Wong, 1997). Interestingly, within the first 6 to 8 weeks after a stroke, speed of finger tapping in the so-called unaffected hand (the hand ipsilateral to the lesion) is most strongly related to the achievement of rehabilitation goals. Further exploration of how to improve speed of information processing and speed of motor function may prove useful.

Conclusions

Research on the cognitive rehabilitation of impairments in higher cerebral functions should not be abandoned even though the present utility of such treatments appears minimal. Data on specific acquisitions skill after brain injury are encouraging. Theoretically, direct retraining of impaired cognitive functions appears to be possible. If accomplished, such retraining would be of substantial help to patients. When the direct retraining of an underlying cognitive impairment is attempted, it should be recalled that both cognitive and affective functions are intimately interconnected. Consequently, they must be addressed simultaneously to maximize their usefulness for the patient. As Merzenich and colleagues (1996b) have recently observed, cognitive neuroscience studies also reveal the most effective strategies for driving brain change. The subject must be attentive and motivated. The training must be progressive and adapted to each training subject. The training schedule must be repetitious and intense.

I would add that training must help patients adjust to whatever permanent disabilities they have sustained and provide them with appropriate methods for doing so from both cognitive and psychotherapeutic perspectives.

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A Contextualized and Routine-Based Approach to Cognitive and Behavioral Rehabilitation: A Historical Perspective

Mark Ylvisaker, Ph.D.

During the initial period of intensive program development in TBI rehabilitation, extending from the mid-1970s through the 1980s, rehabilitation specialists expressed considerable enthusiasm for an approach to rehabilitation quite different from that described in this presentation. Popular interventions targeted the underlying cognitive, behavioral, perceptual, communication, or other impairment; were delivered by specialists working in relative isolation; and were delivered in clinical settings using training tasks largely unrelated to the individual's real-world tasks and stressors. Thus, for example, cognitive rehabilitation came to be understood by many practitioners as an enterprise based on precise neuropsychological delineation of the individual's underlying impairments, followed by an intensive program of hierarchically organized exercises designed to remediate those impairments (Sohlberg, Mateer, 1989). In the early stages of clinical research, success was measured by improvement on training tasks or neuropsychological tests. Using these measures of success, cognitive retraining exercises seemed to have an important treatment effect (Ruff, Baser, Johnston, et al., 1989). However, in some areas (e.g., memory retraining), that effect has been found to be clinically insignificant (Schacter, Glisky, 1986), and in others, important questions have been raised about reduction of impairment and also about transfer from training tasks to real-world application (Ponsford, 1990). Over the past 15 years, practitioners have increasingly sought to contextualize their intervention with the goal of functional improvement in the persons they serve. That is, the focus of rehabilitation for many practitioners has shifted from decontextualized impairment-oriented interventions to contextualized disability and handicap-oriented interventions.

The Problem of Transfer: Generalization and Maintenance

Many investigators in behavioral and cognitive psychology have amassed persuasive evidence supporting the following heuristic principle, which is applicable to many disability groups: *Behaviors or skills acquired in a laboratory or training context are unlikely to transfer to functional application contexts and be maintained over time without heroic efforts to facilitate that transfer and maintenance* (Martin, Pear, 1996; Singley, Anderson, 1989). Recognition of the impact of this principle has led to the development and validation of increasingly contextualized interventions in many clinical fields, including vocational rehabilitation, special education, strategy intervention for students with and without specific disability, behavioral intervention, and language and social skills intervention.

History of Intervention in Related Fields

A broad historical survey of attempts to improve cognitive functioning suggests that developments over the past 25 years in cognitive rehabilitation for people with TBI have replicated earlier histories with other populations. For example, 19th century faculty psychology supported attempts to train components of cognition with targeted exercises (that is, “discipline the forms or faculties of the mind”). For students with no disability, intensive study of Latin and geometry was recommended to train organized and logical thinking. At the same time, many students with mental retardation were subjected to hierarchically organized exercises similar to those used in late 20th century cognitive rehabilitation, and with the same goal—to eliminate the cognitive impairment (i.e., cure mental retardation). More recently, the field of learning disabilities similarly began with enthusiastic attempts to cure the disorder with remedial cognitive and perceptual exercises aimed at the most basic level of the neurological impairment. In all three cases (educational psychology, mental retardation, and learning disabilities), investigations eventually revealed that improvements on decontextualized training tasks rarely transferred to meaningful academic, vocational, or social tasks. Therefore, intervention increasingly came to be embedded in the contexts of everyday activities and routines. (See Mann [1979] for an illuminating historical review.)

Framework for Intervention

Following TBI, impairment in the domains of cognition, executive functions, communication, and behavior is most commonly associated with frontolimbic injury. Commonly observed impairments related to such injury appear to interfere substantially with successful action, whether success is determined by thoughtful decision-making or by learning from the consequences of past behavior (Damasio, 1994). The “high reason” route to successful action is threatened by a combination of planning and organizational impairment, reduced abstract thinking, impulsiveness, impaired working memory, and difficulty transferring. Efficient learning from consequences is reduced by breakdowns in circuits that tie behavior-regulating somatic markers to stored memories, impulsiveness, and impaired working memory. Unfortunately, restorative exercises in these domains have enjoyed limited success.

A potential escape from the horns of this apparently destructive dilemma is to deliver rehabilitation services through supported everyday routines. Positive routines of action and interaction are created with ample antecedent supports; teaching is done through apprenticeship procedures as opposed to traditional training procedures; services and supports are largely provided by everyday people in the life of the individual with TBI; if necessary, teaching is through implicit memory/procedural memory systems (vs. declarative/explicit memory systems); and teaching occurs largely through involuntary rather than deliberate learning tasks. The approach is based in part on the developmental and recovery theories of Vygotsky (1978), who argued that most nonreflexive components of cognition are gradually internalized from everyday routines of social interaction.

Impairment/Disability/Handicap

In both physical and cognitive rehabilitation, the traditional approach proceeds hierarchically, from (1) attempts to eliminate or substantially reduce the impairment to (2) attempts to reduce functional disability with compensatory procedures if impairment-oriented treatment is insufficiently successful to (3) attempts to reduce social, vocational, and/or educational handicap if impairment- and disability-oriented interventions are insufficiently successful. An alternative approach, which is appropriate in many cases of cognitive, behavioral, academic, and vocational disability, reverses this hierarchy. First, handicap is reduced by modifying everyday routines, including the support provided by everyday people in the environment. Second, disability is potentially decreased by including functional compensatory procedures in the individual's everyday routines and ensuring intensive contextualized practice in the use of those compensatory procedures. Third, the impairment is potentially reduced by ensuring that the individual practices compensatory procedures—in increasingly varied contexts—to the point at which the procedures are internalized and become components of the individual's automatic cognitive or self-regulatory mechanism.

Support for This Approach

Endorsement of an everyday, routine-based approach to cognitive-behavioral-executive function rehabilitation for individuals with TBI is based on (1) extensive clinical experience using this framework, (2) a limited amount of experimental and qualitative research with individuals with TBI (Feeney, Ylvisaker, 1995; von Cramon, Matthes-von Cramon, 1994; Ylvisaker, Feeney, 1996, 1998), (3) evaluation of the cost-effectiveness of this framework within the New York State Department of Health Medicaid Waiver Program, (4) the neuropsychological and developmental theories described earlier, (5) the extensive literature dealing with transfer of training in both behavioral and cognitive psychology, (6) an impressive body of supportive intervention research in related fields of intervention, (7) the relatively disappointing findings from investigations of the effectiveness of traditional impairment-oriented cognitive retraining, and (8) the managed care mandate to generate quality outcomes with dramatically shrinking resources.

Cost-Effectiveness

The Sage Statewide Neurobehavioral Resource Project is a component of the New York State Department of Health Medicaid Waiver Program and is designed to support individuals with behavioral and cognitive impairment after TBI in community settings. In 1997, the cost of the program was \$144,000. Using conservative actuarial and accounting methodology dictated by external auditors, savings of \$1,842,000 were directly attributable to the program during that year (a net savings of approximately \$1,700,000). The program is based on principles of cognitive and behavioral intervention described in this presentation and centers on an apprenticeship component wherein specialists in rehabilitation have as their primary responsibility the training of and support for everyday people in the life of the person with disability.

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Cognitive Rehabilitation: Research Approaches

Ronald M. Ruff, Ph.D.

Traumatic brain injuries (TBIs) lead to cognitive dysfunctions that can manifest in a spectrum of changes in concentration, memory, learning, spatial integration, problem-solving, and intellectual functioning. The aim of cognitive rehabilitation after TBI is to restore specific cognitive functions through strategies and repetitive exercises or to establish compensatory mechanisms (external, prosthetic assistance or cues) to enhance a functional recovery. The evaluation of experimental cognitive remediation poses major challenges.

Heterogeneity of Persons With TBI

Problem. The severity of TBI is one important dimension in a complex array of factors that delineate brain damage. The Glasgow Coma Scale (GCS), the size and location of the lesion, the extent of axonal shearing, the presence of intracranial pressure, vascular changes, and hypoxia can all play a role. Other bodily traumas, such as pain, depression, spinal cord injuries, and comorbid features need to be considered. Moreover, the pre-injury history of individuals with TBI can vary significantly in terms of psychiatric and neurological disorders as well as demographic features of age, gender, time of onset, education, socioeconomic status, vocation, ethnicity, and cerebral dominance.

Searching for Solutions. Research would benefit if the TBI classifications were expanded to incorporate this heterogeneity. In addition, the present cognitive, emotional, psychosocial, and vocational status should be carefully delineated. The period between the accident and the implementation of the cognitive remediation protocol (chronicity) also needs to be described, comparing those functions that remain stable with those that have changed. Moreover, the patient's premorbid physical, emotional, mental, psychosocial, and vocational status should be estimated (Ruff, Mueller, Jurica, 1996). Thus, a multidimensional schema is proposed that would include the dimensions of (1) present status, (2) severity of TBI, (3) chronicity, (4) highest functioning levels, and (5) premorbid status.

Spontaneous Recovery Versus Relearning

Problem. Since healing results in tremendous benefits for almost every TBI patient, spontaneous recovery presents a major challenge for the researcher. During spontaneous recovery, cognitive functions can improve at different rates. The challenge remains to separate the effects of cognitive remediation from those of spontaneous recovery.

Searching for Solutions. Some researchers have taken the approach that patients with TBI should wait to receive cognitive remediation until a year or two post-injury, because most

spontaneous recovery takes place during that time. However, another solution is a group comparison study, which is the optimal research design to evaluate the efficacy of cognitive remediation. A further refinement is to evaluate each patient in a multiple baseline design that can be juxtaposed with an experimental and control group comparison. Thus, single-case designs can be added to group comparisons (Niemann, Ruff, Baser, 1990). Although group comparisons are extremely expensive, granting agencies need to be persuaded to finance comprehensive rehabilitation programs if we are to base our conclusions on scientifically rigorous methodologies. Reasonably large sample sizes are obviously advantageous.

Standardization of Therapy

Problem. Research typically limits ongoing nonstandardized treatments. Thus, in most studies, members of a group of TBI patients have been exposed to the same cognitive remediation program. A problem with that approach is that the patients may need to be enrolled in concurrent treatments, such as speech therapy or individual psychotherapy. These concurrent treatments may assist with emotional adjustment, which then can interact with the cognitive gains. A second problem is that patients may benefit differently from various regimens of cognitive remediation. A dynamic or flexible approach, however, becomes too unwieldy within the context of experimental research. Thus, the ideal clinical approach of tailoring cognitive remediation techniques to each patient is frequently compromised in experimental designs that emphasize standardization of treatment.

Searching for Solutions. Wilson and colleagues (1997) and Ponsford and Kinsella (1998) designed research paradigms that set clinically valuable treatment goals. In each of the studies, individuals were measured on specified variables before the intervention (baseline phase), during the intervention (treatment phase), and after the cessation of intervention (return-to-baseline phase). We have recently taken the approach of providing a standardized training protocol, then adding tailored memory training to evaluate what further benefits could be gained, and then comparing the standardized with the tailored approach.

Level of Generalization

Problem. The generalization of newly learned techniques is recognized as a principal goal of any intervention. For cognitive remediation to have a lasting impact on an individual's life, it must be available across various situations and over time. Generalization is often regarded as a phenomenon that happens without any special interventions, as a natural consequence of traditional therapy. However, this needs to be carefully evaluated. Most cognitive remediation research protocols are labor-intensive, and adding followup protocols to these hours, 6 to 12 months post-treatment, becomes extremely laborious.

Searching for Solutions. For evaluating cognitive remediation, three levels of generalization have been proposed: (1) gains measured according to the training material, (2) psychometrically captured therapy gains, and (3) measurements of everyday life functioning. The third level represents the key challenge, because of the scarcity (or absence) of useful

measurements that link cognition with everyday functions (ecological validity). This is tied to the challenge of operationalizing valid outcome measures. If the desired outcome is not defined, then the generalization of cognitive gains on everyday functioning is elusive. One of the possibilities of formulating outcome with respect to day-to-day living is to identify the following three dimensions: (1) meeting the basic needs, (2) selecting the appropriate living arrangements, and (3) self-management or determination. Basic needs include medical care, safety, feeding, physical fitness, education, employment, income, social interaction, recreation and leisure, self-identity, and self-worth issues. An appropriate living arrangement is paramount to good outcome and may directly affect how specific needs such as shopping and medical care can be met. The patient's living arrangement should be carefully chosen to minimize problems. Finally, self-management is pivotal to a successful outcome. This view is anchored in the notion that individual freedom is a fundamental human right. Thus, each patient should have input into how each of his own needs should be met and at what level he is capable of self-management.

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Institute of Medicine Model of Disability

Diana D. Cardenas, M.D.

In the 1997 report *Enabling America: Assessing the Role of Rehabilitation Science and Engineering*, the Institute of Medicine (IOM) proposed a new enablement-disablement model that expanded the 1991 IOM model in several important areas. First, the 1991 model implied that the disabling process is unidirectional, progressing toward disability without the possibility of reversal. Second, the 1991 IOM model did not include the environment except as a risk factor involved in the disabling process. Finally, the 1991 IOM model did not adequately represent societal limitation as stressed by the 1993 National Center for Medical Rehabilitation Research disablement model.

Models of disability have been evolving since the 1950s. As yet, there is no single comprehensive paradigm or universally accepted theoretical model of the enablement-disablement process. The new IOM model emphasizes the interaction of the person with the environment and is intended to be viewed as a three-dimensional model. The model is no longer unidirectional but allows the possibility of movement in the direction of no disability. The environment includes not only physical but also social and psychological components. The environment is represented as a flexible three-dimensional mat. The strength of the mat is related to the support systems available and the existence of barriers. Disability is represented as the interaction of the person with the environment or displacement of the environmental mat. The greater the displacement, the greater the disability.

The IOM model is applicable to the consequences of traumatic brain injury (TBI). For example, cognitive impairment may create functional limitations. The person with impaired executive function may have functional limitations that result in difficulty with initiation, monitoring his or her performance during an activity, inhibiting irrelevant information, and maintaining attention. This makes independent living and productive work difficult. Deficits in reasoning and problem-solving are also impairments that may be caused by TBI. Functional limitations may occur because the person cannot put steps together in a sequence to accomplish a goal or to perform a task. This in turn makes tasks such as driving a car, paying bills, preparing food, and using the telephone difficult, depending on the extent of the impairment. Another example is memory impairment, another possible consequence of TBI, which affects day-to-day functioning. Deficits in short-term memory can make new learning difficult, which can affect the patient's ability to learn compensatory techniques or therapeutic interventions for other coexisting impairments.

Cognitive impairments may thus create functional limitations and disability, defined as a limitation in performing socially defined activities and roles. The rehabilitation professional team attempts to provide appropriate training strategies to help overcome the functional

limitations imposed by cognitive impairments and, it is hoped, does so in the context of the patient's social roles.

The process of rehabilitation has focused on impairment-level interventions and functional limitations, and the latter have become more important because of the push for discharge in a managed health care environment. Rehabilitation has always involved changing the environment to accommodate functional limitations, for example, by adding a raised toilet seat or providing specialized computer interfaces. The patient who is easily distracted may require a separate therapy locale where there are no distractions. The patient who is agitated may require a special protective bed or room. Use of memory books is another example of strategies used to compensate after brain injury. Numerous environmental modifications are not only physical; many are cultural, psychological, political, and economic and may be appropriate and therefore enabling for persons with TBI.

Strategies that utilize assistive technology, such as use of computer programs for cognitive retraining, have been criticized for lack of generalization; however, such strategies provide direction for further research and can be used to test the potential benefit of pharmacological agents in enhancing concentration, attention, or memory. New research ideas need to emerge through the interaction of scientists, clinicians, engineers, and consumers. Many research advances have been made in the areas of pathology and impairment and have involved the administration of experimental and neuropsychological tests. More is being understood about performance of functional, real-world tasks. Investigators have learned that the patterns of life's behaviors differ from those predicted from paper and pencil testing. The changes in emotion, social interaction, and communication that may occur anytime there is a cognitive impairment are difficult to understand, much less measure.

The 1997 IOM report suggested that further research related to cognitive function should include (1) determining how individuals with brain injury can improve their performance of functional, real-world tasks, for example, self-care, meal preparation, parenting, and employment; (2) further development and testing of rehabilitation strategies to overcome problems with aphasia, agnosia, and apraxia; (3) understanding the impact of cognition on the individual and society and the potential effects of environmental and learning strategies on recovery and functioning; (4) determining whether certain aspects of affective disorders can be distinguished from the cognitive sequelae of TBI, (5) determining whether the brain has different processing pathways for different types of information after brain injury; and (6) determining how deficits in inhibitory control affect everyday functioning, that is, how different aspects of attentional processing predict everyday functioning.

Other research questions posed by the IOM report are as follows: How does cognitive activity relate to specific environmental contexts? What role does the environment play in the internal representation and processing of visual information? How is it possible to prepare spouses and families for the multitude of tasks required for life with a person who has had a severe brain injury? These questions can be addressed only when we have the appropriate tools to measure cognitive deficits in real-life activities. Preventing disabilities in those with cognitive impairments cannot be left at the level of functional limitation. New means of addressing the

cognitive needs of persons must come to the forefront in science to reduce the devastation of cognitive impairments on the lives of those with TBI.

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Models of Head Injury Care

D. Nathan Cope, M.D.*

Short- and Long-Term Outcomes of ABI Managed by Paradigm

Paradigm Health Corporation is a privately held, for-profit, national, integrated care system for catastrophic injuries; a large proportion of its clients are patients with acquired brain injury (ABI). These ABI cases are referred to Paradigm by its customers both immediately after injury and years after injury.

Paradigm manages care on the basis of the collection and analysis of extensive prospective clinical and other data (leading to formal severity risk adjustment for each case), process of care, and outcome measures. Both clinical-functional and financial parameters are extensively measured. Paradigm is able to predict appropriate resource use and clinical pathways needed to achieve appropriate clinical-functional results. A formal system of expert case management, specialist physician direction, and data-supported decision-making works to achieve the specific outcomes for each patient. Paradigm is able to write risk-bearing contracts with its customers based on the achievement of objective clinical and functional results. The outcome measures utilized by Paradigm include level of global outcome, e.g., return to home, community, and productive activity; medical stability; functional status; type and frequency of complications; community reintegration; return to work; attorney retention; degree of handicap; resources projected; and resources consumed.

Comparison of Results With Outcome Evidence From Acute and Chronic Quasi-Matched Samples From Other “Nonmanaged” Systems of ABI Care

An analysis is given of Paradigm’s management of *acute* ABI cases. Case rate costs for achievement of specific outcome are reported. Experience and estimates for these severe ABI cases are contrasted with traditional “unmanaged” actual and projected cost experiences. For the *chronic* group, the analysis shows extraordinary actual and projected medical, support, and social lifetime costs. Near normal life expectancies characterize this group. Both sets of data suggest a benefit of rehabilitation and coordinated care.

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Research Needs of the ABI Models of Care

Support is offered for the basic research needs of the ABI field. These needs have been delineated recently by the Neurobehavioral Conference at The Given Institute in Aspen, Colorado (1998). These needs include:

- Development of a severity classification system for ABI that can identify comparable ABI patient groups and specific subgroups and account for the multiple interacting ABI injury, individual patient characteristics, and social support system.
- Establishment of severity risk-adjustment models that include uniform standards and measures that are objective and cross the continuum of recovery.
- Development of adequate process-of-care measures.
- Development of outcome measures for the short, intermediate, and long term that include medical, functional, social, and economic (cost) dimensions.
- Establishment of uniform descriptions of rehabilitation services, process-of-care elements, and levels of care, including frequency, intensity, duration, content, setting, and milieu of interventions.

These measures must be developed by wide consensus and be available to multiple investigations and systems of care so that appropriate analyses are ultimately possible.

Dangers and Limitations of Reaching Conclusions About Appropriateness of Care Based Solely on Class I Evidence

Clinical evidence is now categorized as class I, II, or III (Walters, 1998). The premium evidence is from class I studies based on the randomized controlled trial (RCT). These studies are challenging to design, are expensive, and have the potential for creating ethical dilemmas. Class I evidence has other limitations, which have been highlighted recently (Birch, 1997; Hart, 1997). When class I evidence is not available, all remaining treatments are likely to be labeled as experimental. The conference should remain aware that some ABI rehabilitation management has face validity. Development of consensus statements, including standards and guidelines for ABI rehabilitation, must therefore rely on class II and class III, as well as class I, evidence. Conclusions must, in the end, be based largely on these levels of evidence, including expert opinion, because of the limitations and lack of objective class I data (Eddy, 1996; Naylor, 1995).

The consequences of such conclusions are far from academic. There are increasing pressures to look at health benefits from a cost-effective and cost-benefit perspective, in short, to look at health benefits as measured only by whether the intervention saves money. The driver in health care insurance benefits is cost containment. Any conclusion that a service is not “proven effective” will have the practical effect of eliminating that service from clinical practice, whatever the clinical opinion of merit.

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Access to Brain Injury Rehabilitation and Other Post-Acute Services

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There is widespread concern that many individuals with brain injury do not have access to rehabilitation and other post-acute services that they presumably need. Individuals with brain injury, their family members, and providers often cite case examples of individuals who have been unable to obtain services. Although the problem of access may be real, the empirical evidence for this concern remains lacking.

The issue of access is confounded by a larger issue, namely, the efficacy of brain injury services and the ability of individuals to benefit from these services. The issue of access is material only in those instances where brain injury services are effective. In other words, if certain types of post-acute services are not effective, there is not an access issue. The effectiveness of post-acute brain injury services is beyond the scope of this paper and is the subject of other papers represented in this consensus conference.

The Multidimensional Nature of Brain Injury Services and Access

In considering the issue of access, we need to understand that brain injury services are not uniform and that the concept of access is not a unitary one. Both are multidimensional. Brain injury rehabilitation consists of a collection of diverse interventions that may be provided in different combinations in different settings in different sequences for different brain injury sequelae. Thus, when we speak about access, we need to be clear as to what it is that we are seeking to access.

The concept of access is similarly complex (Aday, 1993). The issue of access may be geographic: Is there a source of services within reasonable geographic proximity to the individual's home and family support system? The issue of access may be timeliness: Can the individual obtain the services when he or she can most benefit from them? The issue may be organizational: Does the service-providing organization provide the necessary case-management and support services that help channel the individual to the types of services he or she needs? The issue may be financial: Does the individual have access to resources, for example, own resources or health insurance that will pay for brain injury services? Can an individual obtain services without ruining the financial well-being of the household?

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In speaking about access in health services research, we usually mean financial access although we should not overlook access issues that stem directly or indirectly from the capacities of the service delivery system to meet individual needs. For the most part, the concept of access used here means financial access.

What Do We Currently Know About Access to Rehabilitation and Post-Acute Services?

An exhaustive review of the peer-reviewed literature uncovered no scientifically or empirically rigorous evaluation of the problem of access apart from anecdote and individual case studies. The brain injury literature has been more concerned with the effectiveness of rehabilitation clinical interventions than with access to these services. In the absence of systematic empirical data, the author wishes to convey what is known in terms of the nature, not the extent, of financial access to brain injury services.

Unless an individual is independently wealthy, his or her financial access depends in large part on the source of third-party coverage—health plan, workers' compensation, automobile insurance, veterans' benefits, a structured settlement for an at-fault injury, State-funded brain injury programs, or another outside source. These sources vary widely in their coverage of brain injury services, and the individual's access to these sources will vary with the etiology of the injury (e.g., automobile crash, military service connected injury, urban violence), the State or geographic area in which the person lives, and the generosity of an employer-sponsored health plan. Sometimes the level of coverage may seem arbitrary and capricious.

One important difference among funding sources is the duration of the period for which a third party provides coverage. Because of open enrollment seasons, many health plans do not perceive their liability as extending into the indefinite future and thus may be unwilling to make up-front expenditures in order to save long-term costs. By contrast, reinsurers and many workers' compensation carriers perceive that they are "on the hook" for the long term and are prepared to take the long-range point of view and thus are willing to optimize expenditures over both the short and long terms.

Another important difference among funding sources is their level of funding for services that extend well beyond the initial acute care episode of care. Generally speaking, third-party support tapers off as service goals move from medical stabilization to community reintegration. Health plans are more likely to scrutinize or deny payment for rehabilitation and post-acute services, especially if these are expected to be of indefinite duration. Managed care health plans, especially those with various forms of capitated payment, have greater financial incentives to scrutinize or deny payment. Brain injury advocates often cite instances in which extraordinary appeals or public opinion finally motivated a health plan to provide additional coverage. Others note that managed care may provide for services only in a subacute facility when a more structured medical rehabilitation program may be considered necessary.

A major difficulty in acquiring third-party payment for brain injury rehabilitation and post-acute services is the vague and subject-to-interpretation nature of the language used to

describe the benefits package outlined in the health plan contract. Most individuals rarely examine this language carefully at the time they enroll in a health plan, and if they do, they may be surprised by what it really means when they attempt to obtain financial access to the services they seek.

Because private insurance often limits post-acute services and typically does not pay for long-term services, individuals and their families may exhaust their personal resources and need to rely on public programs, especially the Medicaid program. Medicaid is one of the few payers of long-term care and long-term services aimed at community reintegration. In a multistate study, however, the General Accounting Office (GAO) found that access to public programs for individuals with brain injury was at best uneven (U.S. General Accounting Office, 1998). To meet the needs of people with brain injury, some States have acquired exemptions from the Federal Government known as “home and community-based waivers” that enable States to target individuals with specific disabilities. The GAO study reports that several States also have funded service programs for individuals with brain injury exclusively from their own resources. These State-only funded programs tend to serve only a very limited number of individuals in each State.

The GAO identified three types of individuals who are most likely to have difficulty in accessing post-acute brain injury services. These include (1) “individuals who are cognitively impaired but lack physical impairments,” (2) “individuals without personal advocates,” and (3) “individuals with problematic behaviors.” GAO informants report that “many of these people ultimately end up homeless or in nursing homes, institutions for mental illness, prisons, and other institutions.”

In Terms of Research, Where Do We Go From Here?

In the ideal world, we would evaluate access by having an objective standard by which we could determine what services individuals should obtain and in what settings, following the onset of their brain injury. We would then attempt to determine what services people actually received relative to this “gold standard” of need and then evaluate their different outcomes to determine the outcomes and costs of not providing needed services in an optimal setting. Unfortunately, such a standard does not exist, nor is it likely to exist in the foreseeable future.

We are thus left to consider second-best approaches to evaluating access. One second-best approach is to examine how, whether, and where similarly situated individuals obtain their rehabilitation and other post-acute services and evaluate the different factors that increase or decrease the probability that an individual will obtain rehabilitation and other services. The factors may include, for example, individual characteristics (age, gender, education, employment status at time of injury); injury-related characteristics (site of lesion, Glasgow Coma Score, Abbreviated Injury Score); health plan status (yes or no) and type of health plan (managed care, fee-for-service); and system variables (level of trauma center and rehabilitation center integration). Then the contribution of each of these factors or variables to the probability of obtaining services would be ascertained.

Closing Observation

The problem of access is rooted in a health care system in which health care coverage is not uniformly available and in a health care marketplace in which payers and providers face financial incentives that may lead to clinically suboptimal outcomes. Thus, even if the problems of individual financial access could be addressed, significant market distortions may still remain and lead to flawed clinical and placement decisions that compromise access to optimal care.

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The Consumer Perspective on Existing Models of Rehabilitation: The Rehabilitation of Persons With Traumatic Brain Injuries

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This discovery project serves to acknowledge the consumer perspective on a multiplicity of issues regarding traumatic brain injury (TBI) rehabilitation, but it is not designed to provide systematically collected data on what actually works in TBI rehabilitation practices. Consumers, as a national community of individuals and families, have been at work for almost two decades to understand this relatively uncharted domain of complex medical, self, family, and social challenges. The presentation of an analysis of themes and trends in TBI rehabilitation from the viewpoint of the consumer is a work in progress:

1. What were perceived as the most effective rehabilitation practices resulting in reintegration with the family, community, and work/school for individuals with TBI?
2. What were perceived as the least effective rehabilitation practices for individuals with TBI?
3. Were the goals of rehabilitation for persons with TBI established by consumers, family members, clinicians, or a combination of these?
4. Were the goals perceived as satisfactory by consumers?
5. Are there recurring themes about the goals, organization, or administration of TBI rehabilitation that are perceived to be overlooked by the scientific and/or medical community?

The scope of this consumer-driven and consumer-oriented project involved developing a search strategy focusing on locating the networks of consumer publications. The literature that was reviewed included 107 sources with approximately 1,300 items collected from the national and community offices and through contact with Web site resources. The literature relevant to community integration is presented in terms of (1) issues as summarized from the consumer literature and (2) consumer statements illustrating the issues.

Quality of Life: The Most Effective Rehabilitation Model

Consumers recovering from TBI diagnosed as mild, moderate, or severe tended to perceive the most effective rehabilitation practices for community integration as those that focused on person-centered planning and enhancing the quality of their life: physical well-being,

cognitive processing, emotional/family health, behavioral/social skills, vocational/educational activity, and community living.

The most effective rehabilitation component from the family perspective is identified as education and family systems therapy. The families require a TBI curriculum to learn the language and systems of services that they will be required to navigate after acute or post-acute rehabilitation.

Access to Care

Consumers tend to perceive the least effective rehabilitation practices as those that do not address the access to care, the systems issues of the TBI, and long-term real-world functional issues. The systems-focused rehabilitation model focuses on coordinating rehabilitation services within a lifelong continuum of care in order to understand all dimensions of an injury and discover real-world patterns of function (Dolen, 1991) . The medical model addresses the physical injuries, but the family finds itself searching for brain injury diagnosis and rehabilitation. Consumers report these areas of concern:

1. The under-diagnosis or misdiagnosis of TBI.
2. Inappropriate diagnosis and placement.
3. Failure to provide person-centered supports for related problems such as substance abuse treatment, adapting to the disability in terms of sexuality, and neurologic impairment.
4. Difficult access to long-term rehabilitation and case management.
5. Cultural diversity and cultural healing belief systems.

The existing health care delivery system provides no choices or options for people who really need services in the areas of dual diagnosis (substance abuse and mental illness) and chronic illness or pain and depression. The physical, cognitive, psychosocial, and behavioral supports that a person needs after becoming medically stable continue to be limited in scope. Additionally, the current rehabilitation models need to prepare the consumer and family for assuming a management role in securing specialized treatment and needed services.

Measurement of Effectiveness of Rehabilitation

Consumers present their perspectives in the larger term of recovery, not just clinical rehabilitation; the individual copes with the life-valuing process, which is not complete until individual and family quality of life is re-established and maintained. Therefore, an important discovery of this paper is recognizing that the language spoken in reference to rehabilitation goals by the medical/scientific community is different from the language of consumers and families. Consumers face an ongoing search for access to systems and appropriate services when

talking about rehabilitation goals. “Providing the service that the individual needs at the appropriate time in the recovery process is the most effective and empowering rehabilitation practice” (Cannon, 1994).

Consumer Satisfaction

Consumers report dissatisfaction with the outcomes of goal-setting in TBI rehabilitation due to lack of information, options, assistance for problem-solving and decision-making, and coordination among programs and service providers. The goal-setting process may not even begin until after several years of survival when the consumer discovers a new resource or community of support.

Effective Models for Rehabilitation and Consumer Involvement

Community-Based Life Skills Rehabilitation Practices: Project LINCS. The process of relearning is critical to successful integration back into the family, community, and work or school. This process is more effectively facilitated when learning takes place in natural settings in addition to the classroom or rehabilitation setting. Project LINCS (Learning in Natural Community Settings) was designed to provide followup with the real life needs of survivors and their families. This model views the rehabilitation process “as essentially educational, requiring skilled instructional training and long-term maintenance support in community settings” (Windsor, 1993).

Participant Action Research. The current research models are being reconfigured to acknowledge the critical component of consumer-driven Participant Action Research (PAR). Established in 1993 at the Mt. Sinai Medical Center in New York, PAR integrates persons with TBI and their significant others directly into all aspects of a program of action-oriented research.

Summary

The reality for consumers is that the medical model of rehabilitation may adequately address physical survival, but the other rehabilitation models are currently not successful in addressing consumer and family needs for positive outcomes and education for recovery beyond rehabilitation. The primary missing piece in the goals, administration, and overall organization of TBI rehabilitation is the consideration of the consumer perspective.

Recommendations

Given the fundamental changes in the health care environment, including the shift from inpatient to outpatient care, the need for community-based research and innovations in rehabilitation models is evident.

1. Establish research on consumer and family well-being in longitudinal studies to track the progress of persons with TBI throughout the course of specific rehabilitation processes and then beyond in order to assess family and community integration. The need to address the complex clinical sequelae within a lifelong continuum of care is a discovery project for a collaborative research panel.
2. Conduct community-based studies of the consumer-driven paradigm shift. Examples of innovative models include Project LINCS, “the least expensive cooperative continuum of community reintegration services for persons with brain injuries” (Windsor, 1993), implemented through the San Diego Community College District; the Participant Action Research model at the RTC of Mt. Sinai Medical Center (Campbell-Korves, 1995); and the Head Coach/TBI Curriculum component to educate and empower the consumer (Brain Injury Association of Virginia, 1994).
3. Establish a qualitative research project for the analysis of themes and trends in consumer literature to be conducted as a collaborative team of consumers and researchers. This project has a ready Web site network capable of a national endeavor to create the template for accessing and analyzing such information.

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Quality of Life and Life Satisfaction Studies

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The goals of this presentation are to highlight methodological problems inherent in quality of life (QoL) and life satisfaction studies; describe difficulties in conceptualizing QoL and the inadequacies of available measures; identify means of overcoming these inadequacies; highlight new, unpublished, or important but little-known findings; and identify important deficiencies in our knowledge about traumatic brain injury (TBI) and QoL that require further research. Considerable confusion exists about how QoL is defined. One central distinction concerns the perspective one takes (Dijkers, 1997). *Subjective* approaches define QoL in terms of congruence between aspirations and achievements as judged by the person himself or herself. *Objective* approaches focus on observable characteristics such as income, neighborhood poverty level, lifespan, education, and diagnosed disorders. *Health-related QoL*, the focus of this presentation, emphasizes aspects of life that may be affected by health; these characteristics typically include functional status, energy level, pain, participation in social and daily activities, and ability to leave one's home. QoL evaluation has been a focus of research in the chronic illness and cancer literature, and it has recently become a concern in rehabilitation (Tate, 1997).

A variety of instruments have been developed for use in such diverse undertakings as multicenter clinical trials, monitoring of outcomes in various clinical, severity- or "risk-adjusting" outcomes (Iezzoni, 1994) and development of care protocols (U.S. Department of Health and Human Services, 1995). Many QoL instruments abound because the needs of different users vary, scales have divergent properties, the experiences of different clinical populations are different, a high level of sophistication is needed to understand and interpret these instruments, and investigators desire both generic and disease-specific measures. Typical applications include aggregation across individuals and comparison of outcomes over time.

Levels of QoL components are sometimes viewed in a pyramidal hierarchy in which multiple, specific components constitute a bottom level, broad domains constitute a higher level, and an overall appraisal of well-being constitutes the top level. Domains often referenced include (1) physical status and functional abilities, (2) psychological status and well-being, (3) social interactions, (4) economic and vocational status and factors, and (5) religious and spiritual status. Spilker (1996) categorizes the foci of QoL instruments into five *realms*: (1) universally agreed-on aspects of health-related QoL applicable to everyone, (2) components of health-related QoL applicable to everyone, (3) components of health-related QoL applicable to persons with specific conditions, (4) components sometimes viewed as aspects of health-related QoL that are usually classified as clinical measures (e.g., depression, pain, or cognition), and (5) tangential aspects of QoL that are used occasionally. Schipper and colleagues (1996) describe QoL as a multifactorial construct, subjectively appraised, and related to a concept of reintegration to normal living. It reflects the "net consequences of disease and its treatment on the patient's perception of his ability to live a useful and fulfilling life."

In summary, QoL is a multifactorial construct that includes functional status as an element, is typically assessed from the perspective of the care recipient, and can serve to monitor outcomes and compare groups or change over time. QoL is related to a concept of reintegration to normal living and reflects the net consequences of disease and its treatment on individuals' perceptions of their ability to live a useful and fulfilling life.

Most instruments use rating scales that have the usual limitations of ordinal level of measurement: unequal intervals between points of a scale, limited reliability information, and unknown person applicability. Interval-level measures have the advantage of equal intervals between units of the scale and can be subjected to parametric analyses. Rating scale analysis (Rasch, 1980; Wright, Masters, 1982) provides a means of creating an equal-interval measure (calibrating items), describing a person's level of QoL (calibrating persons), evaluating the extent to which items cohere in defining a construct (item fit), and evaluating the extent to which a person's responses to a set of items are dominated by the one dimension it purports to measure (person fit). Criteria used to judge and improve the adequacy of a measure include (1) person separation (the range of QoL represented by the persons in the sample), (2) item separation (the range of QoL covered by the measure), (3) item fit (the extent to which the sample as a whole responds unexpectedly to specific items), (4) person fit (the extent to which individuals or subgroups respond idiosyncratically to the item set), and (5) scale structure (the extent to which raters use the steps in the scale correctly and consistently). Other applications of rating scale analysis include (6) providing a method of describing extent of QoL in persons undergoing rehabilitation, (7) extending scales across a continuum of settings, (8) identifying persons for whom a common scale is not useful, and (9) identifying items that do not work well to define a unidimensional construct.

Wade (1992) proposed five criteria by which to evaluate the utility of measures:

1. *Context of use*: Who can use the test? Is it appropriate for the purpose of the study?
2. *Development*: How were the items selected? Is the format suitable for the intended population?
3. *Validity*: For what populations have construct, concurrent, and predictive validities been established?
4. *Reliability*: How consistent are scores across raters? occasions? settings? Is there any bias?
5. *Sensitivity*: Has the test been used in placebo-controlled trials? in a trial of known efficacy?

The critical question that one must consider in test selection is "Will the test provide the required information?" A satisfactory answer requires stating *in advance* what one wants to measure in order to select an appropriate test.

Although QoL measures should possess the usual psychometric properties of reliability, validity, sensitivity to change, and ability to discriminate among levels of performance, few useful instruments exist to measure these characteristics across a range of settings. For example, QoL measures are often targeted at patients in specific settings (e.g., inpatient oncology treatment) and are “too easy” for patients in other settings (community). An important task is to co-calibrate items from across tests targeted at low, medium, and high levels of QoL to provide estimates of QoL regardless of which test was administered. A major goal of some QoL investigators is to create measures that are useful for persons in the general community who are receiving treatment for a variety of conditions. A sensible approach is to co-calibrate items from two or more tests and rescore items as necessary to maximize the range of the instrument, item fit, and utility. It may be necessary to revise instructions, develop additional items, delete items because of poor fit, identify patients for whom the instrument may usefully be applied, and develop refined scoring criteria.

The wealth of QoL instruments makes the task of selecting representative instruments daunting. Excellent guides are those of McDowell and Newell (1996), Spilker (1996), and Bowling (1997) as well as the journal *Quality of Life Research*. Two of the most widely used instruments are the Short Form Health Survey and the Sickness Impact Profile. John Ware and colleagues at the Rand Corporation developed the Short Form-36 for use in the Health Insurance Study Experiment/Medical Outcomes Study (1993). Their intent was to develop a generic measure of subjective health status that could be applied widely to persons with a variety of conditions. The items measure eight dimensions: physical functioning, social functioning, role limitations caused by physical problems, role limitations caused by emotional problems, mental health, energy/vitality, pain, and general health perceptions; a ninth category addresses perceptions of health changes over the past year. Separate versions allow assessment of health perceptions over the past 4 weeks and the past 1 week. The Sickness Impact Profile was developed as a performance-based measure of perceived health status that is sensitive to changes over time or differences in health status between groups (Bergner, Bobbitt, Carter, et al., 1981). Three uses are as (1) a health survey to determine general health levels of a population and to compare groups or communities, (2) an outcome measure to compare treatments and measure patient change in studies of specific diseases, and (3) an outcome measure for evaluating various approaches to the delivery of health care services. Its 136 statements are combined in 12 daily activity, behavior, well-being, and social functioning categories. Seven categories are collapsed into two dimensions measuring physical and psychosocial health.

QoL has been described inconsistently and imprecisely in the TBI literature. Most often the term has been equated with post-TBI adjustment. Vague and idiosyncratic definitions have been proposed in the TBI literature. For example, Jacobs and colleagues (1990) discuss issues affecting QoL after TBI but do not provide a definition of QoL. Bergquist and colleagues (1994) define QoL as (1) developing interpersonal relatedness or a sense of community among self and others, (2) achieving a sense of productivity, and (3) establishing a sense of self-control, self-efficacy, or self-competency. Although these are important concepts, they are more encompassing than the way the term is used in the larger health literature. Moore and Stambrook (1995) provide an interesting discussion of cognitive moderators of outcome following TBI and a multidimensional model of QoL outcomes, although their review does not reflect the larger QoL

literature. Hall and Johnston (1994) recommend that investigators focus on life satisfaction because QoL “is so all-embracing as to be nebulous.”

A variety of QoL measures have been used in the TBI literature. For example, Boake and High (1996) used the CHART as a QoL indicator; Baker and colleagues (1998) used the Katz Adjustment Scale; Burleigh and coworkers (1998) used the LSIA-A and CIQ; Webb and colleagues (1995) used the LSIA-A; and Granger and associates (1995) and Heinemann and Whiteneck (1995) used a single item to define life satisfaction or QoL. One measure developed expressly for adults with TBI is the CIQ. Willer and colleagues (1994) described the CIQ’s development and derivation of measures of integration into home, social, and productive roles. This measure may come closest to tapping a QoL construct that overlaps with the larger literature on QoL.

In summary, sophisticated psychometric methods allow us to conceptualize more clearly what we mean by QoL. In turn, we have benefited from measuring these constructs with improved reliability, validity, and sensitivity. We must co-calibrate items from different instruments and explore the pattern of misfitting items and persons to measurement models. The increasing prominence of injury and chronic diseases in the health literature, changing population demography, and growing cost containment concerns all converge to support QoL as a major focus in TBI rehabilitation. Research recommendations include using standardized QoL measures as outcome indicators following TBI more consistently and examining both objective and subjective aspects of QoL in addition to life satisfaction. It is time for TBI rehabilitation to join the mainstream of health services research by adopting terminology and measures that are used more widely. Doing so will enhance communication and understanding about adaptation following TBI.

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Ethical Considerations in Research Design Involving Persons With Traumatic Brain Injury

John Banja, Ph.D.

The central ethical issue in recruiting and maintaining persons with traumatic brain injury (TBI) as research subjects consists of implementing procedural safeguards that protect their rights and welfare, because these persons frequently lack adequate judgmental capacity to give informed consent to research participation. The obligation to respect personal rights and dignity—which John Rawls (1971) emphasized in *A Theory of Justice* by saying, “Each person possesses an inviolability founded on justice that even the welfare of society as a whole cannot override” (p. 3)—is at the heart of contemporary research ethics and usually represents the linchpin in indicting research efforts as less than honorable or simply disreputable. Not surprisingly, in the immediate aftermath of World War II, with the horror of the Nazi monstrosities still reverberating throughout the world, the tribunal that composed the 1947 Nuremberg Code specifically forbade research among persons unable to give informed consent. The Helsinki Declaration, which appeared in 1964, permitted such research but, like Rawls, insisted that “concern for the interest of the subject must always prevail over the interest of science and society.”

Contemporary research ethics promotes respect for persons as a formal and categorical obligation. It is never the case in a research scenario that the good of the many—or the importance of gaining new knowledge—outweighs the good of the one. Most important, the American comprehension of individual rights along with an emphasis on liberal democratic values holds that no argument or policy exists that obligates individuals to engage in research, nor does a persuasive ideological basis exist to support the argument that certain persons can force others to subordinate their interests or welfare to the pursuit of knowledge. Among persons who are judgmentally impaired, this point is all the more pronounced and the obligations imposed on the researcher all the more intense because judgmentally incapacitated persons are frequently unable to protect themselves and thus constitute a population whose rights are especially vulnerable.

The observation that the goal of research is to secure knowledge serves to contrast research with the clinical enterprise. In straightforward treatment scenarios, the explicit presumption of the patient and the professional is that the good of the patient is the immediate, singular, and overriding objective. The patient is an end in himself or herself and has every right to assume that he or she will be treated as such. In research scenarios, on the other hand, the research subject might not, and usually does not, significantly benefit because his or her immediate good is not fundamentally at issue. What is at issue is confirming a hypothesis, developing a knowledge base, and evolving principles and laws about scientific phenomena. In research scenarios, these objectives never take precedence over the discrete good and welfare of

the research subject. This moral principle is of great importance in designing research protocols involving individuals with cognitive impairments or mental disability.

Protecting Research Subjects With Judgmental Impairments

In conducting research on TBI, researchers should first attempt to recruit subjects who are symptomatic but not judgmentally impaired. This practice would obviate ethical concerns about rights violations among vulnerable populations. Of course, this effort will frequently prove impossible in TBI research because the research often targets precisely those impairments that cause or constitute the subject's inability to give informed consent to research participation (i.e., inadequate ability to understand, reason, exert insight, appreciate decisional consequences, etc.).

Nevertheless, research protocols should incorporate evaluational mechanisms whereby competent subjects can be distinguished from incompetent subjects. Such competency assessments should be task specific, that is, tailored to the intellectual demands of the research study rather than to a demand for "mental status" variety. Among individuals who are determined to be judgmentally unable to give informed consent but who can "assent," that is, give "uninformed" consent, a proxy or surrogate must be in place to protect the patient's interests. Identification of the surrogate should proceed in accordance with State law or regulation (assuming such law exists). The surrogate should be informed of the research protocol as comprehensively as would a competent research subject. This includes disclosure to the effect that the subject might not benefit from the research in any substantive way or, if some benefit might be anticipated, what its probability and magnitude would likely be. The surrogate should also be informed that he or she can withdraw the subject from the research without penalty.

Enrollment of subjects with judgmental incapacities requires consent or assent from both the surrogate and the subject. If the subject is unable to assent, no evidence should be present that he or she wishes to refuse or withdraw. Despite their judgmental impairments, subjects with cognitive impairments who have initially assented to participation but who appear to desire discontinuation must be allowed to withdraw. The argument that their cognitive impairment disempowers them from understanding the nature or consequences of their withdrawal (and therefore somehow moots their withdrawal decision) will usually not trump the argument that respecting their personhood requires acknowledging the nonobligatory nature of research participation and their authority as free, rights-bearing citizens to refuse research participation (despite whatever cognitive impairments they have). This argument holds even if the subject's surrogate insists on the subject's continuing, a possibility that requires an additional safeguard to monitor whether the surrogate's decisions proceed in "good faith." A small group of cases that might provide an exception to the general rule of always respecting the subject's right to withdraw are those in which the uncomprehending subject's desired withdrawal would entail an excessive burden to him or her. This scenario includes only directly therapeutic research interventions that are known to have promise and whose discontinuation would plunge the uncomprehending subject into a menacing situation (for example, suicide or the relentless progression of a terminal illness). Such scenarios, in the general scheme of research, are somewhat unusual, although one occasionally sees them among pediatric populations.

Research protocols in TBI should incorporate mechanisms that ensure that neither the subject nor the surrogate is in any way coerced, threatened, or manipulated to comply with the researcher's objectives. These ethical worries are especially prominent during the subject recruitment phase of research, when subjects and/or surrogates might believe that refusal to participate will result in some penalty or that assent will lead to some benefit. Some ethicists worry about this possibility so much that they recommend subjects be recruited and, with their surrogates, be "consented" by individuals not directly involved in the research (and who, therefore, would not be tempted to dilute the gravity of information that might cause subjects and/or surrogates to withhold assent/consent).

Last, one needs to recognize that Federal mandates and regulations defer to State law, institutional review boards, or ethics review boards in matters that involve protecting subjects with judgmental impairments. An extremely important function of such review frequently includes assessing the gravity of risk presented to subjects enrolling in a research project. With risk understood as the probability of an adverse event occurring, research risks have traditionally been classified into three categories: minimal risk, minor increment over minimal risk, and greater than minor increment over minimal risk. These classifications have led one commentator to remark that "these concepts are sufficiently vague to permit substantially varied interpretations." Ethics or institutional review boards should receive guidance on interpreting these terms because a consensus does not appear to exist on their definitions even though ethics review boards are frequently asked to approve projects whose risks constitute a "minor increment beyond minimal."

At issue is how the meanings of these risk classifications are affected and complicated by the nature of subject specificity and context specificity. Thus, 45 Code of Federal Regulations Section 46 defines minimal risks as risks not greater "than those ordinarily encountered in daily life." But "ordinary encounter" might differ dramatically among persons—e.g., the lumberjack versus the college professor—whereas the context of the scenario—e.g., one in which the research subject experiences an extremely low quality of life—might reduce the gravity or magnitude of a particular research risk considerably below its estimation by a healthy individual.

Future Directions

To contemplate ethical issues in TBI research, it is important to gather morally problematic examples "from the trenches." Two interesting areas that should be examined include describing the continuum of research questions in traumatic brain injury—from pure science to immediately therapeutic—and then listing and discussing the ways that differing magnitudes and probabilities of risk penetrate each stage and are affected by the gravity of the subject's condition. Thus, one might identify at least four categories of human research in TBI: (1) research that deals only with a pure knowledge issue, not a clinical question, (2) research that is therapeutic in nature but holds out no benefit whatsoever to the enrolled research subject, (3) research that may be therapeutic to the subject but with unknown probability and magnitude of the benefit, and (4) research that is known to have therapeutic value with a direct chance of benefit to the research subject. After refining the criteria whereby examples of the above can be

classified, ethics researchers might then examine how the three levels of risk mentioned above (i.e., minimal, minor increment beyond minimal, greater than minor increment beyond minimal) can be understood within these various contexts. For example, an important area of ethical research would be to gather knowledge that would assist ethics review boards in authorizing research that poses risks that constitute a “minor increment beyond minimal risk.” How does one develop an operational understanding of this term? Under what conditions should such research proceed? Should a National Ethics Advisory Board on Research, similar to the President’s 1983 Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, be developed to facilitate answers? It would be interesting to determine whether any consensus on these questions exists among researchers, whether their opinions would be at significant variance from the general public or from patient advocacy groups, and, if so, how public policy formation might proceed.

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Approaches to Resolving the Dilemma

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Three issues affecting the implementation and interpretation of clinical outcome research in traumatic brain injury (TBI) will be presented: (1) the selection of designs appropriate for examining rehabilitation outcomes in TBI, (2) the distinction between outcomes that are therapeutically important versus statistically significant, and (3) the importance of replication in establishing the clinical validity of research in TBI.

Issue 1. Research Design

Randomized clinical trials (RCTs) are frequently advocated as the only scientifically legitimate design to use in clinical research (Andrews, 1991; Colditz, Miller, Mosteller, 1989; Gladman, 1991; Ottenbacher, 1995). However, RCTs are often difficult or impossible to implement in a clinical setting. The practical limitations of RCTs have been discussed by many investigators, including Kramer and Shapiro (1984), who note that “despite the obvious advantages and impressive track record of RCTs, clinical investigators have become increasingly aware of certain difficulties in their interpretation, feasibility and ethics.” The difficulty of meeting the requirements of RCTs in clinical settings has forced researchers to develop new approaches to conducting effectiveness investigations. For example, Guyatt and colleagues (1990, 1986) demonstrated the use of alternative designs using small numbers of subjects in clinical medicine. They refer to these designs as randomized trials involving individual patients, or N of 1 randomized trials. Variations of these same designs are more commonly referred to as interrupted time series or single-subject experimental designs (Guyatt, Sackett, Taylor, et al., 1986). Other alternative design strategies include Sequential Clinical Trials (Whitehead, 1997), Regression Discontinuity Designs (Cook, Campbell, 1979), and Goal Attainment Scaling (Kiresuk, Smith, Cardillo, 1994). Also available to clinical investigators in cognitive rehabilitation are a large number of qualitative and ethnographic approaches that allow investigators to explore complex person-environment interactions (Bogdan, Taylor, 1984).

The way research design is usually taught to students and portrayed in professional journals implies that the design is an open window through which the phenomenon of interest can be studied in an unobstructed manner (Andrews, 1991). This window analogy suggests that the design allows researchers to uncover a phenomenon but that the design does not directly contribute to the results. Evidence now exists that this assumption is false (Colditz, Miller, Mosteller, 1989; Gladman, 1991; Ottenbacher, 1995). The findings of a clinical trial, no matter how well designed the trial is, do not provide a picture of the world independent of the methods used to collect the information. Therefore, no investigation can isolate a relationship between treatment and outcomes beyond the context of the design.

The discussion above should not be interpreted as an argument against the use of randomized clinical trials or against the consideration of design quality factors in the evaluation and synthesis of clinical research. On the contrary, design attributes are of the utmost importance. Design characteristics should be examined in relation to specific research outcomes whenever any attempt is made to integrate and interpret multiple clinical trials (Ottenbacher, 1995). If investigators adopt such a practice, they will avoid the rigidity that sometimes allows empirical habit to overpower scientific originality and subordinates research problems to methodology.

Issue 2. Statistical Versus Clinical Significance

Rehabilitation researchers and clinicians often operationalized clinical significance by equating it with statistical significance (Anscombe, 1990). This is a practice that has caused considerable confusion in the research literature on rehabilitation outcomes. Positive results are usually interpreted as those associated with statistically significant outcomes. The tendency to treat the $p < .05$ alpha level as a probability cliff represents a misinterpretation of significance testing. As a result of this misinterpretation, research results supporting the null hypothesis are treated in a qualitatively different way from research reports failing to support the null hypothesis (Ottenbacher, 1995).

The limitations of significance testing have been well documented, and numerous supplements or alternatives have been proposed (Andrews, 1991; Cohen, 1988). One frequently advocated supplement to statistical significance testing is the calculation of effect size measures. Various measures of effect size appropriate for a wide range of designs and statistical procedures have been proposed by Cohen (1988). Another frequently advocated supplement to statistical significance testing is the use of confidence levels. Focusing on the therapeutic inferences in clinical trials instead of the statistical probability will enhance the clinical relevance of rehabilitation research.

Issue 3. The Importance of Replication

Successful replication is generally taken to mean that a null hypothesis that has been rejected in the original trial will be rejected in a second or subsequent investigation (Ottenbacher, 1996). If the null hypothesis is rejected in followup studies, we conclude that a successful replication has been achieved and that the theory tested or intervention under investigation has been supported. Conversely, if the first study produces statistically significant results and the second investigation nonsignificant results, then the conclusion is that the results of the two studies conflict and that there is a failure to replicate. The standard model of replication based on statistical significance testing (Rosenthal, 1990) is presented below.

		Original Study	
		$p > .05$	$p < .05$
Second Study	$p < .05$	Failure to replicate	Successful replication
	$p > .05$	Failure to find effect	Failure to replicate

If a replication study uses the same sample size and thus has the same power as the original study, then the probability of a replication is $p^2 + (1 - p)^2$. If the investigator conducting a replication study is examining a genuine effect (the true research [alternative] hypothesis, H_a) then power becomes a critical factor in determining the success of any replication effort (Ottenbacher, 1996).

The impact of low statistical power on successful replication is easily illustrated with an example. Assume a researcher has conducted a series of appropriately designed replication studies with a mean power of .40, the probability of replication p (replication) = $.40^2 + (1 - .40)^2$ is .52. This value is even less encouraging if we consider that because of the low power, the majority of the replications in this example represent confirmations of a false impression. In fact, $(1 - .40)^2 + [.40^2 + (1 - .40)^2] = .88$, or 88 percent of the replications strengthen a false impression (a type 2 error) (Ottenbacher, 1996).

Implications

The three research issues described above are not mutually exclusive. They interact in a complex manner to potentially obscure the interpretation of rehabilitation effectiveness. The first factor limits the number of investigations we consider in developing a knowledge base regarding rehabilitation outcomes. The second and third factors reduce our ability to accurately interpret the results of individual clinical trials and, perhaps more importantly, prevent us from synthesizing existing research to determine whether a consensus exists regarding the effectiveness of various rehabilitation interventions.

Many investigators have displayed a tendency to be overzealous in their use and promotion of traditional experimental methods and associated statistical procedures, much like the young child who, when first given a hammer, finds that everything he encounters needs pounding. Not all rehabilitation research questions need to be hammered with statistical null hypothesis testing. The evolving discussion concerning the merits of various research strategies makes it clear that traditional experimental designs are a valuable empirical option, but they are not the absolute ideal in every situation (Whyte, 1994). The debate concerning research approaches forces investigators to address not only traditional outcomes but also the rehabilitation process and the ecology of disability. To develop a useful body of knowledge, researchers must become proficient in a variety of strategies so that they can explore research

problems without quantitative or qualitative parochialism. Investigators should be modest in their claims regarding specific designs and realize that in clinical settings, all designs and statistical procedures are fallible. The discovery of a bias or weakness in a research strategy is not a reason to reject the method but is instead a challenge to improve it, just as we strive to improve or refine a theory in the face of disconfirming data.

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