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EXECUTIVE SUMMARY

The National Center for Medical Rehabilitation Research (NCMRR) portfolio has continued to grow at a rate that exceeds the growth of the National Institutes of Health (NIH) as a whole, and that of the National Institute of Child Health and Human Development (NICHD). This growth is largely driven by an increase in the number of quality applications from rehabilitation researchers and researchers from allied fields who are building up the research base and addressing the needs of people with disabilities. The NCMRR alone annually supports $75 million in rehabilitation-related research; additional support for such research comes from other NIH Institutes that have an interest in rehabilitation approaches and outcomes.

Throughout its tenure, the Center has emphasized training new investigators and recruiting established investigators from allied fields. The NCMRR continues to focus on building research infrastructure and integrating cutting-edge technologies and approaches to address the broad rehabilitation research agenda developed by the National Advisory Board on Medical Rehabilitation Research in 1993 in conjunction with the wider rehabilitation community.

The Center includes the following five programs:

- **Traumatic Brain Injury (TBI) and Stroke Rehabilitation**, directed by Beth M. Ansel, Ph.D., CCC-SLP
- **Biological Science and Career Development**, directed by Ralph M. Nitkin, Ph.D.
- **Pediatric Critical Care and Rehabilitation (PCCR)**, directed by Carol Nicholson, M.D.
- **Behavioral Sciences and Rehabilitation Engineering Technologies**, directed by Louis A. Quatrano, Ph.D.
- **Spinal Cord and Musculoskeletal Disorders and Assistive Devices**, directed by Nancy Shinowara, Ph.D.

In keeping with the NICHD’s shift to improve the transparency of and public input in strategic planning for its components, the NCMRR went through a portfolio review and discussion of future research plans in preparation for its report to the National Advisory Child Health and Human Development (NACHHD) Council.

Unlike other NICHD Centers and Branches, the NCMRR has its own Advisory Board, which meets twice a year to discuss the Center’s portfolio and to assess possible research directions. Therefore, rather than re-invent this process for its report to the NACHHD Council, the NCMRR relied on the National Advisory Board on Medical Rehabilitation Research to assist in examining the Center’s current portfolio and making recommendations for future NCMRR research directions.
With the forecast constraints on the growth of research funding in general, NCMRR has developed a set of new priorities for research funding emphasizing opportunities for investigator-initiated grant applications:

- Translational Research: Bench to Community
- Basic Research to Advance Rehabilitation
- Plasticity and Adaptation of Tissue in Response to Activity and Environment
- Reintegration of Persons with Disabilities into the Community

At the same time, the NCMRR will strive to achieve several cross-cutting objectives:

- Develop mechanisms to support new investigators
- Enhance consumer input and outreach
- Extend the interdisciplinary model from basic research through applied research and community studies

**NCMRR PROGRAMS AND PROGRAM DEVELOPMENT**

To accomplish its mission—fostering development of the scientific knowledge needed to enhance the health, productivity, independence, and quality-of-life of people with physical disabilities—the NCMRR supports a broad range of basic and applied research to enhance the daily functioning of people with disabilities. The Center’s mission also brings the health-related problems of people with disabilities to the attention of America’s best scientists so that researchers can apply the myriad advances occurring in the biological, behavioral, psychosocial, and engineering sciences to improving outcomes of people with disabilities.

The Institute of Medicine report, *Enabling America: Assessing the Role of Rehabilitation Science and Engineering* (National Academy Press, 1997), highlighted the national need for research advances to improve the effectiveness of rehabilitation services and the practices for promoting the health of people with disabilities. The incidence and prevalence of people with disabilities continue to mount in parallel with dramatic increases in medicine’s ability to prevent deaths due to injury, disease, and conditions associated with aging. An estimated 49 million Americans¹, about one of every seven citizens, have disabling conditions so severe that they are unable to carry out the major activities of their age group, such as attending school, working, or providing self-care.

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As a health care discipline, medical rehabilitation provides the means for combating disability. Medical rehabilitation services are made more effective by putting them on more solid scientific footing. Improved outcomes are reflected by improved integration of people with disabilities back to family, community, vocational, and educational settings, rather than placement in long-term care facilities. The result is both improved quality-of-life for service recipients and long-term cost savings for society.

Remarkably, no focus for facilitating medical rehabilitation research existed within the NIH until 1990, when legislation established the NCMRR (P.L. 101-613). This legislation also established two other entities that are integral to the Center’s operations:

- **The National Advisory Board on Medical Rehabilitation Research** consists of 12 scientists and clinicians in medical rehabilitation, six people from the public domain, and several ad hoc members from government agencies that fund research or service programs of relevance to medical rehabilitation (see Appendix C for a list of current Board members). The Board’s principal function is to advise the NIH on research opportunities and to evaluate NCMRR activities. The Advisory Board helped to develop the initial NCMRR Research Plan, which was mandated in the founding legislation. The resulting *Research Plan for the National Center for Medical Rehabilitation Research* (DHHS, NIH Publication 93-3509, 1993) continues to guide priority setting for the Center’s programs. This Research Plan outlined seven research areas for the Center, including:
  - Improving functional mobility;
  - Promoting behavioral adaptation to functional losses;
  - Assessing the efficacy and outcomes of medical rehabilitation therapies and practices;
  - Developing improved assistive technology;
  - Understanding whole body system responses to physical impairments and functional changes;
  - Developing more precise methods to measure impairments, disabilities, and societal and functional limitations; and
  - Training research scientists in the field of rehabilitation.

- **The Medical Rehabilitation Coordinating Committee** makes recommendations to the NICHD and NCMRR directors regarding the Center’s Research Plan and activities that are carried out in conjunction with other entities, both within the NIH and throughout the federal government. The Committee includes representatives from other NIH institutes that have interests in rehabilitation research: National Institute on Aging (NIA); National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); National Cancer Institute; National Institute on Deafness and Other Communication Disorders; National Heart, Lung, and Blood Institute (NHLBI); National Institute of Neurological Disorders and Stroke (NINDS); National Institute of Nursing Research; National Eye Institute; National Institute on Drug Abuse; National Center for Complementary and Alternative Medicine; National Institute of Biomedical Imaging and Bioengineering; and National Institute for General Medical Sciences.
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The remainder of this report describes the Center’s research programs, highlights findings from NCMRR-supported research, and outlines possible areas of research for the Center to support in the future.

**THE NCMRR RESEARCH PORTFOLIO**

**NCMRR Research Priorities**

As the NCMRR and others viewed the field of rehabilitation research in 2000, there was general agreement that an urgent need existed to enhance research capacity. The strategy adopted by the NCMRR was deliberately ecumenical: to develop new investigators into rehabilitation researchers and to attract established investigators to address rehabilitation research questions. The NCMRR promoted training and research opportunities aggressively by attending national scientific and professional meetings and by drawing attention to new opportunities, such as the Rehabilitation Research Network Centers (see the *Infrastructure Development at the NCMRR* section of this report for more information on the networks). In addition, NCMRR also issued various Requests for Applications (RFAs), Program Announcements (PAs/PARs), and other solicitations during this time period (*Appendix A*) and supported a number of conferences (*Appendix B*).
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The Center’s annual expenditures for research and research training grew from $37.7 million in fiscal year 2000, to $75 million in fiscal year 2005—an average annual growth of 20 percent (Figure 1). The number of NCMRR projects funded for these fiscal years increased from 190 to 303 (Figure 1). Consistent with Advisory Board recommendations, the NCMRR has provided disproportionately greater support for research training (Figure 2), as compared, for example, to other NICHD Centers. As with all of the NIH, the greatest proportion of the annual research budget goes to support continuing grants (Figure 3). Also consistent with the culture of NIH, fully half of all grants from NCMRR go to support R01 applications (Figure 2).

Evaluation of the research portfolio over the years 2001-2005 (Figure 4) revealed a reasonably broad distribution of support for projects in all of the priority areas identified by the Advisory Board. Support for evaluation of therapies and practices accounted for the largest share of grants (22 percent), reflecting a growing interest in translational studies that attempt to evaluate the efficacy of rehabilitative approaches, as well as the large costs of conducting clinical studies. Developing improved assistive technologies accounted for 17 percent of grant support, reflecting both the exciting opportunities to utilize new technologies to address the needs of the disabled, and the relative availability of Small Business Innovation Research (SBIR) grants that are particularly well suited for some of this work.

Analyzing the research portfolio with respect to clinical conditions under study (Figure 5) revealed a similarly broad distribution of funding across different conditions. As expected from the large proportion of disabled individuals who have limitations of mobility2, about 35 percent of the NCMRR research portfolio addressed issues related to mobility. Cognitive issues were the subject of 18 percent of research funding and secondary conditions, including bladder and bowel dysfunction, also accounted for 18 percent. Research on promoting participation and health services research represented 11 percent of the portfolio.

The NCMRR plays a unique role in focusing the expertise of the biomedical research enterprise on the problems of rehabilitation and recovery.

The Center’s lead role does not mean, however, that other federal agencies and NIH Institutes do not support research related to rehabilitation. For example:

- The NINDS supports research on neuropathology, particularly with respect to stroke, spinal cord and brain injury, and neuromuscular disorders;
- The NIAMS supports research on muscle and joint physiology, bone, and skin;
- The NIA supports research on geriatric issues; and
- The NHLBI supports research on exercise and cardiovascular function.

Outside the NIH, the National Institute on Disability and Rehabilitation Research (NIDRR) supports a significant amount of work on participation and socio-behavioral issues; the Centers for Disease Control and Prevention (CDC) support work on demographics, prevention, and secondary complications; and the Veterans Administration supports research on issues of particular concern to the health care of veterans.

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The role of the NCMRR is perhaps best appreciated by its lead in developing the trans-NIH initiative, *Research Partnerships for Improving Functional Outcomes* (PAR-04-077). Rather than specifying research on a particular disease entity, this initiative solicits work on a broad array of conditions, but with specific attention to improving the function of individuals with those conditions. Applications for this initiative can focus on basic mechanisms of recovery, treatment methodologies, evaluation, or outcomes, thus spanning diverse expertise and methodologies ranging from molecular biology to health services research. The initiative also emphasizes the development of cross-disciplinary research partnerships that will bring new science and insights to bear on improving rehabilitation and recovery. A key feature of this effort is that nine NIH Institutes and the Agency for Healthcare Research and Quality accept applications submitted under this PA, thus providing new venues for investigators who are interested in rehabilitation issues to apply for research support from NIH Institutes that are not usually thought of as interested in supporting rehabilitation research.

**TRANSLATIONAL RESEARCH APPROACHES IN THE NCMRR**

Even though studies of acute tissue damage and pathology are generally supported by other parts of the NIH, the NCMRR has a special role in supporting studies to translate this research into improved function, reduced secondary complications, and increased participation of people with disabilities. To this end, the NCMRR supports a range of basic research approaches on the response of the substrate to injury and on strategies to promote regeneration, recovery, plasticity, adaptation, and recovery of function. Many of these studies are initially carried out in animal models in which cellular, molecular, physiological, and biomechanical processes can be examined in greater detail. More promising results can then be carried into human studies for further validation, tests of safety and efficacy, and translation into clinical practice.

Animal models are particularly well suited for studying certain pathological processes, tissue responses, and functional interventions, provided that investigators account for anatomic, physiological, and functional differences and that they have a clear vision of potential translation into human studies and clinical practice. Animal models may even be appropriate for studying cognitive and behavioral processes in limited contexts. However, for other studies, especially those involving relatively non-invasive approaches, the most appropriate animal model may indeed be the human, especially with respect to studies of joint mechanics, gait, muscle physiology, activity-mediated processes, and exercise physiology.

Recent studies in animals and pilot studies in humans suggest that stimulatory compounds (e.g., amphetamines) may promote recovery in stroke, possibly through activity-mediated pathways. To encourage more research in this area, the NCMRR issued the RFA, *Pharmacological Approaches to Enhance Neuromodulation in Rehabilitation* (RFA-HD-02-023), which led to a series of studies in animal models on the effects of pharmacological compounds on recovery of function in the somatosensory and motor systems.

Studies on spinal-cord injured rodents and cats have provided some interesting results on the possibility of enhancing functional circuitry within the spinal cord and restoring walking.
Treadmill training and other rhythmic activities appear to activate pattern generators and latent circuitry within the damaged spinal cord; this activation can initiate rhythmic motor activity (e.g., walking) even in the absence of appropriate connections with the motor centers of the brain. To translate these findings into humans, the NCMRR supported two clinical trials on body-weight supported treadmill training for spinal cord injury (SCI) and stroke patients. One of these studies, a multi-site clinical trial demonstrated that well-supervised conventional therapies were as effective as treadmill training for patients with partial SCI. This finding has spurred further research in the field.

Although cerebral palsy represents a cluster of developmental disorders that primarily affect the central motor system, it often leads to severe musculoskeletal dysfunction in the affected limbs. Chronic muscle inactivity and spasticity present unique challenges in the clinical management of cerebral palsy. Current treatments (e.g., splinting, muscle-tendon lengthening, or dorsal rhizotomy) often focus on treating the symptoms without appropriate consideration of the underlying dysfunction or the likely neurological and musculoskeletal responses to the intervention. The NCMRR supports a range of studies on gait modeling in cerebral palsy, as well as clinical follow-up studies of surgical interventions that highlight the subtle heterogeneity of cerebral palsy deficits and the implications for clinical management of the condition.

In the extreme case, chronic disuse of muscle can lead to contractures, a severely disabling condition associated with overgrowth of connective tissue cells and reduced contractility and joint function. To date, however, few studies have addressed the molecular and cellular bases of contractures, or the therapeutic strategies that can reduce disability and restore function. Recently, the NCMRR issued *Molecular and Cellular Basis of Contractures for Design of Therapeutic Interventions* (RFA-HD-02-022). As a result of this RFA, the Center funded three grants addressing: contractures, in terms of cellular and molecular genetic changes in different regions of inactive muscle; biomechanical changes in individual muscle fibers; and alterations in contractile and other structural proteins. Another interesting approach, funded by the NCMRR to address musculoskeletal problems, is the use of cultured cartilage cells to explore the effects of cyclic tensile stress on these cells. In response to cyclic tensile stress, cultured cartilage cells produce significant quantities of anti-inflammatory cytokines. This tissue culture system may be a useful model for exploring the basic mechanism that underlies the beneficial effects of passive joint manipulation. Efforts are under way to determine whether cartilages from different regions (e.g., vertebral joints) behave similarly.

Another new direction for rehabilitation research is the consideration of genomic factors. Researchers have long known that patients can have different outcomes, despite similarities in predisposing conditions and in subsequent clinical management. Some of this variation may result from subtle differences in the localization or extent of initial insult, prior state of health, clinical follow-up, or even patient compliance; newer evidence also indicates that genomic factors could impact on clinical outcome and recovery. Thus, allelic differences among individuals could translate to subtle differences in key molecular and cellular responses and, ultimately, in rehabilitative outcomes. Genomic differences could manifest themselves at several levels, including: modulation of predisposing health and clinical factors; initial pathological processes; extent of plasticity and recovery; responses to therapeutic interventions; and even behavioral and psychosocial coping and adjustment.
To stimulate research in this area, the NCMRR developed an initiative titled *Genetic Basis of Recovery and Rehabilitation* (RFA-HD-03-025). Several of the submitted proposals represented unique collaborations among rehabilitation researchers, genetic epidemiologists, and other basic and clinical specialists. The five grants funded under this initiative are exploring the influence of potential differences among various aspects of genetic factors on outcomes in TBI, muscle disuse atrophy, respiratory stress, and other conditions.

Another interesting application of basic research is in the use of specially engineered bacteria to treat urinary tract infections. Chronic bladder dysfunction, which is associated with SCI, spina bifida, and stroke, is a critical issue for many nursing home residents that often requires the repeated use of in-dwelling catheters. However, this remedy makes these patients prime candidates for bacterial infections, which have a major impact on morbidity and mortality. To treat this problem, NCMRR-funded researchers proposed a strategy of bacterial interference; that is, intentionally seeding the bladder with benign bacteria to out-compete pathogenic strains and thereby prevent their growth. By examining the range of bacteria found in the bladder and the potential of each for causing symptomatic infections, the researchers created a genetically altered strain of *Escherichia coli* that is benign, but that tightly adheres to catheter surfaces, preventing the pathogenic strains from gaining a foothold. Preliminary studies in mixed culture conditions and later in clinical trials with able-bodied volunteers indicated that the engineered strains were completely benign and the patients who received them asymptomatic. Initial pilot studies in spinal-cord injured subjects indicated that this engineered bacteria could successfully colonize bladders with no adverse effects. The strategy’s long-term effects on preventing urinary tract infections and reducing mortality will require larger follow-up studies.

**APPLIED RESEARCH—REHABILITATION TECHNOLOGY**

This component of the NCMRR research program focuses on improving the human–environment interface and involves development and testing of novel assistive technology to restore or enhance an individual’s capacity to function in his or her environment. Projects supported in this program include, but are not limited to, prosthetics to enhance mobility, communication, cognition, and environmental control. The NCMRR supports a wide range of projects, using both research mechanisms (R03, R21, and R01) and SBIR mechanisms, to address complex and difficult engineering problems. For example, the portion of the NCMRR portfolio that applies state-of-the-art biomechanical modeling and imaging to predict the effects of therapeutic interventions for neurologic and musculoskeletal interventions has grown steadily since the last report to the NACHHD Council.

This section highlights four research efforts that have resulted in products either on the market or about to launch. These projects illustrate different domains of applied research supported by the NCMRR.

**Trail Assessment Technology**

A project from Beneficial Designs, Inc.—called TrailWare 2.0—offers a sophisticated database that allows land managers to enter data into a computer program and generate extensive, detailed
reports regarding the grade, cross slope, tread width, obstructions, and surface firmness and stability of trails. TrailWare 2.0 also generates summary reports and signage that trail managers can use to provide information to the public. All hikers—from families with young children to older individuals to those with limited mobility—benefit from having this information for selecting appropriate trails to hike. More aggressive trail users can also use TrailWare 2.0 to select options that offer a greater challenge.

Other NCMRR-funded work built on TrailWare 2.0 successes to develop the Wheelchair Work Measurement Method, a process that determines the work needed to propel a wheelchair over different surfaces in relation to the work needed to propel it up different ramp grades. Because existing accessibility standards are based on specific ramp grades, the work necessary to propel the chair up those grades should be consistent with any standards for firmness and stability; the Wheelchair Work Measurement Method makes this consistency possible.

This highly successful project and other NCMRR-funded SBIR research on trail-related technologies have not only resulted in a suite of tools and research results on the topic, but have also made a tremendous impact on the development of accessibility standards for outdoor recreation. The provision of access information for outdoor recreation is critical to the health and well-being of persons with disabilities and helps to create and maintain access to all environments for all people.

Magic Wheels
Wheelchairs with rear push wheels and front casters have changed very little since they were first patented in 1869. Now, a manual wheelchair push wheel with innovative features has resulted from nine years of research with NCMRR support. This SBIR/Small Innovative Technology Transfer (STTR) product offers two easily shifted mechanical gears, which help in navigating ramps, hills, and uneven terrain. Users with full or limited hand and arm strength are able to use the shifter. Another important feature of the chair is a “hill holder,” which eliminates rollback when climbing hills or long ramps when in low gear. This feature permits the user to rest between pushes without rolling backwards. In addition, the breaking feature requires 50-percent less force to stop, when in low gear going downhill.

Magic Wheels (http://www.magicwheels.net) will give users greater independence and easier access to their environments without fear of running out of power or adding substantial weight to their wheelchairs. The researchers are now using clinical rehabilitation research to confirm the product’s other indirect benefits. For instance, providing consumers with more independence may reduce the burden on caregivers; and reduced effort necessary to propel the wheel may translate to prevention or reduction in onset of shoulder pain or upper limb injury, both common problems for persons in conventional wheel chairs.

The High-Impact Telemetry (HIT) System™
In sports such as football, impacts with the potential to cause injury might go unnoticed, and resulting physiological damage may be cumulative. To address these issues and improve safety, Symbex, with support from the NCMRR, developed the HIT System™—the first device to continuously monitor, analyze, and record a football player’s on-field head impact experiences in both game and practice situations. The HIT System™ measures head acceleration and captures
its data from sensors embedded in the padding of a helmet that automatically and continuously measure and record blows to the head. Almost instantly, the system computes the magnitude, location, direction, and duration of each impact. The impact information is then transmitted wirelessly to a laptop computer housed in a compact, sideline console. Sideline staff can then review several richly detailed images and graphs of the impact on the HIT System™ display.

The HIT System™ not only monitors and records the impact history for all players simultaneously, but can also alert the sideline staff to the occurrence of an impact that conforms to a Suspect Impact Profile™—criteria identifying impacts that might have caused damage. The system monitors standard impact measures, including maximum G force, Head Impact Criteria, Gadd Severity Index, or customized metrics based upon impact location, magnitude, duration, linear and angular acceleration components, and the exact times of single or multiple impacts. The result is improved player protection and injury prevention, detection and care. This system is now in clinical trials at Virginia Polytechnic Institute and State University.

StepWatch™

Long-term collection of accurate ambulation data is important for the evaluation of status, function, outcome, and behavior of individuals with many types of conditions or impairments (e.g., lower-limb prosthetics, total hip replacement, total knee replacement, hip fracture, stroke, surgical efficacy, and diabetes). Phase I and Phase II SBIR awards from the NCMRR enabled principal investigator Kim Coleman and Cyma, an activity-monitoring company, to conduct and complete research and development for the StepWatch™ System Activity Monitor (SAM). StepWatch™ is now commercially available on four continents. The NIH Web site offers a report of the company’s success at http://grants1.nih.gov/grants/funding/sbir_successes/158.htm.

The StepWatch™ monitor—a highly adjustable, unobtrusive, extremely durable, and maintenance-free device—is useful for both research and clinical evaluation. Users wear this computer-programmable instrument on the ankle. StepWatch™ records the number of steps taken every minute for up to two months between downloads, with an accuracy that can exceed 98 percent, regardless of walking styles that range from completely functional to highly impaired. The device is also an accurate option for persons who are obese to monitor low-impact weight-bearing activities, such as water aerobics. This instrument provides both patterns and intensity profiles of activity, as well as overall activity level, and has a built-in database for tracking individuals over time. StepWatch™ also generates a standard report that can be printed for inclusion in medical records.

RESEARCH ON SECONDARY CONDITIONS

If untreated, the physical and psychological conditions that often follow trauma and disease may not only lead to chronic disabilities, but may also impact the functional limitations of the individual or patient responses to long-term treatments. To achieve rehabilitation goals for recovery of function and for maintaining and/or improving the quality-of-life, preventing and treating secondary conditions are important for individuals who have disabilities from traumatic injury (e.g., SCI), neurological disorders/diseases (e.g., stroke, multiple sclerosis, cerebral palsy, amyotrophic lateral sclerosis, Parkinson Disease), and metabolic diseases (e.g., diabetes).
Secondary conditions or complications can be varied, numerous, and synergistic and can result in serious health risks and very costly medical care. For example, SCI is associated with many secondary conditions that have significant impacts on medical rehabilitation management, long-term outcome, and quality-of-life of the individuals. All of the NCMRR’s programs support research on many secondary conditions, including an emphasis on obesity, muscle atrophy, and bone loss. Researchers are increasingly appreciating that these three conditions are serious problems, especially for persons with impaired mobility and/or inadequate or inaccessible opportunities for exercise.

Between fiscal year 2002 and fiscal year 2005, the NCMRR supported approximately 143 different research projects that addressed issues relevant to the following areas of secondary conditions (in order of increasing total award):

- Bone loss ($580,343)—4 projects
- Obesity ($1,013,875)—4 projects
- Muscle atrophy ($3,134,936)—7 projects
- Pressure ulcers ($4,192,313)—15 projects
- Bladder/bowel disorders ($5,474,398)—13 projects
- Cardiovascular dysfunction secondary to injury ($9,370,999)—44 projects
- Pain ($12,125,868)—32 projects
- Psychosocial factors, depression, adjustment to illness, etc. ($24,964,287)—46 projects

These data are approximate and include overlapping projects because research in these areas tends to be integrative and interdisciplinary. In addition, a large category of musculoskeletal and disability research ($71,090,258) also includes research on spasticity and pain (see Figure 5).

NCMRR staff are encouraged that important research areas, which have long needed more attention, have shown growth trends during this time period. Such areas include bladder and bowel, depression, muscle atrophy, and pressure ulcer research. Fiscal year 2004 and fiscal year 2005 saw jumps in research dollars and in the number of projects concerning pain and disability, as well as in pain and obesity research—two areas of research focus across the NIH. While the dollars in support of obesity and disability research within the NCMRR show a three-fold increase during this time period, the number of projects is still small relative to the seriousness of obesity complications confronted by persons with disabilities, including those with SCI, who are at greater risk for obesity, diabetes, and subsequent medical complications.

In many cases, advances in research on the care and prevention of secondary conditions, as well as on other areas pertinent to rehabilitation would be more forthcoming if a greater number of collaborative partnerships existed among experts from basic science, engineering, and clinical communities. The NCMRR is continuing efforts to bring together these experts through meetings, discussions, and initiatives. For example, the Center is planning a workshop to address increased bone loss, another poorly understood complication in conditions such as SCI and multiple sclerosis, in which individuals have neurological disorders coupled with limited or no mobility.

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NCMRR-sponsored research has made and continues to make contributions toward the assessment, therapeutic interventions, treatments, and understanding of secondary conditions and their effects on the quality-of-life of individuals with disabilities. For five years, the NCMRR has sponsored a program project on urological research in SCI that includes four collaborative projects on: detrusor hyper-reflexia after SCI, alterations in bladder mechanics in SCI, biomarkers of bladder cancer in SCI, and novel intervention strategies for neurogenic bladder. This P01 is a good example of the synergistic benefit from collaborative research involving many diverse areas of expertise on the problem of secondary conditions.

Individuals with SCI frequently have uncoordinated activity of the bladder and urethral sphincter that prevents normal, controlled voiding. The project on detrusor hyper-reflexia uses an SCI animal model to study the response of the lower urinary tract to microstimulation of the spinal cord, in both the normal and chronic SCI bladder, and the effects of perineal and pudendal afferent nerve stimulation on the function of the SCI bladder. Researchers have made progress toward developing methods for the modulation of neural pathways to the urethra and bladder that could be applied to alleviating detrusor-sphincter-dyssynergia. They reported that high-frequency electrical stimulation of the pudendal nerve can block external sphincter contraction. They also published about computer-modeling results, which identified patterns of electrical activity—a process that could provide differential nerve blocks.

Researchers have also used animal models to describe the profound alterations in the composition and tissue structure of the SCI bladder wall that affect bladder-wall mechanical properties and function in SCI bladders compared to normal bladders. One goal of this research is to develop a structural constitute model for the normal bladder and for the SCI bladder. These efforts should enable future work to determine whether structural changes are affected primarily by the lack of neural control, and/or by the changes in the bladder’s mechanical environment.

Biomarkers for bladder cancer are pertinent to the general population, as well as to spinal-cord injured individuals, for whom the incidence of bladder cancer can be 460-fold higher than in other populations and for whom it often occurs at a younger age. An overall goal of this project is to identify the most accurate and cost-efficient test for monitoring and detecting bladder cancer in patients with SCI. The research team for this NCMRR-supported project has developed an immunoassay that detects urine-based bladder cancer protein, BLCA-4, in patients who have bladder cancer. The researchers reported that, in SCI individuals, BLCA-4 is not elevated by other factors such as cystitis, smoking, and positive urine cultures.

Research on novel intervention strategies for neurogenic bladder includes both clinical and animal model research on the mechanisms underlying bladder overactivity in SCI patients, and on the development of new therapeutic targets for treating overactive bladder in persons with SCI. Conventional therapies have serious limitations for treating neurogenic bladder due to SCI and other neurological diseases. Currently, major bladder reconstructive procedures or chronic indwelling catheters are the only options for SCI patients who are unable to tolerate or benefit from anticholinergic drugs; therefore, this project holds great significance for improving SCI patient outcomes.
The investigators have found that anti-muscarinic agents play a new role in afferent modulation for the treatment of overactive bladder. They also demonstrated that nicotinic receptor activation is an important mechanism for inducing bladder overactivity, meaning that the nicotinic receptor could be a new target for the treatment of SCI-related bladder dysfunction. A recent publication reported encouraging results from injecting botulinum toxin (BTX-A) into the urethra or bladder as an effective treatment for several voiding dysfunctions (i.e., neurogenic detrusor overactivity and/or detrusor sphincter dyssynergia, bladder neck obstruction, and interstitial cystitis). The 110 clinical cases analyzed included patients with multiple sclerosis, SCI, stroke, overactive bladder, and interstitial cystitis. These preliminary findings could lead to new therapeutic applications of BTX-A, such as treating conditions associated with increased afferent nerve excitability, a situation that occurs in SCI and chronic inflammation.

Since the Center’s last report to the NACHHD Council, it has issued the following PAs and RFAs related to secondary conditions (for a complete list of NCMRR-issued solicitations, please see Appendix A):

- Biobehavioral Pain Research (PA-03-152)
- NIH Exploratory/Developmental Research Grant Award (R21) (PA-03-107)
- Innovative Technologies for Pediatric Critical Care and Rehabilitation (SBIR/STTR) (RFA-HD-03-014)
- Increasing Quality-of-Life in Mobility Disorders (PA-02-111)
- Long-Term Care Recipients: Quality-of-Life and Quality-of-Care Research (PA-02-162)
- Innovative Technologies for Enhancing Function for Individuals with Disabilities (PA-02-071)
- Clinical Trial Planning Grants to Guide and Improve Timing, Intensity, Duration, and Outcomes of Pediatric Critical Care and Rehabilitation Therapeutic Interventions in Childhood Cardiopulmonary Arrest (RFA-HD-02-026)
- Pilot Clinical Trials in the Prevention, Epidemiology, and Treatment of Respiratory Failure in Children (RFA-HD-02-027)

**Behavioral and Biopsychosocial Issues in Rehabilitation**

Persons with disabilities often face unique behavioral and social challenges in achieving good health. For instance, implementing fundamental scientific advances is often contingent on an individual’s willingness or ability to adapt, to make behavioral changes, or to change the environment. Vaccines to prevent disease or the identification of environmental conditions that result in injury or disease serve as constant reminders of these issues because they illustrate that an individual’s behavior plays a pivotal role in improving health. In addition, direct effects of chronic conditions can include emotional and cognitive effects, in addition to other disorders, all of which affect everyday life activities. When considered with ever-shorter lengths of stay in health care settings, the result is that increased responsibility for continuing rehabilitation rests on individuals or their families. Therefore, one cannot underestimate the importance of behavioral and social research on improving rehabilitation outcomes. Continued research on
behavioral and psychosocial issues and the advances that result from this research are integral to improving the health of persons with disabilities.

Because this research can take place between any of the stages of rehabilitation—from pathophysiology to societal integration—the NCMRR supports research on:

- The study of human functioning at the level of the individual, small group, institution, organization, and/or community;
- The study of the interactions among biological factors and behavioral or social variables and how they affect each other; and
- Development of procedures for measuring rehabilitation outcomes for persons with disabilities.

The Center also supports clinical research studies designed to predict or influence health outcomes for persons with disabilities. The following section describes supported research in this area and highlights findings from selected projects.

**Behavioral and Social Processes**

Research on behavioral and social processes can occur at the time of impairment, at the functional limitation level, or at the societal level. Such studies include research on: family processes of low-income African American families, interactions between disability and stress, cognitive rehabilitation, interactions between environment and disability, and language development in persons with disabilities, to name a few.

In one such NCMRR-supported effort, a four-year longitudinal, urban, multi-method ethnographic study, researchers will examine cross-cultural health care encounters. The outcomes of this project will describe and interpret: the knowledge and strategies that families bring into situations to shape encounters and generate desirable outcomes; how families and practitioners revise their strategies; how practitioners shape intervention to the unique needs and strengths of family and child; how families and practitioners challenge and attempt to disconfirm stereotypes; and the cultural resources practitioners and families draw upon. The study will also examine the role of non-health care professionals in the provision of care for disabled children and the negotiations between family members and practitioners in the delivery of care that are critical to understanding how culturally competent care evolves.

As children grow and develop, many factors within the child, within his or her family, and within the environment have the potential to influence participation in everyday activities. It is difficult to plan interventions to enhance participation without knowledge of factors that influence this participation. To learn more about these influences, the NCMRR funded a longitudinal study of children with physical disabilities, ages 5 to 13 years, to determine the child, family, and environmental factors that enhance participation in formal and informal activities of childhood. The investigators then used results from this initial study to develop a family-centered intervention. Building upon the information from the first study, the second project evolved into a multi-site clinical study to evaluate the efficacy of a family-centered functional therapy versus regular therapy care for improving performance of functional tasks, mobility, participation in everyday activities, and quality-of-life of 220 children who have cerebral palsy.
In a similar line of study, researchers are examining traumatic brain injury (TBI) in younger children, which typically results in more severe and persistent sequelae than does TBI in older children. Little is known about the effects of early TBI on the family or about the factors that facilitate or hinder recovery among these children. This ongoing study uses a prospective cohort design to examine family adaptation following TBI in young children to understand the relationship between the social environment and child recovery, over time. Understanding the relevance of the environment to the child’s recovery following TBI will allow the investigators to design and develop interventions to improve outcomes.

Behavioral Interventions

Multiple Sclerosis (MS) is among the most disabling diseases and affects approximately 400,000 people in the United States[^4]. Studies have revealed that quality-of-life among persons with disabilities is lower than quality-of-life among people with other chronic illnesses. To learn more about this concept, the Center is supporting a randomized trial to determine whether cognitive behavioral therapy customized for MS patients can reduce disease activity and progression (as assessed by MRI and clinical measures) compared to treatment as usual. The study results could have an immediate impact on clinical practice for MS patients, as well as broader implications in the field of psychoneuroimmunology.

Another vein of NCMRR research addresses alleviating pain in children who are undergoing rehabilitation. Excessive pain is common during a variety of rehabilitation and medical procedures. Several studies are under way examining the use of virtual reality as an intervention to relieve pain for children as they go through rehabilitation. Evidence suggests that the distraction of virtual reality can serve as a powerful non-pharmacologic analgesic, which can be used in addition to traditional analgesic pain medication. For example, among burn patients who undergo painful daily wound care, researchers have devised a virtual reality distraction that allows patients to go inside a three-dimensional computer-generated world named Snow World. Patients who go into Snow World during wound care appear to experience less pain. To better understand the mechanisms underlying distraction effectiveness, one investigator has proposed three studies to help identify the components of distraction that enhance acute pain control in children. This research will increase the scientific knowledge of cognitive-behavioral aspects of pain in children, thus increasing clinicians’ ability to relieve or prevent children’s suffering. If successful, these distraction methods may also offer options for relieving pain in adults.

The long-term effects of acquired brain damage (ABD) can create major public health problems, ranging from deficits in attention/concentration and memory, to higher-level executive functions involved in reasoning, planning/organizing, problem solving, and judgment. These types of problems can compromise a person’s capacity to resume pre-injury work and to act within social roles. Post-acute rehabilitation programs often offer cognitive rehabilitation to handle these issues, even though the evidence to support its effectiveness and efficacy is limited. Recent evidence-based reviews indicated a need for systematic study of treatment outcomes to determine practice guidelines. To begin gathering such evidence, the NCMRR is supporting an investigator-initiated randomized clinical study that will extend treatment methods to address the needs of outpatients who have more severe cognitive deficits. The objectives of the research are

to: evaluate the efficacy of an individual problem-solving treatment geared toward persons with more severely compromised cognitive skills; demonstrate the applicability of problem-solving treatment methods to individuals with ABD due to stroke, and to those with ABD due to TBI; and clarify the relationship between baseline performance on timed attention tasks and treatment gains. Successful completion of this project will not only contribute to the evidence base regarding the effectiveness of cognitive rehabilitation, but will also have immediate, practical benefits for enhancing community integration of individuals with ABD.

**Studies of Protective Factors and Risk Factors**

A significant proportion of Americans living with a disability experience impaired mobility. Mobility-impairing conditions impact quality-of-life and human potential across disease category, age span, and economic and cultural classifications. People with such disabilities are at a greater risk than the general population for health problems such as pressure sores, urinary tract infections, high blood pressure, and obesity.

Recent evidence also suggests that persons with disabilities experience the same health benefits—including improved sense of well-being, better cardiovascular fitness, reduced anxiety, improved lipid profile, and improved self-image—from exercise as does the general population. To date, most research to encourage and promote physical activity is based on theories such as planned behavior, social cognitive theory, stages of change, and relapse prevention. The NCMRR is supporting an intervention study, based upon components of these theories, on physical activity among manual wheelchair users. The study is designed to assess: the effectiveness of the intervention in promoting physical activity adoption and maintenance among this population; the physical and psychosocial effects of intervention; and the complex interplay of factors that influences the effectiveness of the intervention. Results of the study will contribute to the knowledge base about strategies to promote physical activity among manual wheelchair users. The findings will also elucidate the effects of physical activity on the physical and psychosocial health, function, and participation in the community of manual wheelchair users.

Power-assisted wheelchairs seem to provide users who have limited arm strength or compromised hand-motor control with a means for mobility that also provides beneficial exercise. Documentation of improved quality-of-life is often necessary to justify the high cost of the power-assisted chairs over fully powered chairs to comply with current insurance plans and federal reimbursement programs. Currently, however, few studies are available to assist clinicians in selecting the most appropriate mobility aide for a patient’s clinical characteristics. The Center is supporting a study to examine the impact of power-assisted wheelchairs on the everyday life of the user, with the overall goal of defining the characteristics of successful users of this type of wheelchair. The study outcomes will provide necessary evidence about the impact of this new technology on patients’ lives in the real world.

The NCMRR also supports research on identifying and understanding behavioral and social risk factors, and on protective factors associated with the onset and course of illness and health conditions. These studies examine the associations among specific behavioral and social factors

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and mental and physical health outcomes, as well as the mechanisms that explain these associations. Findings from this research will describe behavioral and social factors that may be health-damaging (risk factors) and/or health-promoting (protective factors), both of which are critical to defining clinical rehabilitation plans.

**PEDIATRIC CRITICAL CARE AND REHABILITATION (PCCR)**

The population of disabled American children and young adults is expanding rapidly. As more children survive critical illness and injury, and as more medically fragile and disabled children live longer, there is increasing need for research to evaluate longer-term outcomes after pediatric critical care. To address these issues, the NCMRR established a new program in PCCR focused on developing research that links PCCR medicine and science to the epidemiology, prevention, and treatment of childhood disabilities. This new program sponsors competitive research projects on all aspects of PCCR—a breadth of scope in research for the benefit children that is somewhat unique to the NCMRR. The Center supports critical analyses of outcomes for children who are survivors of trauma, congenital anomalies, neonatal asphyxia, infectious processes, septic shock, and many other less common, but still devastating childhood processes.

**Linking Physical Medicine and Rehabilitation (PM&R) with Pediatric Critical Care**

The research interests, issues, and methods germane to PM&R and pediatric critical care medicine are quite complementary. Although certain fundamental differences—the clinical paradigm or scenario, the research unit of analysis, and the time scales of interest—exist between the two fields, there is common interest in the same children: those with critical birth disorders, those with childhood illness, and injury survivors, who have many years of life and development ahead once the immediate threat to survival is ameliorated.

Research in pediatric PM&R is scarce and the scientific underpinnings of pediatric rehabilitation practice remain understudied. Because enhanced or maximized function is the desired outcome of such interventions, existing research has focused on activity and participation, differentiating between the disability and the limitations it imposes. The mechanisms by which a given rehabilitation practice—such as physical, occupational, educational, or pharmacologic therapy—achieves improved outcomes for children are incompletely understood. Newer imaging techniques, including molecular visualization in organ-tissue beds *in vivo*, may substantially alter the limitations of PM&R in the near future to enable descriptive and therapeutic research for disabled children on a scale previously unimagined.

Pediatric critical care outcomes, on the other hand, are traditionally measured in terms of child survival. With the development of pediatric critical care medicine as an officially certified subspecialty of pediatrics in 1986, mortality in pediatric critical care units has plummeted from about 35 percent, to its currently reported low levels of between 5 percent and 8 percent, nationally, even in very tertiary pediatric intensive care units (PICUs). This change occurred despite persistently elevated mortality rates among critically ill and injured children in certain diagnostic categories (e.g., pediatric malignancy and TBI). It is unlikely, then, that mortality will ever regain its prominence as a meaningful outcome measure for pediatric critical care practice. The National Pediatric Trauma Registry, a collaborative project between PM&R clinicians and
pediatric trauma surgeons launched in the 1980s, is an example of the attempt to measure outcomes after acute care using functional rehabilitative criteria across a broad population and bridging many organ systems and parameters.

In pediatric critical care, the evolving agenda for pediatric intensivists lies in the relationship of morbidity to patterns and techniques of acute care practice. For instance, choice of ventilatory and cardiovascular support techniques, choice of pharmacologic agents in sedation and analgesia, and their longer-term effects on child health and development are all emerging issues within pediatric critical care research. Because resource utilization is such a central issue in most pediatric critical care services, comparisons of nursing hours and other measures of service consumption are of interest in weighing the eventual benefits for children and families. Many questions about the relationship of pediatric critical care practice to child health and disability remain unanswered, and the NCMRR’s PCCR program seeks to support research to find those answers.

Research sponsored by the new PCCR program at the NCMRR addresses a major part of the Center’s mission. Since its inception four years ago, the program has published six NIH/NICHD scientific initiatives that utilized a diverse array of funding mechanisms, but that all centered on linking longer-term childhood outcomes and morbidity to acute care practice. As of September 1, 2005, the program had received 215 applications, of which 117 were investigator initiated and 98 were in response to published initiatives. Overall, the program funded 46 applications.

Approximately two-thirds of the applications came from acute or critical care scientists (often pediatric intensivists and surgeons), and the remaining one-third came from pediatric rehabilitation practitioners of varied disciplines. The trans-disciplinary nature of the PCCR program is most evident in the number of applications that had a focus beyond the acute care period. Specifically, 46 applications focused research on longer-term processes, without prominent acute care components, and 13 such applications were from pediatric surgeons, anesthesiologists, or intensivists.

Thus far, program achievements of note include the discovery of differential patterns of cerebrospinal fluid proteins in children with inflicted critical head trauma, as compared to age peers with accidental head trauma, and a developmental evaluation of children following liver transplant. In addition, one Center-supported pediatric anesthesiologist addressed the important issue of ameliorating post-operative pain in severely disabled children, and a pediatric trauma surgeon developed a trans-disciplinary approach to pediatric trauma decision-making and triage using neuroinformatics.

The Collaborative Pediatric Critical Care Research Network (CPCCRN)
The new NICHD CPCCRN, which the NCMRR began funding in April 2005, will serve as a national resource for studying the scientific bases of pediatric critical care medicine. The Network consists of six clinical centers, chosen on the basis of proposed scientific work, patient ethnicity, and concordance with programmatic objectives. A Data Coordinating Center supports the Network using cutting-edge informatics to manage the complexities of the emerging collaborative research.
Several convergent developments in critical care medicine, as well as in the larger medical, scientific, and national communities, were fundamental to the NICHD decision to develop and maintain a collaborative infrastructure in the form of the CPCCRN. For example, critical care medicine has introduced a number of management and innovative methodologies without evidence from controlled observation and objective evaluation to support their use. Another major problem is in attempts to balance assuring prompt implementation of new technologies, procedures, treatments, and drugs with evaluating their safety, efficacy, cost/risk/benefit ratios, and effects on developmental and family outcomes. In addition, modalities of mechanical ventilation, non-invasive ventilation, circulatory support, organ transplantation, and extracorporeal life support have extended therapeutic options to children previously thought to be beyond the reach of state-of-the-art therapy. The use of less-invasive techniques in neurosurgery, general, orthopedic, reconstructive, vascular, and cardiovascular surgeries, as well as in the implementation of newer techniques for respiratory and circulatory support, are also central to the radical changes in mortality now achievable with state-of-the-art pediatric critical care medicine.

As a result, children in higher risk groups who are victims of critical illness and/or injury, and those who might benefit from surgical interventions that were once infeasible are benefiting from pediatric critical care in increasing numbers. In light of these issues, the NICHD intended the CPCCRN to support a substantial range of research activities, reaching across traditional disciplinary lines and transcending customary thinking and organizational structures to achieve innovative research in the care of critically ill and injured children.

**MEASUREMENT AND OUTCOMES RESEARCH**

Many within the rehabilitation community have voiced concern about the limitations of existing assessment instruments for capturing the effects of interventions or monitoring the quality of services provided to patients. The content of the instruments, the breadth of coverage, and measurement precision are all at issue. Measuring rehabilitation outcomes is a cross-cutting issue that holds great interest for the NCMRR. For instance, the Center initiated pilot studies to examine different strategies for measuring rehabilitation outcomes among different populations. One investigator-initiated project examined the use of computer-adaptive testing (CAT) approaches in pediatric populations. The researcher contrasted the score accuracy, validity, precision, and response burden of simulated and real-time CAT administrations using a standard scale of pediatric functional mobility. The results revealed that the CAT score had good-to-excellent comparability and validity, but had reduced precision on individual scores in comparison to the full-length form.

An NCMRR-initiated RFA in rehabilitation outcome measurement resulted in exploratory grants that will pursue different topics and use innovative approaches. The RFA was intended to encourage multidisciplinary research utilizing techniques, such as CAT or simulations, to improve the quality and scientific power of data to more accurately measure the health of persons with disabilities. Five of the applications rely on theory methodologies and CAT for planning instruments to measure topics, such as: health status of children with chronic...
conditions; outcomes of TBI interventions; and participation, communicative participation, and physical activity. Two projects propose to develop measurement instruments using simulation techniques: one project addresses setting meaningful patient goals and computing health-related outcomes weighted by quality-of-life, and the other is designed to measure executive function in children. The remaining application proposes to develop objective measures of functional movement performance.

Upon completion of these exploratory grants, investigators will submit regular research grants to complete the development of detailed health assessments for the rehabilitation field. This approach could be useful for developing an assessment tool to diagnose or to document the impact of a rehabilitation intervention. In addition, it could result in a tool for better evaluating medical interventions at the impairment level, while providing better understanding of the relationships between health challenges and disability concepts for individuals in widely differing circumstances.

Rehabilitation outcome measurement is also an interest for the NIH as a whole, specifically via the NIH Roadmap activities. Therefore, the NCMRR is also involved in an NIH Roadmap initiative to develop instruments that measure symptoms of chronic conditions and that investigators who are implementing clinical studies can use to document outcomes.

The NIH Roadmap initiative, *Patient-Reported Outcomes Measurement Information System (PROMIS) Network*, established a collaborative relationship between the NIH and individual research teams through cooperative agreement mechanisms. The broad objectives of the PROMIS Network are to:

- Develop and test a large bank of items measuring patient-reported outcomes;
- Create a CAT system that will allow for efficient, psychometrically robust assessment of patient-reported outcomes in clinical research on a wide range of chronic diseases; and
- Create a publicly available system that can be added to and modified periodically and that will allow clinical researchers to access a common repository of items and CAT methods.

The Network includes rehabilitation researchers who will collaboratively collect self-reported data from children and adults who have a variety of chronic diseases, using agreed-upon methods, modes, and questionnaires to measure symptoms, such as pain and fatigue. The outcome of this effort will provide a standard instrument that can be used by clinical researchers worldwide.

In many disciplines, cost-effectiveness analysis is often criticized for discriminating against people with disabilities, for harming the elderly, for ignoring issues of fairness, and for undervaluing the benefit of treating severely ill patients. These problems become more critical as the U.S. population ages because the elderly have chronic disabilities that limit the degree to which they can improve their quality-of-life with health programs. As a result, cost-effectiveness measures of programs targeted toward the elderly seem relatively unfavorable. Regardless, though, the country’s aging population demands such efforts move forward. One project sponsored by the NCMRR sought to improve value measurement in cost-effectiveness analysis so that it is fair to the elderly and to people with disabilities. This study investigated how people with chronic conditions view these problems, as well as how those who do not have
such conditions view them, to identify health-state valuations for specific conditions. The research then examined the cognitive factors that contributed to the discrepancies in the valuation. The results of this research could influence medical decision-making by identifying the different perspectives of patients, physicians, and the unaffected toward various medical conditions and treatments. The research could improve methods for valuing health programs and improve the acceptability and usefulness of assessments for decision makers.

**CLINICAL RESEARCH IN REHABILITATION**

The unique mission of the NCMRR is reflected in its conceptual model of rehabilitation research, which emphasizes the individual person and successful reintegration and functioning in the community as central foci of the medical rehabilitation process. (See the *Future Research Directions for the NCMRR* section of this report for more details.) The NCMRR supports a range of clinical research that addresses not only physical function, but also issues of quality-of-life and societal and functional limitations. This research encompasses projects in the areas of evaluation, treatment, and applied technologies, with an emphasis on both clinical and basic research, and includes studies across the life span and across etiologies, such as injury and trauma (e.g., SCI, TBI), stroke, tumor, degenerative neurological diseases, and congenital conditions. The Center also focuses its research efforts on treatment outcomes, mobility impairment, secondary conditions, and cognitive impairments associated with these conditions. The NCMRR continues its commitment to rehabilitation research through the development and support of clinical research programs that combine targeted initiatives and investigator-initiated research.

Before any treatment is approved for general use, it must be studied carefully to understand how the treatment works, how effective it is, and what potential risks may exist. The safety and benefits of the therapy for humans must then be proven through an orderly series of tests. Over the years, medical research has succeeded in converting many diseases that were once considered life-threatening into more chronic, treatable conditions. Although rehabilitation research has made strides in this direction, progress for rehabilitation research in clinical settings is slower—a fact that only reinforces the need for the NCMRR’s continued support of these initiatives. Clinical research remains a complex endeavor that requires an efficient approach to discovery and clinical validation of research results. The challenge of accommodating the physical, intellectual, societal, and emotional characteristics and needs of individuals makes clinical research even more challenging.

Rehabilitation is beneficial for promoting improvements in functional areas such as mobility, performance of self-care, and community integration; however, important questions remain regarding the effectiveness of individual treatment strategies, as well as the organization and intensity of rehabilitation services across disorders. The design of clinical rehabilitation research is particularly challenging because it demands that a complex combination of personal and societal issues be placed within the context of enhancing the health, productivity, independence, and quality-of-life of individuals with physical disabilities. The rehabilitation process may
present a time-limited window of opportunity for recovery or accommodation. Research is needed to help determine how best to maximize the benefits of rehabilitation throughout the course of illness and/or injury. This process is particularly important given the constraints of the current health care system and the likelihood of even more constraints in the future.

The NCMRR is uniquely poised to address the important aspects of clinical rehabilitation research via a combination of funded investigator-initiated projects and targeted clinical research initiatives that have generated subsequent studies. These studies:

- Consider the management of chronic disease, new diagnostics, and therapeutic approaches;
- Evaluate the safety and efficacy of interventions;
- Adapt existing interventions to new populations;
- Design meaningful measures of functional outcomes and attention to community integration; and
- Provide evidence-based clinical care that can drive health care management and policy, in some cases challenging previous assumptions of current clinical practice.

**THE CONTINUUM TOWARD RANDOMIZED CONTROLLED TRIALS (RCTs)**

The benchmark for clinical research is the RCT, a study in which people are allocated at random to receive one of several clinical interventions, including a standard of comparison or control. The control may be a standard practice, a placebo, or no intervention at all. RCTs seek to measure and compare outcomes through quantitative, comparative, and controlled experiments in which investigators study two or more interventions among individuals who receive them in random order. The RCT is one of the simplest yet most powerful tools in clinical research. However, not all scientific questions or areas of science are ready for a large-scale RCT investigation—a situation more common than not in rehabilitation research. It is valuable, then, to consider clinical research along a spectrum related to the development of the scientific field and the requirements of the specific research question. A variety of programmatic tools are available to meet clinical research goals, and they can be viewed along a continuum of research opportunities, building on each other in an ongoing fashion. That continuum is described here, within the context of NCMRR research.

**Pilot Research Studies**

Before undertaking a large clinical study, pilot information is necessary to provide the preliminary building blocks that lead to optimal trials and allow investigators to structure a well-designed trial. The NCMRR recognized the need for pilot clinical studies and adopted a mechanism to provide support for investigators as they obtain preliminary data and establish the clinical basis to support the rationale for subsequent full-scale RCTs. Through the R21 mechanism, applicants are encouraged to obtain preliminary data, to refine research design, statistical components, intervention strategies, outcome measures, and target population, and to incorporate creative and realistic solutions for difficult problems in clinical neurological research for a particular intervention.
Over the past decade, research has supported the development of many neuroprotective agents to improve outcomes for patients with acute cerebral disorders, such as stroke, subarachnoid hemorrhage, and head injury. Such efforts tested a number of different classes of drugs (e.g., calcium-channel blockers, glutamate antagonists, cholinesterase inhibitors) in head-injured adults across the stages of recovery to facilitate behavioral management and functional outcome. Even though case studies in adults suggested that some of these agents may be useful for improving attention and memory and, possibly, for enhancing plasticity, little data is available on appropriate dosages or on effects of these agents in pediatric TBI patients.

Using the small existing research base, a number of investigators received NCMRR support to evaluate the efficacy of pharmacological interventions for the physiological and behavioral sequelae of TBI. Examples of funded work include studies to: evaluate the efficacy of hypertonic saline to treat intracranial hypertension in children with severe head injury; evaluate pharmacological intervention to improve arousal and recovery; and examine the overall safety and efficacy of specific pharmacotherapy (e.g., amantadine, aripiprazole) for improving the behavioral management, functional outcome, and neurological status of children following TBI. Having completed the preliminary pilot work necessary to form the building blocks for further study, this research now continues via larger scale investigations that will answer important clinical questions to further define the requirements and needs for RCTs.

**Clinical Trial Planning Studies**

Current constraints on clinical researchers make the complex and time-consuming process of planning Phase III clinical trials problematic, especially in the medical rehabilitation field, which lacks a well-established clinical research infrastructure. To assist researchers, clinical trial planning grants provide a mechanism for early peer review of the rationale and design of a potential RCT and support the development of detailed RCT study plans and research collaborations.

The NCMRR supports a number of clinical trial planning grants that facilitate clinical projects by supporting pilot studies and enabling investigators to obtain preliminary data, refine intervention strategies and outcome measures, and establish the theoretical basis to support subsequent larger scale RCTs at a future date. This program supports the establishment of the research team, the development of tools for data management and oversight of the research, the definition of recruitment strategies, and the finalization of the protocols and identification of other essential elements of the study included in a manual of operations/procedures.

The Center currently supports several studies that address the problem of identifying objective and effective rehabilitation interventions for children, a problem complicated not only by the adaptation and recovery processes taking place at different stages following injury, but also by the additional uncertainties of the process of biological maturation. These studies include: evaluating the longitudinal impact of assistive technologies on children with disabilities; a sensory-based rehabilitation technique for children following traumatic birth injury; and the development of an RCT of Constraint-Induced (CI) Movement Therapy in children. Taken together, these studies form a cohesive first step toward developing a clinical trials research program in pediatric rehabilitation.
Patients at the other end of the age span also present unique challenges for conducting RCTs. For example, stroke and hip fracture are among the leading health care problems that require rehabilitation services among the elderly. Together, these two diagnoses account for the majority of days spent in rehabilitation for this age group. In addition, the rehabilitation needs and goals of individuals with stroke vary considerably. Because of the diverse needs and goals of this population, there is little agreement among professionals as to treatment strategies, the efficacy of rehabilitation, or desired outcomes. There is also no clear evidence concerning the timing of interventions, nor the intensity of physical rehabilitation for patients. The NCMRR provided clinical trial planning grants to help investigators develop clinical trials that will evaluate models for providing rehabilitation while considering timing, intensity, and duration of treatment. On the basis of the work performed in these projects, investigators are submitting applications for large-scale clinical trials to determine best practices for the treatment of these patients.

**Multi-Center Clinical Trials**

Once the goals of a small-scale research project are achieved, a larger study may be appropriate; such a trial is the expected progression of the research process, especially for clinical studies, which require ample patient enrollment to address clinical questions. The majority of large multi-center clinical studies supported by the NCMRR were first supported as smaller scale investigations. Through the smaller projects, investigators are able to refine design and methodological issues that subsequently yield successful multi-center study plans.

One example of this progression of work is a planning grant that developed methods and protocols to run randomized placebo-controlled studies of the effectiveness of drug intervention in combination with behavioral therapy of two different intensities. Having successfully piloted an innovative study design and collaborative arrangements for the initial effort, the currently supported project represents a unique opportunity to perform the first definitive RCT of bromocriptine for enhancing recovery from aphasia, and to determine the interaction between bromocriptine and intensity of speech therapy.

Another example, a multi-site study, examines the factors that contribute to poor social outcomes in children with TBI. The researchers employ multiple methods to study five overlapping areas of social functioning, including the brain regions associated with social behavior and parent/teacher/peer perceptions of social function. The richness of the data collected at five clinical sites in the project lies in the contemporaneous examination of each level in the model (i.e., regional brain abnormalities, social information processing, social interaction, and social adjustment) and their interrelationships. This work is part of the NCMRR’s ongoing interest in addressing the behavioral, cognitive, and social sequelae of TBI.

Persons with TBI also experience high rates of depression, especially during the first six months following their injury. Both neurological and psychological factors appear to contribute to depression in this population. Depression following TBI is associated with poor cognitive, behavioral, and functional outcomes. Preliminary studies suggest that people with TBI and major depression may not respond to antidepressant treatment in the same way as depressed persons without TBI. To date, because no large RCTs have been conducted, basic questions remain about the treatment and outcomes of major depression among persons with traumatic brain injury.
injury. As a consequence, depression is not usually assessed and optimal rehabilitation guidelines for identifying and treating depression have not been established.

To address this gap, an NCMRR-supported clinical study is following a large number of patients who had moderate to severe TBI to identify those who develop major depression, and to address depression that develops after TBI. This double-blind placebo-controlled study examines whether major depression following TBI improves with antidepressant treatment. The research will also determine whether the benefits of treatment are paralleled by improvements in cognitive functional outcomes, or by fewer post-concussive symptoms. Researchers expect this clinical trial to lead to improved clinical care and better functional outcome for many survivors of TBI who suffer from co-morbid depression.

As mentioned earlier in this report, MS is one of the most frequent causes of disability in early to middle adulthood. The cognitive impairment that affects approximately half of patients with MS is a primary cause of disability, and it exacts a tremendous socioeconomic and interpersonal toll on patients and their families. One investigator examining this disorder obtained exciting results in a small NCMRR-funded pilot clinical trial to treat cognitive impairment in MS. Findings from the initial work suggested a benefit from acetylcholinesterase inhibitor (AchEI-donepezil) intervention for memory impairments in MS. This medication enhanced the learning and memory of impaired MS patients on standardized outcomes as compared to patients who received placebo. However, researchers have not tested the pharmacological intervention in RCTs with adequate sample size. Confirming the efficacy of AchEI-donepezil for improving memory in MS patients will provide valuable insights that could improve the standard of care for this population. Further study is therefore critical to confirm positive results obtained in a relatively small sample at a single clinical site.

A follow-up study, funded by the NCMRR and currently under way, builds on the findings from the first study and will serve as a crucial test of results across multiple centers in a definitive RCT. The investigators hope that this work will provide documented evidence of treatment effectiveness in a large patient population. Positive results will alter clinical practice for the treatment of cognitive impairments in MS patients and could help to decrease caregiver burden and improve the quality-of-life for those with MS. The importance of this study lies in its opportunity to change clinical practice. This work also illustrates the gradual and persistent pursuit of data—from concept to planning to RCT—that now permits the development of an innovative and successful multi-site RCT based on a single-site trial that revealed safety and efficacy of AchEI-donepezil for cognitive impairments.

Other examples of individual small pilot studies growing into a series of integrated RCTs include those addressing a unique aspect of stroke rehabilitation. Several studies, currently under way, seek to provide answers about the way movements are learned and how this fundamental process is affected by neurologic insult or disease. Along with pharmacological and surgical interventions, physical therapy and exercise might improve mobility of patients with neurologic damage. If therapeutic exercise is to be most effective, it is important to understand how the disease itself may affect the patients’ ability to learn a new movement repertoire.
Profoundly impaired motor function is a major consequence of neurologic disorders, such as stroke, TBI, and degenerative neurological disorders and contributes significantly to physical disability and impaired quality-of-life. Most rehabilitation strategies emphasize compensatory training for the unimpaired extremities to maximize function and prevent complications of immobility. There are, however, few rehabilitation techniques that are known to influence the motor neuroplasticity of a healing brain. A clear need exists to translate unique behavioral techniques, which are shown to have impact on plasticity in the nervous system, into practical evidence-based therapeutic interventions, especially at a time when the duration and number of treatments covered by insurance have been restricted.

NCMRR-funded investigators are developing strategies to facilitate the motor recovery of stroke patients and, thereby, maximize function and quality-of-life. One such technique, derived from basic research findings, has produced results that can substantially reduce the motor deficit of patients with mild to moderate chronic strokes, thus increasing their independence. This technique, Constraint-Induced (CI) Movement Therapy or Forced Use, involves motor restriction of the less affected upper extremity for two weeks, during which time repetitive use of the more affected upper extremity is promoted for many hours a day. Massed or repetitive use of the more affected extremity leads to a large increase in use-dependent cortical reorganization, which involves the recruitment of substantial new regions of the brain in the innervations of more affected extremity movement.

NCMRR-funded research is evaluating whether CI treatment is effective for increasing the amount of functional motor performance in patients following stroke, and whether the locus and size of lesions are factors that influence the extent to which motor function is recovered. Studies to date suggest that this treatment produces long-lasting improvements among patients who are more than one year post-stroke, and that it might be as effective for subacute patients, who are three- to six-months post-stroke, as it is for more chronic patients.

Another series of studies draws from this work and examines related areas of function and physiology in children and adults. Studies evaluating caregiver burden indicate a strong correlation between degree of depression and fatigue and the expected impact on functional outcome. Another study is evaluating the effect of CI Movement Therapy on cortical motor reorganization following stroke, using transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI); this work will determine whether TMS motor maps or fMRI activation predictably changes following CI Movement Therapy, whether this change correlates with motor recovery, and what possible mechanisms underlie the change.

The study offers a unique opportunity to use non-invasive methods to study cortical plasticity in subjects who receive a specific therapy intervention, compared to a control group. The project could validate the concept that physiological cortical motor changes after stroke are closely correlated with motor improvement, and that they are influenced by a physical intervention. Such findings could lead to the development of new rehabilitative strategies based on the interactions between therapeutic interventions and the physiology and anatomy of recovery.
The NCMRR TBI Clinical Trials Network

In the continuum of clinical research, a coordinated, cooperative clinical trials network stands at the opposite end of the spectrum from pilot studies. NIH Institutes have successfully used the cooperative clinical trial network model for decades in a variety of clinical populations, with the overarching objective of providing infrastructure to support collaborative research for multi-center studies. This structure has a number of advantages, chief among them the fact that the network facilitates clinical studies by taking advantage of common intervention protocols and outcome measures systematically applied to sufficient number of patients. Researchers are therefore able to provide statistically valid results of treatment efficacy and to address important clinical questions in a cost-effective and efficient manner. The NCMRR’s experience with research on TBI is a prime example of the network structure’s possibilities and benefits.

During the past two decades, understanding of the pathophysiology of TBI has increased dramatically. For instance, clinicians now recognize that not all neurologic damage occurs at the moment of injury, but rather that it evolves over the ensuing minutes, hours, and days. A combination of early imaging in the emergency room, removal of extra-axial masses, support of blood pressure, ventilation, and monitoring of intracranial pressure is well-known to produce improved survival rates. The role of aggressive follow-on intensive care treatment is equally well established. In addition, a growing body of literature suggests that adjunctive pharmacological treatment facilitates behavioral management during the rehabilitation process and might result in better functional outcomes. Despite these advances, researchers have much to learn about the underlying damage and pathophysiology of the deficits associated with TBI and the links among acute care, rehabilitation, and long-term patient outcomes.

To learn more, the NCMRR established a multi-center network of sites that are working together to design clinical intervention protocols and measures of outcome for TBI. Through rigorous patient evaluation, using common protocols and interventions designed for multiple points of care—including the accident scene, emergency room, intensive care unit, rehabilitation and long-term follow-up—the NCMRR TBI Clinical Trials Network can study the required numbers of patients to provide answers more rapidly than individual centers acting alone. This interdisciplinary research Network is designed to evaluate the relationship among acute care practice, rehabilitation strategies, and the long-term functional outcome of TBI patients—that is, to identify which intervention variables result in improvements in long-term outcomes.

Taking advantage of the network model structure has allowed TBI research to progress toward a number of clinical research goals. Specifically, the NCMRR wants to highlight two major achievements to date. First, the TBI Network created a profile of its typical patient to determine the number of patients with different clinical features who might be eligible for future studies and to help estimate recruitment times necessary. Second, Network researchers are developing clinical treatment guidelines and procedures for all points in the continuum of care, including TBI Clinical Trials Network Guidelines for surgical care, systems-based protocol for severe and moderate TBI patients, deep-vein thrombosis prophylaxis procedures, and rehabilitation guidelines for physical therapy, speech-language pathology, occupational therapy, and neuropsychology.
Clinical trials are time-consuming, expensive, and difficult, but are essential to building an evidence base for clinical practice. The NCMRR remains committed to helping the field of rehabilitation to expand the evidence base for clinical practice through the full range of support mechanisms available.

**REHABILITATION TRAINING**

Training and career development has been a priority for the NCMRR since it was founded. In the early years, efforts focused primarily on supporting rehabilitation therapists and clinicians who were seeking to develop research careers. More recently, the NCMRR has expanded its efforts to attract established researchers from allied fields in focusing on rehabilitative questions. Key issues for NCMRR support involve professional training, availability of appropriate research mentors, and career constraints.

In contrast to some other areas of NIH-supported research, medical rehabilitation tends to cross the domains of pathology, impairment, function, and/or disability and cuts across professional domains. Research often focuses on the individual, rather than on the cell, tissue, or organ. Although some studies are conducted in clinical settings, medical rehabilitation often involves longitudinal follow-up in real-world settings, taking interactions among environmental factors such as family, community, and health service constraints into account. Thus, rehabilitation researchers often need broad training in the appropriate clinical, physiological, and psychosocial domains. The NCMRR supports training and career development through a variety of mechanisms, including departmental training grants, individual fellowships and career development grants, national career development programs, infrastructure grants, and research workshops.

Currently, the NCMRR funds 15 institutional training grants (T32), along with 14 programs it supported in previous years but that are no longer active. During the first 14 years of the NCMRR, these programs supported between 600 and 700 students at the predoctoral or postdoctoral level (Ph.D.s outnumber M.D.s by about two to one, along with a handful of M.D.-Ph.D. fellows). These institutional training programs range from cellular/molecular biology and bioengineering, to behavior, to psychosocial and policy issues. Training studies are distributed across the various levels of analysis (i.e., pathophysiology, impairment, function, disability, and societal limitations), although impairment and function are the most prevalent. Follow-up studies of these trainees suggest that more than 75 percent have remained in research careers, and many have risen to faculty positions. They have submitted more than 150 applications to the NIH alone, including 14 successful K awards and 39 research grants (e.g., R01, R03, R21, P01, etc.).

The NCMRR supports an additional 20 postdoctoral fellows (mostly Ph.D.s) through individual postdoctoral awards (F32s). These fellowship grants cluster at the pathophysiological level, although some trainees focus on impairment, function, disability, societal limitations, and/or health policy. The majority of NCMRR-supported F32 trainees have remained in research
careers, and most have developed into independent academic researchers. They continue to publish in peer-reviewed journals, and a few are currently submitting NIH research applications, although none have yet received R01 funding. Within the NICHD, the predoctoral F31 mechanism typically supports individuals who are from an underrepresented minority group or who have a disability. The NCMRR has supported four predoctoral fellows through this mechanism, some of whom are now progressing toward independent research careers.

NIH-wide, candidates who wish to transition to the independent investigator level receive support through career development mechanisms (e.g., K01, K08, K23, and K25), which provide support for intense mentored research, either clinical or basic, to facilitate the transition of clinical fellows into independent faculty careers. NCMRR trainees include rehabilitation professionals (e.g., physical, occupational, and speech/language/communication therapists), PM&R physicians, neurologists, critical care specialists, and bioengineers. Again, in previous years, trainee research clustered at the pathophysiological level, but more recently trainees are conducting research at the level of impairment, function, disability, and/or societal interactions. NCMRR applicants have had moderate success with this mechanism, with roughly 20 percent to 40 percent receiving funding.

Within the NICHD, medical rehabilitation is targeted as a special area of emphasis through the use of the K01 mechanism. Since 2001, this targeting has allowed the NCMRR to support 18 Ph.D. students who were seeking further training in rehabilitation research. An additional 20 NCMRR trainees received support through the K08 and K23 mechanisms, which are designated across the NIH for clinically trained individuals who seek training in basic or patient-oriented research, respectively. The new NCMRR PCCR program has been especially active in attracting pediatric investigators to these career development mechanisms. In addition, researchers with engineering or quantitative backgrounds may take advantage of the trans-NIH K25 mechanism, through which the NCMRR currently supports four bioengineers.

As a group, the NCMRR-funded career development awardees have developed into outstanding, productive researchers. Almost all of them continue to publish in peer-reviewed research journals, and some already have several first-author publications to their credit. About 90 percent of them have submitted independent research proposals to the NIH (e.g., R01s, R21s, R03s, and other mechanisms), and 12 were successful in getting a grant; some even received more than one grant. Other K trainees have received major research grants from other federal agencies, such as the NIDRR and the CDC, and from private research foundations.

Although rehabilitation research crosses many professional domains and patient groups, the field of PM&R is most closely aligned with the clinical interests of the NCMRR. Therefore, using the K12 mechanism, the NCMRR currently supports a national network of established rehabilitation researchers who mentor clinically trained individuals in conjunction with the Association of Academic Physiatrists and various PM&R departments. The program actively recruits and supports a small number of highly motivated trainees from the field of PM&R as they proceed through two to three years of mentored research outside their departments; they also receive continued support at the beginning of their PM&R faculty careers.
Now entering its 11th year, this Rehabilitation Medicine Scientist Training Program has an outstanding reputation for supporting dedicated physician-scientists. Several graduates of this program have assumed faculty positions, and a high percentage has applied for research grants from other NIH Institutes, with some notable successes. The formation of the new PCCR program in the NCMRR provides additional opportunities to attract pediatric researchers to the field of medical rehabilitation. And, two years ago, the Center funded a second K12, the Pediatric Critical Care Scientist Development Program, to provide mentored support to highly motivated pediatric intensivists in research career development in PCCR research. The program has received 32 applications, and funded seven. Most successful applicants are also actively seeking independent research support.

Support of clinical investigators continues to be an important issue across the NIH, especially in recent years as grant funding has become increasingly tight, and as clinicians are trying to balance the competing demands of clinical service, scholarship, and other professional duties. Physiatrists are most closely aligned with the field of medical rehabilitation, but they do not always have the appropriate research experience, nor the negotiated release time to actively pursue research careers; this fact is especially relevant as the distinction between clinical support and research methodology becomes more apparent. Despite increasing constraints in the managed care environment, clinical departments and professional organizations must continue to support research activities and clinical scientist careers because research is essential to justify rehabilitative practices, promote effective therapies, and drive health care reimbursement to cover chronic treatments and extended care. The NCMRR also draws investigators from other, more established clinical disciplines, such as neurology, pediatrics, and medicine. Although these investigators might approach rehabilitation through a commitment to a particular patient population (e.g., stroke, SCI, children), they sometimes develop a broader appreciation of functional outcomes and more long-term follow-up.

Ph.D.s from rehabilitation fields (e.g., physical therapists, occupational therapists, speech/language/communication therapists, and nurses) are in a unique position to contribute to medical rehabilitation research because they have a special appreciation for supporting patients who have chronic disabilities and for understanding the role of environmental factors and real-world settings in rehabilitation. To develop competitive NIH proposals, these professionals need the appropriate grounding in physiological, biomechanical, and/or psychosocial processes and often benefit from some mentoring in research approaches and grantsmanship. Physical therapist Ph.D.s have done especially well in developing successful careers and independent research proposals with the NCMRR, perhaps due to their academic training and network of professional support.

Medical rehabilitation also relies on collaboration with engineering disciplines, especially in the areas of assistive devices, tissue engineering, and assimilating new technologies. Although engineers tend to have a solid grounding in quantitative disciplines, they often need help to understand the needs of the rehabilitation community, the use of appropriate assessments and outcomes measures, and the finer points of biomedical grantsmanship. As mentioned above, the NCMRR has successfully used the K25 mechanism to support career development for mid-level bioengineers. Creating additional support mechanisms for career development for entry level bioengineers is a high NCMRR priority for the future.
In addition to the formal grant mechanisms described earlier, the NCMRR also supports training and career development through infrastructure grants, workshops, seminars, and direct communication with potential grantees. The biennial NCMRR trainee workshop is particularly successful in this regard. This major meeting engages 150 to 200 candidates in two days of research highlights, career development, networking, grantsmanship, NIH peer review, funding opportunities, and clinical trials planning and conduct.

In conclusion, training and career development continues to be a major priority for the NCMRR and its staff. As a result of NCMRR support, there is now a growing cadre of productive rehabilitation researchers and a national network of support, both of which have led to significant increases in quality of research applications submitted to the NCMRR and to the growing success of NCMRR grantees in the highly competitive arena of peer review. The Center also actively seeks to attract established researchers from allied fields to enter rehabilitation research and address such issues as plasticity and adaptation, reducing secondary complications, increasing participation and integration, and promoting healthy outcomes.

INFRASTRUCUTURE DEVELOPMENT AT THE NCMRR

Although medical rehabilitation has a long history of treatments based on physiological and psychosocial principles, specific research studies that define the precise timing and intensity of treatments, the active ingredients of these therapies, and the underlying physiological mechanisms is often lacking. Although this situation is common in other clinical fields, medical rehabilitation has a more immediate need for answers in light of the increasing population of elderly and of individuals with chronic disabilities who seek to retain function and live healthy and productive lives. Research is needed to justify rehabilitative treatments during the chronic phase, when further improvements in function and adaptation are still possible.

On the advice of the National Advisory Board on Medical Rehabilitation Research, the NCMRR launched a multi-million dollar initiative in 1999 to support four regional research networks. Each network would build upon collaborations across three institutions, each with the broad and diverse goals of providing regional outreach, focused scientific expertise, information transfer, and improved research capacity. Funding was provided through the R24 mechanism, which supports scientific workshops, research cores, Web sites, consultations, and seed grants for promising pilot projects. Each of the four networks took a unique, but complementary approach to meeting its goals; the result is a national infrastructure that promotes and supports medical rehabilitation research. During the first five years of funding, the networks had a significant impact on the quality of medical rehabilitation research and on the number of research applications that were submitted to the NIH and other funding agencies and foundations.

The initial group of funded networks included the following:

- The Cognitive Rehabilitation Research Network (in the Northeast) provided specific expertise in the study of brain injury, brain imaging, cognitive rehabilitation, and clinical
trials. It hosted focused workshops and collaborations on cognitive rehabilitation and posted source materials and discussions on its Web site. The network also supported a large database of patients who had TBI and stroke that provided contacts for more than two dozen research studies. The network also developed an effective program for funding pilot projects and a visiting scholars program that provides direct access to key clinical and behavioral approaches.

- The Center for Advanced Research in Neurorehabilitation (in the Midwest) provided expertise in neuroscience, biomechanics, and robotics. Annual research workshops offered a special venue for area researchers to identify collaborators and resources, and to further sharpen their research goals. In addition, the Center provided seed funding for promising investigators that allowed them to obtain the necessary pilot data to develop competitive NIH applications.
- The Network for Enhancing Rehabilitation Research in the South provided expertise in pediatric research, outcome measures, and motion analysis. Aside from promoting scientific collaborations, this network also developed a unique grant-writing retreat that annually provided a few dozen junior researchers with access to a small cadre of top rehabilitation researchers to further their own career development and hone their research applications.
- RehabNet-West provided broad expertise in experimental design and statistics, neuroimaging, and information technology through a series of workshops, Web-based lectures, regional meetings, and consultations. This network supported broad regional outreach through workshops at remote locations, interactive Web-based discussions, and more than 100 one-on-one phone and e-mail consultations. As with the other networks, this network also supported pilot projects and helped launch several dozen research applications.

Using this network infrastructure, the NCMRR launched an additional initiative to address the issue of health disparities. The Center encouraged each network to develop proposals and collaborations that specifically addressed health disparities among/across racial and ethnic minority populations. Pilot projects that were judged to have the potential grow into larger investigator-initiated research proposals received seed money support. Funded pilot projects addressed a variety of health disparities, including health service utilization among stroke patients, genotypic variations in pediatric outcomes, communication of clinical information to families of children with TBI, racial/ethnic differences in clinical trials participation, unique issues of secondary depression and caregiver burden, and differences in clinical management and amputation rates. The projects stimulated unique collaborations among researchers from different disciplines and, in a few cases, have given rise to NIH-funded research grants.

Based on the success of the initial medical rehabilitation regional networks, the NCMRR set about to renew this program, but with more focus on providing access to specific expertise, and less focus on building regional collaborations and providing exposure to the research culture. Through a new competition, the NCMRR solicited applications for programs to support research cores in biomedical, behavioral, and psychosocial approaches particularly relevant to current opportunities in medical rehabilitation research. The networks would accomplish these goals by supporting central research cores to promote didactic interactions (e.g., workshops, courses, written material, and Web sites), consultations, sabbatical opportunities, and pilot funding.
The NCMRR received proposals to develop cores in a variety of disciplines. The Center subjected the proposals to rigorous peer review to determine which networks would provide access to cutting-edge expertise and technology, as well as the appropriate infrastructure and institutional support to deliver these opportunities to the research community. Colleagues in the NINDS provided additional funds for this initiative that ultimately allowed the NCMRR to support six research cores across the United States. The newly funded Rehabilitation Research Infrastructure Network cores provide expertise in bioengineering and robotics, cognitive rehabilitation, neurobiology and clinical neuroscience, molecular genetics and proteomics, and muscle biology. Taken together, this series of cores offers a unique, cost-effective network of infrastructure and opportunities for rehabilitation researchers and for those from allied fields. The only disappointment in the process was the absence of a top-quality research proposal in rehabilitation outcomes or psychosocial research, but the NCMRR will continue to promote opportunities on these topics through other initiatives.

FUTURE RESEARCH DIRECTIONS FOR THE NCMRR

Beginning in 2005, the NICHD has made efforts to improve the transparency of and public input in strategic planning for its components, including the NCMRR. To this end, the Center went through a portfolio review and discussion of future research plans in preparation for its report to the NACHHD Council. To do so, the Center relied on its existing Advisory Board, which was established in the legislation that also established the NCMRR in 1990. The Advisory Board meets twice a year to discuss the NCMRR’s portfolio and to assess possible future research directions. What follows is a summary of the discussions among the NCMRR staff and the NCMRR Advisory Board about the future of the Center’s research.

The NCMRR’s efforts to grow the capacity for rehabilitation research have been highly successful, both by supporting training and career development of new investigators, and by drawing the attention of established investigators to research problems in rehabilitation. This broad effort has covered the span of issues developed by the NCMRR Advisory Board at the inception of the Center. The NCMRR now seeks to capitalize on this research base and, to the extent possible within the NIH structure, to focus the future growth in NCMRR funding along major themes:

- Translational Research: Bench to Community
- Basic Research to Advance Rehabilitation
- Plasticity and Adaptation of Tissue in Response to Activity and Environment
- Reintegration of Persons with Disabilities into the Community

At the same time, the NCMRR will also strive to achieve several cross-cutting objectives:

- Develop mechanisms to support new investigators
- Enhance consumer input and outreach
- Extend the interdisciplinary model from basic research through applied research and community studies
To advance this agenda, the NCMRR will continue to work in collaboration with other NIH Institutes, the NIH Office of the Director, other federal agencies, and organizations in the private sector.

In the remainder of this section, the NCMRR highlights possible future directions in terms of its cross-cutting objectives first, and then explains possible activities within the major themes.

**DEVELOP MECHANISMS TO SUPPORT NEW INVESTIGATORS**

The NCMRR has successfully supported the development of a new generation of rehabilitation researchers. The most recent NCMRR training meeting, for example, attracted more than 175 participants. However, current national climate means that federal funding agencies, including the NIH, are facing a prolonged period of constrained growth. New investigators are particularly vulnerable to tight pay lines because they have less experience in grantsmanship and fewer resources available to them. Developing mechanisms to protect and nurture new investigators will be among the highest priorities for the NCMRR over the next few years. The Center will undertake these efforts in coordination with efforts by the NICHD and the NIH, more broadly.

**ENHANCE CONSUMER INPUT AND OUTREACH**

The NCMRR and the investigators it supports would benefit from enhanced consumer input and outreach. For instance, disability groups and advocates could more effectively participate in developing research priorities if they had more information about the process and outcomes of research. Investigators would benefit from more information about how their work addresses the concerns of individuals with disabilities, and how their work may ultimately be implemented to change people’s lives.

The NCMRR will develop an outreach program to describe its activities to consumers and advocacy groups. The new electronic update—*Innovations: Future Solutions Now, An NCMRR Update*—is an important first step in this program (see Appendix E or visit [http://www.nichd.nih.gov/about/ncmrr/innovations_eupdate_2005.pdf](http://www.nichd.nih.gov/about/ncmrr/innovations_eupdate_2005.pdf)). The first *Innovations* e-update was distributed electronically in November 2005; the Center intends to send out new e-updates about twice a year. The outreach topic would also be ideal for interagency collaboration through the Interagency Committee on Disability Research. Further, the NCMRR Advisory Board provides an important forum for consumer representatives to have input on concepts for targeted initiatives. The NCMRR could also extend this process to encourage consumers educated in scientific issues and to educate those not familiar with the issues to participate in workshops and conferences that develop research agendas.
EXTEND THE INTERDISCIPLINARY MODEL FROM BASIC RESEARCH THROUGH APPLIED RESEARCH AND COMMUNITY STUDIES

The NCMRR has an explicit charge in its mission to promote research that will improve the lives of people with disabilities, meaning that the definition of translational research for the NCMRR must extend beyond “from bench to bedside” to “from bench to community.” To meet this charge, the Center will encourage rehabilitation researchers to consider how their results can extend into community-based settings. The NCMRR will also explicitly encourage effectiveness, as well as efficacy research, i.e., research to determine how well interventions actually work in the community. This effort may proceed in incremental stages, and will likely include educating rehabilitation researchers about successful strategies employed by other fields, developing toolkits, and funding pilot projects.

An important first step in both extending the interdisciplinary model and in enhancing consumer awareness will be documenting the dissemination of research results. The National Library of Medicine effort to link NIH grant information to abstracts listed on PubMed will be helpful in this effort. The NCMRR, following Office of Management and Budget guidelines, sees great value in collecting information from investigators about their NCMRR-supported research projects, such as:

- Who else knows about what you are doing?
- Who else is using the results of your research?
- What difference has your research made?

Another topic for discussion by those in the rehabilitation field is: What are some of the unique challenges to research on rehabilitation and recovery?

In answering this question, it is important to realize that rehabilitation as a clinical field only became well-established after World War II. Further, the research tools to study the basic biology of recovery (e.g., growth factors, functional imaging, etc.) have emerged only in recent decades. RCTs, so important in developing evidence-based medicine, have not been widely mounted to address rehabilitation practice. This results, in part, from the fact that rehabilitation professionals are accustomed to individualizing therapeutic programs for each patient; therefore, they may be less likely to enroll patients in RCTs with pre-specified treatment programs. Specification of therapies and identification of the “active ingredient” is also far more problematic in rehabilitation trials than in pharmaceutical trials. Outcomes of rehabilitation are also more dependent upon factors not controlled by the treatments, such as experience, education, and social and physical environments.

The NCMRR Advisory Board captured the scope of the problem of improving outcomes for individuals with disabilities in its formulation of the stages of the disablement process:

Pathophysiology Impairment Functional Limitation Disability Societal Limitation

The Board envisioned this process as moving from left to right, but recognized that it was not a linear process, and that feedback loops could occur at multiple stages. The Board also recognized that much of the research traditionally supported by the NIH focused on the first two
steps of this process. This model was widely adopted and served, at least in part, to motivate the latest World Health Organization (WHO) effort on the *International Classification of Functioning, Disability, and Health*. However, the rehabilitation community has expended much effort and argument on trying to define these steps and to develop measures of these abstract qualities.

The NCMRR has been working on a new model that focuses attention on the possible interventions in the disablement process and, rather than trying to define abstractions, lists those items that are actually measurable. Thus, rehabilitation interventions become influences, which have the potential to affect the degree of organ system dysfunction or dyscontrol caused by tissue damage, as well as the quality of specific task performance. Other mediating influences act in parallel, and, therefore, the ultimate effects of task-performance deficits on individuals’ roles in society are shaped by attitudes and laws at the individual and societal levels. The NCMRR model appears below.

<table>
<thead>
<tr>
<th>Pathophysiology</th>
<th>Organ Dysfunction</th>
<th>Task Performance</th>
<th>Roles</th>
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<td>Acute Care</td>
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The distinction between these models is not merely semantic, but reflects a difference in orientation. Rather than focusing on characterizing impairments, functional limitations, disabilities, and societal limitations, the NCMRR model seeks to understand and change the influences that mediate transitions between these levels. The NCMRR model emphasizes rehabilitation as an active process with the goal of improving quality-of-life.

What then, distinguishes rehabilitation interventions from other medical interventions? Rehabilitation interventions are activity-based, requiring the active participation of the patient or client. It is now clear that the nervous system is an exquisitely plastic organ, driven and molded by experience; through the actions of the nervous system, those experiences cause a wide range of actions on nearly all other body systems including cardiovascular, musculoskeletal, and immune systems.

The NCMRR model also highlights the special challenges faced by rehabilitation researchers. For example, organ dysfunction can result from many different pathological processes. Until recently, activity-based therapies often lacked specificity for the particular deficits experienced by patients. Although rehabilitation disciplines articulated a very clear philosophy of individualized treatments for patients, few empirical principles existed to guide the process. The complexity of multiple interacting influences on task performance and on role performance,
especially the influences of the environment and patients’ prior education and experience, makes it very difficult to isolate the “active ingredient” of rehabilitation interventions in the clinical setting. Investigators often use surrogate endpoints, such as performance measures on activities of daily living; however, the correlations between these measures and long-term outcomes meaningful to patients and families have not been adequately investigated.

This new model also highlights the importance of individual preferences and values in achieving task and role performance. Even as rehabilitation professionals are eager to avoid “blaming the victim,” individual preferences and values clearly play a central role in determining how well individuals will engage in activity-driven therapies, and how well they will surmount the difficulties of performing tasks and participating in roles. Clinicians are well accustomed to the seeming paradox of patients with apparently modest deficits whose lives are devastated, versus those facing seemingly overwhelming obstacles, who, nonetheless, engage in rich and fulfilling lives. More investigations into factors that enhance individual motivation are needed.

**TRANSLATIONAL RESEARCH: BENCH TO COMMUNITY**

The challenges facing patients, clinicians, and policy makers have never been greater. The increasing opportunities to apply cutting-edge science to promote recovery and to improve the lives of individuals with disabilities are balanced by rapidly growing demands on both health system resources and research resources. A solid base of empirical evidence on which to ground the clinical practice of rehabilitation is desperately needed to establish the effectiveness of individual treatment strategies, as well as the organization and intensity of rehabilitation services across disorders. At the same time, rehabilitation faces the same challenge as the rest of medical practice: developing cost-effective, community-based services that promote self-care and maximize independence in the community.

Clinical research in rehabilitation must surmount the difficulties in trial design engendered by interventions that are difficult to blind and must continue to work toward specifying therapeutic interventions so that they are repeatable—the method of science. Concurrently, progress is needed to develop outcomes measures that are sensitive and meaningful to patients’ goals. It is important that rehabilitation professionals acknowledge differences between patients, while also understanding how and why those differences may lead to different outcomes and may require different interventions. This effort will require the judicious use of RCTs, quasi-experimental studies, and observational studies. Studies are also needed to develop a knowledge base and toolbox for moving the results of clinical trials and laboratory-based studies out into the community. For research results to make meaningful changes in the lives of individuals with disabilities, these results must ultimately be applied in community settings. Thus, the focus of rehabilitation research must expand to include effectiveness as well as efficacy.

Much of the work supported to date has focused on clinical outcomes at the individual level. The rehabilitation field may need to examine the life course of individuals with disabilities to predict trajectories that are realistic for them, a process that may include a combination of cross-sectional and longitudinal studies of populations to capture the factors that influence the lives of individuals with disabilities across the life span. Other areas that need attention include:
development of statistical modeling techniques; improved methods for assessing memory, behavior, and cognitive function, especially in the community setting; application of psychophysiological methods; measurement of adherence to diet, exercise, and treatment regimens; measurement of activity and participation in community settings; and application of ethnographic and qualitative research methods to problems of disability.

As mentioned earlier in this report, prevention and treatment of secondary conditions is an area of special concern to individuals with disabilities. In particular, treatment strategies, drug dosages, and self-management strategies for an individual who may have one or several secondary conditions at a given time require additional study, especially because treatment and care management of symptoms in people with chronic disabilities often differs from that in the general population. The NCMRR will continue to promote research on the prevention and treatment of secondary conditions and disabilities.

Another vexing problem for individuals with disabilities and the clinicians who care for them is the lack of evidence on treatments for unrelated conditions in individuals with disabilities. This gap in evidence stems from the exclusion of individuals with disabilities from clinical trials. The NCMRR will make efforts to highlight this lack of data among researchers in the rehabilitation field and will assist the NIH in building the evidence base on this issue.

**Basic Research to Advance Rehabilitation**

A vast range of contemporary basic science now has applications in rehabilitation. For instance, tissue engineering and the potential for introducing new genetic information in dysfunctioning cells creates the potential to replace or repair damaged tissue. Gene-expression techniques provide novel means of analyzing the recovery process and identifying potential therapeutic targets. Cell therapies and trophic factors can augment tissue recovery. However, a tremendous amount of basic and clinical work is required before these technologies can move into clinical use. Genetic epidemiology could help optimize therapeutic interventions and better predict the course of recovery. Genetic analyses may not only inform clinicians about individuals’ responses to pharmaceuticals, but also to their responses to activity-driven therapies. Although the major focus of basic research on activity-driven therapies has been on plasticity in the nervous system, it is now clear that activity plays a major role in modulating the shape and function of many organ systems—from bone, connective tissue, and muscle to cardiopulmonary, immune, and endocrine systems. The optimal patterns of activities to engender recovery and restoration of function in these systems for different patterns of illness and injury are what remain unclear. Appropriate animal and tissue culture models may be valuable in developing suitable hypotheses for clinical evaluation.

Advances in imaging have also allowed for earlier diagnosis, more objective outcome measures, and increased insight into mechanisms, especially in rehabilitation. Researchers are just now beginning to be able to view the changes in nervous system activity after injury. Continuing advances in imaging are necessary to extend the view of the recovery process to the cellular level, as well as to bring quantitative measures of neural activity and plasticity into real-time. Studies in the neuroregulation and biomechanics of motor control and the mechanisms of disuse...
and over-use syndromes are highly relevant to medical rehabilitation. Modern biomechanical modeling, based on accurate anatomical data obtained from imaging, is beginning to transform the prescription of musculo-skeletal therapies. These methods may allow the therapeutic exercises and orthotics prescribed to be tailored for individual patients, precisely targeting the muscles and tendons needed to improve function.

There is also increasing need to understand the physiological changes associated with the transition from the acute to the chronic phase of disability. Biobehavioral research on patient preferences and values can support rehabilitative strategies. Likewise, the study of cognitive enhancement, applied behavior, and generalizability has direct relevance to the treatment of learning and memory deficits. In physical disability, the research agenda on behavioral and social processes must expand beyond the family process and social networks to include topics such as: emotion and motivation, resiliency, relearning and memory, and others. For example, one of the major goals of rehabilitation is to return to work. Government agencies are now exploring guidelines that provide some benefits to individuals with disabilities who return to work. Research is needed to examine the effects of work on the health of persons with disabilities and on other family members and caregivers. In addition, research is needed on developing new models of rehabilitation for individuals who cannot return to work.

The NCMRR will encourage the application of all areas of technology to rehabilitation engineering. The Center will place an emphasis on the development of bioengineering teams to promote rehabilitation research and development, and on transdisciplinary communication. Cellular and molecular approaches may also inform and enhance the use of more traditional technologies. Studies on how to enhance recovery of tissues as well as how to integrate assistive technologies directly into tissues may result in enhanced function and improved cosmesis. Turning these prospects into reality (e.g., direct skeletal attachment and implantable devices, advanced mobility aids, robotically aided therapy, etc.) will require basic investigation of the interface between tissue and machine, as well as careful evaluation of ergonomics, patient learning, and patient values and preferences. Appropriate avenues of research include not only extending the performance of persons using assistive devices, but also reducing the stress of assistive devices and preventative strategies (e.g., reducing the chance of falls among the elderly and frail) on those who use them.

Outcomes research has long been a strong point of rehabilitation research; however, important advances are yet to be made. For instance, measuring activity and participation in community settings continues to be a challenge, as does quantifying quality-of-life measures for disabled populations. Application of psychometrics and CAT to functional evaluation of patients could improve the accuracy and cost-effectiveness of clinical evaluations. The NCMRR will encourage projects and collaborations to help elucidate these topics.

**PLASTICITY AND ADAPTATION OF TISSUE IN RESPONSE TO ACTIVITY AND ENVIRONMENT**

Among the hallmarks of clinical rehabilitation interventions are activity-driven therapies, i.e., therapies that require the active participation of the patient, both on cognitive and motor levels, and consideration of the effects of environment on patient function. Advances in neuroscience,
biology, technology, engineering, and pharmacology have provided new information on the mechanisms that underlie individual responses to activity-driven therapies and environmental manipulations. These findings provide encouragement about the plasticity and capacity of the body to repair and regenerate and the potential for recovery of function, prevention of secondary conditions, and improved quality-of-life.

Research during the previous decade has established the roles of plasticity and regeneration in the central nervous system as the central mechanisms responsible for relearning, compensation, and adaptation after neurological injury. Much work remains to define and learn to optimize the signals and trophic factors that regulate synaptic plasticity, as well as to define activities and environments that produce the desired patterns of activity. As mentioned earlier in this report, advances in imaging have been and will continue to be crucial to developing this field.

Identification of stem cells in the adult, and especially in the adult brain, ranks as one of the most remarkable discoveries in contemporary neuroscience. The potential for changing the response of the central nervous system from creating a glial scar to creating functional replacement nervous tissue is enormous, especially in the field of rehabilitation. This effort represents a huge undertaking, which just now in its infancy. Scientists are just beginning to understand the factors that control the differentiation and proliferation of stem cells, and researchers do not yet fully understand the differences between fetal and adult stem cells. The field is also beginning to understand the factors that inhibit the growth of axons in damaged nervous tissue and promote glial scar formation, and the first clinical trials of antibodies to such factors are just getting under way. Moreover, for engineered neural tissue to function, it will have to connect with existing nervous systems; therefore, more research is needed on characterizing the types of axons that regenerate in systems with stem cells, enhancing connectivity with appropriate targets, and demonstrating functional outcomes.

Advances in understanding plasticity and regeneration in the nervous system will require support from a wide range of funding agencies, including multiple Institutes of the NIH, other federal agencies, and non-federal partners. The NCMRR has two major roles to play in this effort:

- Ensuring that rehabilitation researchers have access to state-of-the-art technology and expertise in these areas, so that they are able to address research questions in rehabilitation most effectively; and
- Promoting research, especially efforts on the interactions among activity-driven therapies and pharmacological and cellular interventions.

The NCMRR has taken major steps toward achieving the first goal by funding the Rehabilitation Research Infrastructure Network. Work to meet the second goal is just beginning and will form the basis of the clinical practice of neurorehabilitation for the future.

Plasticity and adaptation occur in many other tissues in addition to the nervous system, e.g., muscle, bone, cardiac, etc. Changes in plasticity and adaptation also mediate individuals’ responses to injury and illness as well as recovery. Understanding tissue responses to activity and environmental adaptation is expanding, and the time is ripe for systematic investigation of optimal activities to promote recovery and regeneration throughout body tissues. Much work remains at the preclinical level, utilizing tissue culture and animal models, to develop fruitful
hypotheses along these lines that can be tested in clinical studies. The NCMRR can play a role in further expanding the field’s understanding of these issues by supporting such investigations.

**REINTEGRATION OF PERSONS WITH DISABILITIES INTO THE COMMUNITY**

The primary mission of the NIH is to foster fundamental creative discoveries, innovative research strategies, and their applications as a basis to advance significantly the nation’s capacity to protect and improve health. It is not enough, then, to develop interventions that have efficacy in the laboratory or university hospital clinic. For rehabilitation interventions to have real effects on individuals’ lives, they must be implemented in communities. The special challenge for the NCMRR in this regard is to foster the development of research on how to accomplish translation of research findings into community practice and to establish effectiveness of these interventions in community settings. This effort requires careful implementation and evaluation of research protocols into community-based settings and integration with modern communications systems.

Additionally, much work remains on understanding patient preferences and values and on the implications of these preferences for patients’ participation in community-based exercise programs, especially in regard to long-term health maintenance programs. Measurement of activity and participation in communities remains a challenge, and the influences of culture and ethnicity cannot be ignored in these efforts.

The NCMRR has promoted the development of technologies to improve function for individuals with disabilities. This effort will continue, with special emphasis on factors that determine success in community settings, such as: utility, cosmesis, affordability, and adaptability. Principles of universal design clearly hold great promise for commercial success and public acceptance. Continued development of assistive technology is also imperative if the nation is to have the capability to provide assistance to an ever-increasing elderly population.

For disabled individuals to remain in the community, the rehabilitation field must become more successful in preventing secondary conditions and disabilities. Specific challenges that the Center will have to consider in this regard include:

- Research directed toward understanding the metabolic and behavioral factors that lead to obesity in persons with disabilities and new approaches to preventing obesity;
- Better understanding and evidence-based assessment of the incidence and progression of secondary conditions and how these conditions affect quality-of-life; and
- Substantially improved clinical training and education of consumers about the prognosis of, prevention of, and treatment options for secondary conditions.

Studies are also needed to elucidate the risk and preventive factors related to conditions including depression, medication misuse, and violence in persons with disabilities. Issues such as dietary and cultural practices, smoking, and substance abuse and their effects on recovery and disability also need investigation.
FIGURES AND TABLES

FIGURE 1: NCMRR FUNDING LEVELS AND GRANT TOTALS, FISCAL YEAR 1992 THROUGH FISCAL YEAR 2005

FIGURE 2: NCMRR FUNDING BY MECHANISM, FISCAL YEAR 2004
Figure 5: NCMRR Cumulative Funds for Clinical Issues Established in the 1993 NCMRR Research Plan, Fiscal Year 2001 through Fiscal Year 2005

- **Paralysis, Spasticity, Tremor, & Peripheral Muscle Issues**: $45.6 Million, 14.9%
- **Movement/Coordination Disorders, Gait, Balance, & Multi-Joint Issues**: $47.6 Million, 15.6%
- **Basic Research on Plasticity & Recovery**: $30.3 Million, 10.0%
- **Promoting Participation, Health Service Usage, & Quality-of-Life**: $31.8 Million, 10.4%
- **Secondary Conditions**: $39.1 Million, 12.8%
- **Cognitive, Behavioral, Emotional, & Communication Issues**: $55.1 Million, 18.1%
- **Other (Broad Studies, Training)**: $23.5 Million, 7.7%
- **Bowel & Bladder Dysfunction**: $4.5 Million, 1.5%
- **Dysreflexia**: $0.1 Million, 0.5%
- **Pain/Sensory Dysfunction**: $12.0 Million, 4.0%
- **Skeletal & Joint, Amputation & Prosthetics**: $13.8 Million, 4.5%

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APPENDIX A: NCMRR SOLICITATIONS, FISCAL YEAR 2001 THROUGH FISCAL YEAR 2005

- NSF-04-607: *Interagency Opportunities in Multi-Scale Modeling in Biomedical, Biological, and Behavioral Systems*
- RFA HD-04-015: *Data Coordinating Center for National Collaborative Pediatric Critical Care Research Network (CPCCRN)*
- RFA HD-04-005: *Medical Rehabilitation Research Infrastructure Network*
- RFA HD-04-004: *CPCCRN*
- RFA HD-03-025: *Genetic Basis of Recovery and Rehabilitation*
- RFA HD-03-023: *Innovations in Powered Mobility Devices: SBIR/STTR*
- RFA HD-03-019: *Training Materials on Surgical Amputations, Prosthetics, and Orthotics: SBIR/STTR*
- RFA HD-03-015: *Pediatric Critical Care Scientist Development Program*
- RFA HD-03-014: *Innovative Technologies for Pediatric Critical Care and Rehabilitation: SBIR/STTR*
- RFA HD-03-013: *Accessible Health Promotion and Fitness for Persons with Disabilities: SBIR/STTR*
- RFA HD-03-011: *Biomechanical Modeling of Movement*
- RFA HD-02-027: *Pilot Clinical Trials in the Epidemiology, Prevention, and Treatment of Respiratory Failure in Children*
- RFA HD-02-026: *Clinical Trial Planning Grants to Guide and Improve Timing, Intensity, Duration, and Outcomes of Pediatric Critical Care and Rehabilitation Therapeutic Interventions in Childhood Cardiopulmonary Arrest*
- RFA HD-02-024: *Dynamic Health Assessments for Medical Rehabilitation Outcome*
- RFA HD-02-023: *Pharmacological Approaches to Enhance Neuromodulation in Rehabilitation*
- RFA HD-02-022: *Molecular and Cellular Basis of Contractures for Design of Therapeutic Interventions*
- RFA HD-02-002: *Augmentative and Alternative Communication Strategies for Treatment of Acquired Cognitive-Linguistic Disorders*
- RFA HD-01-022: *Clinical Trial Planning Grants to Guide Timing, Intensity, and Duration of Rehabilitation for Stroke and Hip Fracture*
- RFA HD-01-007: *Cooperative Multi-Center Traumatic Brain Injury (TBI) Clinical Trials Network*
- PA-04-153: *Health Disparities Among Minority and Underserved Women*
- PA-04-101: *Characterization, Behavior, and Plasticity of Pluripotent Stem Cells*
- PAR-04-077: *Research Partnerships for Improving Functional Outcomes*
- PAR-04-023: *Bioengineering Research Partnerships*
- PA-04-006: *Neurotechnology Research, Development, and Enhancement*
- PA-03-167: *Aging Musculoskeletal and Skin Extracellular Matrix*
- PA-03-152: *Biobehavioral Pain Research*
- PA-03-085: *Competing Continuation Awards of SBIR/STTR Phase II Grants for Device Assessment or Preclinical Studies*
- PA-02-162: *Long-Term Care Recipients: Quality-of-Life and Quality-of-Care Research*
- PA-02-156: *Studies into the Causes and Mechanisms of Dystonia*
- PA-02-155: *Informal Caregiving Research for Chronic Conditions*
- PA-02-136: *Precursor Cells in Skeletal Muscle Repair and Hypertrophy*
- PA-02-115: *Women’s Health in Sports and Exercise*
- PA-02-111: *Increasing Quality-of-Life in Mobility Disorders*
- PA-02-071: *Innovative Technologies for Enhancing Function for Individuals with Disabilities*
- PAR-02-017: *Jointly Sponsored NIH Predoctoral Training Program in the Neurosciences*
- PA-02-014: *Functional Tissue Engineering of Musculoskeletal Tissues*
- PA-02-011: *Bioengineering Research Grants*
- PAR-02-010: *Bioengineering Research Partnerships*
- PA-01-141: *Orthopaedic Implant Wear*
- PA-01-115: *The Management of Chronic Pain*
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- PA-01-109: *Cachexia: Research into Biobehavioral Management and Quality-of-Life*
- PA-01-080: *Research Supplement for Individuals with Disabilities*
- PA-01-078: *The Biology of Non-Human Stem Cells in the Environment of the Nervous System*
- PA-01-044: *Research on Emergency Medical Services for Children*
APPENDIX B: NCMRR-SUPPORTED MEETINGS AND CONFERENCES, FISCAL YEAR 2001 THROUGH FISCAL YEAR 2005

- Rehabilitation Research Agenda: Improving Functional Ability for Patients with Musculoskeletal Impairments, January 9-10, 2006, Bethesda, Maryland
- NCMRR Biennial Training Workshop, December 5-6, 2005, Rockville, Maryland
- Translating Evidence into Practice: Linking Movement Science and Intervention, a III Step Conference, July 15-21, 2005, Salt Lake City, Utah
- Workshop on the Biology of Manual Therapies, June 8-10, 2005, Bethesda, Maryland (Co-sponsored by the NICHD, the National Center for Complementary and Alternative Medicine, the NIAMS, the NINDS, and the Canadian Institutes of Health Research)
- Increasing the Quality and Quantity of Multiple Sclerosis Rehabilitation Research, May 2005, New York City, New York
- Research Opportunities: Translating Defense and Civilian Technologies for Pediatric Critical Care and Rehabilitation, May 16-17, 2005, Rockville, Maryland
- Workshop to Develop a Research Agenda on Appropriate Settings for Rehabilitation, February 14-15, 2005, Bethesda, Maryland
- Biennial NCMRR Training Workshop, December 9-10, 2003, Bethesda, Maryland
- Physical Disabilities Through the Lifespan, July 21-22, 2003, Bethesda, Maryland
- Workshop on Rehabilitation for Stroke and Hip Fracture, August 4, 2001, Rockville, Maryland
- Medical Rehabilitation on the Move: Spotlight on Bioengineering, January 4-5, 2001, Bethesda, Maryland
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APPENDIX D: NCMRR STAFF

Beth M. Ansel, Ph.D., CCC-SLP, joined the Center in 2000, as director of the Clinical Practice Program. Dr. Ansel received her undergraduate education in biology at State University of New York (SUNY) Stony Brook. She completed her master’s and doctoral education in speech-language pathology at the University of Wisconsin-Madison, and her postdoctoral research and clinical fellowship at the Johns Hopkins University School of Medicine and the John F. Kennedy Institute of Handicapped Children. During that time, she worked extensively with children as a member of an interdisciplinary pediatric rehabilitation team, which considered the assessment, treatment, and long-term care of trauma patients. Prior to joining the NIH, she served on the faculty of Purdue University’s Department of Audiology and Speech Sciences.

Carol Nicholson, M.D., is the program director for the PCCR Program at the NCMRR. Dr. Nicholson is a graduate of the University of Southern California School of Medicine and completed residency training in general pediatrics at the University of California, San Diego, and pediatric critical care medicine fellowship training at Children’s Hospital Los Angeles. She is a diplomate of the American Board of Pediatrics, as well as of the sub-board of Pediatric Critical Care Medicine, and a fellow of the American Academy of Pediatrics. Her research background includes early experience (before medical school) in genetics, prenatal diagnosis, virology, birth defects, and child development. Since coming to NICHD, she has become the program scientist for the new Collaborative Pediatric Critical Care Research Network, as well as a visiting scientist in the Department of Resuscitative Medicine at the Naval Medical Research Center.

Ralph Nitkin, Ph.D., is the program director for Biological Sciences and Career Development in the NCMRR. He received his undergraduate and master’s degrees from the Massachusetts Institute of Technology in the area of biological sciences, and his Ph.D. from the University of California, San Diego, in cellular neurobiology. His postdoctoral studies at Stanford University and later work as an assistant professor at Rutgers University focused on the cellular and molecular basis of nerve-muscle synapse formation. For the past 16 years he has worked as a science administrator at the NICHD, first in the area of mental retardation and developmental disabilities, and currently in medical rehabilitation research. Within the Center, Dr. Nitkin is also active in the area of training and career development.

Louis A. Quatrano, Ph.D., is a psychologist who joined the NCMRR in 1991. Dr. Quatrano’s undergraduate education was at SUNY at Geneseo, and he received his doctorate degree from Northwestern University. He initially joined the NIH as a health scientist administrator in the Prevention, Education, and Manpower Branch of the Division of Lung Diseases at NHLBI, where he was involved in transferring basic science into clinical practice and directing the training program in pulmonary research. He went on to become the scientific review administrator for the Human Development and Aging Study Section and the referral officer for SBIR applications in the NIH Division of Research Grants, which is now the Center for Scientific Review. Dr. Quatrano is director of the NCMRR’s Behavioral Sciences and Rehabilitation Technology Research Program.
Carol Ann Sheredos, P.T., M.A., joined the Center in November 2000 as a program support specialist and policy fellow. She graduated from Ithaca College-Albert Einstein College of Medicine with a bachelor’s degree in physical therapy, and received her master’s in adulthood and aging from the College of Notre Dame of Maryland. Ms. Schredos practiced physical therapy in New York, and then joined the Veterans Administration Prosthetics Center as a research physical therapist and performed gait analyses and clinical application studies, primarily of upper- and lower-extremity prosthetics. Ms. Schredos is active in the disability community, having served as chairperson of the Maryland Governor’s Advisory Council on Individuals with Disabilities for the State of Maryland from 1996 to 2004.

Nancy L. Shinowara, Ph.D., is director of the Spinal Cord and Musculoskeletal Disorders and Assistive Devices Program. Prior to joining the Center in 2003, she was with the NIH Center for Scientific Review for nearly eight years, serving as scientific review administrator for several study sections, including those for small business proposals in rehabilitation medicine and orthopedic medicine, and special reviews for grant mechanisms involving biotechnology and bioengineering. Dr. Shinowara received her bachelor’s in biology from Mount Holyoke College and her Ph.D. from Northwestern University in biological sciences/neurosciences; she was also a Spencer Foundation Fellow in the Division of Biology, California Institute of Technology, and a senior staff fellow in the Laboratory of Neuroscience at the National Institute of Aging. Prior to returning to NIH, Dr. Shinowara was assistant professor of medicine at SUNY Stony Brook and director of Renal Cell Biology and Electron Microscopy at Winthrop University Hospital in Mineola, New York. Her research interests include: functional morphology of peripheral nerve, neuromuscular junction, and intercellular junctions; and the cell biology and permeability mechanisms of the blood brain, eye, and peripheral nerve barrier systems and renal epithelia.

Janice Wahlman joined the NCMRR as a secretary in 2005. Prior to coming to the NCMRR, she worked in the NICHD’s Demographical and Behavioral Sciences Branch within the Center for Population Research.

Michael Weinrich, M.D., assumed directorship of the NCMRR in February 2000. He received his undergraduate and medical degrees from Harvard University and was trained in neurology at the University of Chicago, and in neurophysiology at the NIH. Dr. Weinrich has served on the faculties of Stanford University and the University of Maryland. Prior to joining the NCMRR, Dr. Weinrich was professor of neurology at the University of Maryland and medical director for rehabilitation at Kernan Hospital in the University of Maryland Medical System. From 1998 to 1999, he served on the staff of Congressman Benjamin Cardin (Rep MD-D) as a health policy fellow. His research has focused on applications of computer technology to problems in rehabilitation, and on health policy for vulnerable populations.
APPENDIX E: INNOVATIONS—FUTURE SOLUTIONS NOW: AN E-UPDATE FROM THE NCMRR (RELEASED IN FALL 2005)

Welcome!
This e-update is in response to several requests from our Advisory Board and constituents for a periodic update from the National Center for Medical Rehabilitation Research (NCMRR), within the National Institute of Child Health and Human Development (NICHD). It is intended as a means of recognizing progress and disseminating information about the many innovations made in the field of medical rehabilitation as a result of NICHD funding. We hope that you share our excitement over these developing technologies, the emerging evidence for various treatment options, and a growing portfolio of innovative research.

Carol A. Sheredos, P.T., M.A., NCMRR

Director’s Message
The NCMRR Advisory Board suggested that we develop this electronic update to improve communications with the NCMRR’s constituents—consumers, advocates, and investigators. In that spirit, we invite your suggestions on ways that we can improve these updates, and on items that you would like to see featured in future updates. Please feel free to e-mail us with your comments and suggestions.

The number of rehabilitation grant applications to the NICHD continues to rise, and rise proportionately faster than appropriations for the NICHD, resulting in tighter pay lines for investigator-initiated applications, and reduced resources for targeted initiatives. This dynamic is not expected to change in the foreseeable future. Despite this fact, I am pleased to report that applicants to the NCMRR are continuing to succeed under these challenging conditions.

The total number of funded applications and funds committed to NCMRR-sponsored research has also continued to rise. The NCMRR has issued a solicitation and will fund the second generation of Rehabilitation Research Network Centers, as well as the Medical Rehabilitation Scientist Development Program. We have also taken the lead in developing a trans-NIH program (PAR-64-677) to encourage collaborative research on problems in rehabilitation.

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Small Business Innovative Research (SBIR)/Small Business Technology Transfer (STTR) Corner
Featured in each issue of Innovations! Visit these links to see a glimpse of what’s new in the world of NICHD-funded technology.


An NCMRR E-Update
Director's Message

The NCMRR continues to participate in planning and funding conferences to develop and promote an agenda for rehabilitation research. Our collaborations with other agencies are especially noteworthy, including:

- The White House Department of Veterans' Affairs (VA) Conference on Emerging Technologies (co-sponsored with the VA and the Office of Science and Technology Policy);
- Translating Defense and Civilian Technologies for Pediatric Critical Care and Rehabilitation (co-sponsored with the Departments of Energy and Defense);
- Increasing the Quantity and Quality of Multiple Sclerosis Rehabilitation Research (co-sponsored with the National Multiple Sclerosis Society); and
- Workshop to Develop a Research Agenda on Appropriate Settings for Rehabilitation (co-sponsored with the Center for Medicare and Medicaid Services).

Together with its Advisory Board, the NCMRR will be drafting a new strategic plan for the next five years. At the December 2004 meeting, the Advisory Board broke into three work groups that recommended the following research priorities:

- The first group recommended support of research in: biological basis of rehabilitation (including influence of gender, genetics, and ethnicity); artificial intelligence, robotics, and teledermatology; neural prosthetic interfaces; advanced assistive technologies; clinical trials to promote novel rehabilitation interventions; and use of nanotechnology to build devices that integrate with dysfunctional tissue; and research on outcomes and quality-of-life measures.
- The group also supported the use of: three-year center-planting grants; national training K12 grant program for rehabilitation engineers; workshops focused on new and emerging technologies; more R24 infrastructure grants; and collaborative clinical trials to determine optimal intensity, duration, and content of rehabilitative therapies, as well as the optimal target populations.

- The second group focused on: plasticity, adaptation, and accommodation; translational research; medical intervention to sustain life; and needs assessment with a focus on the person and quality of life.
- Priorities include: translating emerging knowledge from basic sciences into implementation; technology, research, and development that leads to evidence-based interventions and accommodations; qualitative and quantitative evaluation of therapeutic interventions (e.g., duration and frequency); and improving the practice of rehabilitation medicine.

- The group also noted opportunities in stem-cell technology and outcomes research (e.g., defining positive health and wellness). Members encouraged collaborations with other NIH Institutes on common topics (e.g., stroke, cancer) to extend outcomes through rehabilitation and participation. It recommended the continued support of investigator-initiated research and encouraged the NCMRR to evaluate the success of ongoing programs and research initiatives.

- The third group felt that rehabilitation research was grounded in studies of: adaptation and plasticity at the level of cells, organs and systems; approaches that go beyond healing and reversal of injury; and studies of retraining reflex functions.

- Research goals include: reconceptualizing cancer outcomes between bench science and clinical studies; examining quality of life and impact on families; secondary effects of impairments on disabilities (e.g., wearing spinal cord injury patients, positive psychosocial impact, breaking out of the cycle of cumulative illness and disability); and long-term management of chronic disabilities and conditions (including pressure sores, effects of long-term drug use, inactivity, and obesity).

- The group recommended conferences on universal design for living, family and support systems, contrasting the medical model with the social/functional model, and outcome measures.

We invite suggestions and comments on these proposed research areas. Please check our Web site at http://www.nichd.nih.gov/ncmrr/research/for the forthcoming draft report to the NICHD Council. We invite your comments and suggestions on this draft.

Michael Weirich, M.D., Director, NCMRR
The information in this document is no longer current. It is intended for reference only.
IN THE NEWS

Workshop at Walter Reed Army Medical Center

On January 14, 2005, the Human Engineering Research Laboratory (HERL) at the University of Pittsburgh, in collaboration with Physical Medicine and Rehabilitation at Walter Reed Army Medical Center in Bethesda, Maryland, presented a workshop entitled State-of-the-Art Workshop: Wheelchair Research and Clinical Practice—Featuring Wheelchair Skills Training. The workshop was free to all military, Department of Defense, NIH, and VA personnel and families.  For more information, visit http://www.herpitt.org/home.html.

Focus on Training

Each issue of Innovations will highlight one of the NCMRR’s institutional training grants (T32 or K12).

This issue focuses on the Medical Rehabilitation Research Training Program at the University of Michigan. This T32 grant (T32 HL007422) has been ongoing, with several competitive renewals, since 1991. Theodore (Ted) Cole was the founding Principal Investigator. The current principal investigator is Denise Tate, Ph.D., professor, Department of Physical Medicine and Rehabilitation. Dr. Tate earned her Ph.D. in rehabilitation psychology from Michigan State University.

The University of Michigan Medical Rehabilitation Research Training Program (U-M MRRTP) was one of the first T32 programs funded by NCMRR with three grant cycles: 1992-1997; 1997-2001; and 2001-2006. The program emphasizes an interdisciplinary approach to research and is designed to prepare fellows for careers in growing biological and health care fields.

Research training is offered in three core areas:

- Motor performance and function;
- Recovery and treatment of brain and spinal cord injury (SCI); and
- Health and wellness.

This program received an NICHD MENTOR award, which goes to the Institute’s most productive training programs. Visit the Program Web site for more information at http://www.med.umich.edu/pm/mentor.htm.

Do you have any questions for NCMRR staff?

For example, do you need assistance with identifying an appropriate funding mechanism for your application? If so, please e-mail us at sherece@gmail.com. Thank you!
Spotlight on Technology

Innovative Body-Powered Voluntary-Closing Prehensor

Principal Investigator: Bradley D. Veatch
(R44|HD30048)

This project is currently gearing up for a commercialization effort. It is a good example of a successful research effort funded under PA 02-071, Innovative Technologies for Enhancing Function for Individuals with Disabilities. This Phase II SBIR project focuses upon optimizing a body-powered voluntary-closing prehensor offering variable mechanical advantage and passive holding-assist. For more information and to view videos of this invention in action, go to http://www.adatech.com/getesLESA4 or to http://www.adatech.com/getesLESA4_in_Motion.

Development of the Game-Cycle Exercise System

Principal Investigator: Rory A. Cooper
(R41|HD39536)

The GameCycle exercise system is an interface between an arm ergometer and a computer game that was designed to provide motivation for individuals who use wheelchairs to exercise on a regular basis. Exercise is important to the physical health and well-being of all people and helps in the prevention of cardiovascular disease, high blood pressure, obesity, and diabetes. It is especially important for persons with disabilities, who tend to have lower activity levels in general. For a presentation on the GameCycle, visit http://www.berlinpitt.org/Presentations/RESNA2002/GAMECYCLE_EXERCISE_SYSTEM.ppt

Magic Wheels: Two-Speed Manual Wheelchair Wheel

Principal Investigator: Steve Meginniss
(R43|HD35793)

Wheels for manual wheelchairs are essentially unchanged since invented more than 150 years ago. Traditional non-powered wheels have limited ability in varying terrain (e.g., hill climbing, hill descending, rough/uneven surfaces) and high-speed riding can cause repetitive stress injuries of shoulder, arm, and hand. These problems are amplified for patients with limited upper body capability.

The Magic Wheels product was designed from the ground up expressly to meet the needs of long-term wheelchair users. The unique design not only meets all the design criteria, but also includes two important, but unarticulated additional features: hill holding with override and finger-tip assistive braking. Magic Wheels two-speed wheels have also been designed to allow after-market retrofitting in the field. To view video clips of Magic Wheels in action, visit http://threshold.com/magicwheel/gallery/video.html.

For additional information on Magic Wheels, visit http://www.magicwheels.net.

The NCMRR Advisory Board

The director of NIH was mandated in PL 101-613 to establish the National Advisory Board on Medical Rehabilitation Research. The Board advises the directors of NIH, NICHD, and NCMRR on matters and policies relating to the Center’s programs.


Minutes from past Advisory Board meetings are available at http://www.nichd.nih.gov/about/nccmr/nncmrboard.htm.
Investigator Profile

Amy Bastian, Ph.D., P.T.

Dr. Bastian is a physical therapist who is known for her work with movement disorders, particularly looking at the role of the cerebellum. One of her major projects, "Mechanisms and Rehabilitation of Cerebellar Ataxia" (HD404589), funded through January 2006, focuses on cerebellar function in dynamically adjusting the relative motion of multiple joints and limbs to make movement smooth and accurate.

"We know that cerebellar circuits must process complex temporal and kinetic relationships between body segments predictively to avoid inaccuracies caused by long feedback delays," Dr. Bastian said. "Cerebellar control processes must also be continually calibrated via adaptive mechanisms in order to be useful in a constantly changing environment."

Although rehabilitation is the major treatment for most cerebellar conditions, there is minimal evidence to demonstrate the efficacy of existing rehabilitation techniques and mechanisms. Dr. Bastian has proposed to test:

- If there are maneuvers that can improve movement performance of people with cerebellar damage;
- If adaptive capacity can be enhanced in people with cerebellar damage; and
- If adaptive capacity predicts outcome (i.e., learning).

Dr. Bastian also hypothesizes that, to improve movement performance and adaptation capacity, it may be possible to enhance residual cerebellar function and/or tap into extra-cerebellar mechanisms, and that adaptive ability will correlate with learning capacity in this population, allowing researchers to predict who will best respond to rehabilitation.

"As we perform these studies, we will evaluate different theories of cerebellar function (e.g., dynamics control, timing) by determining which aspects of movement performance and adaptation are most compromised in cerebellar patients. Thus, this work will test motor control theories, while at the same time evaluating new strategies for rehabilitation."

Dr. Bastian received her B.S. in physical therapy from the University of Oklahoma, and her Ph.D. in movement science from Washington University in Missouri. She was on the faculty of Washington University from 1997-2001. In 2001, she moved to Baltimore, Maryland, where she is an associate professor in the Neurology & Developmental Medicine Department at the Johns Hopkins School of Medicine. She is also the director of the Motion Analysis Laboratory at Kennedy Krieger Institute.

Dr. Bastian is the 1999 recipient of the American Physical Therapy Association - Eugene Mihals New Investigator Award. You can contact her at bastiani@kennedykrieger.org.

NCMRR Mission

The mission of the NCMRR is to foster the development of scientific knowledge needed to enhance the health, productivity, independence and quality of life of persons with disabilities. This goal is accomplished by supporting research on the functioning of people with disabilities in daily life.

The research initiatives and opportunities recommended in the Research Plan (154 KB) for the NCMRR are discussed in terms of seven cross-cutting areas in which increased research effort is needed. Those areas are:

- Improving functional mobility;
- Promoting behavioral adaptation to functional losses;
- Assessing the efficacy and outcomes to medical rehabilitation therapies and practices;
- Developing improved assistive technology;
- Understanding whole body system responses to physical impairments and functional changes;
- Developing more precise methods of measuring impairments, disabilities, and societal and functional limitations; and
- Training research scientists in the field of rehabilitation.

To fulfill this plan, the NCMRR is very interested in receiving applications for funding from investigators, and its support of rehabilitation research is limited only by the number of quality applications received.

To encourage new investigators, there are various training grant mechanisms available to support individuals in different stages of their careers. Information regarding specific training grants is available at http://www.nichd.nih.gov/training/training.htm or by contacting Dr. Ralph Nitkin at RN21e@nih.gov.

In the next Innovations:

- Who's Who in the NCMRR Advisory Board
- Profile of NCMRR Staff Member
- News to Use from the NCMRR
- And More...