

Supporting a Research Career in Rehabilitation

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National Institutes of Health (NIH)



- Overview of the NIH and NCMRR
- Research Support Mechanisms
- The NIH application and review process
- Research Resources and Institutional Contacts
- Unique issues in Rehabilitation Research
- What's Hot in Rehabilitation Research?

The NIH is made up of 28 Institutes, Centers, Divisions:

<u>OD</u>	<u>NIDA</u>	<u>NCI</u>	<u>NIEHS</u>
<u>NEI</u>	<u>NIGMS</u>	<u>NHLBI</u>	<u>NIMH</u>
<u>NHGRI</u>	<u>NINDS</u>	<u>NIA</u>	<u>NINR</u>
<u>NIAAA</u>	<u>NLM</u>	<u>NIAID</u>	<u>CIT</u>
<u>NIAMS</u>	<u>CSR</u>	<u>NIBIB</u>	<u>FIC</u>
<u>NICHD</u>	<u>NCCAM</u>	<u>NIDCD</u>	<u>NCMHD</u>
<u>NIDCR</u>	<u>NCRR</u>	<u>NIDDK</u>	<u>CC</u>

National Center for Medical Rehabilitation Research (NCMRR)

- ♦ Established 1990 by Public Law 101-613
- ♦ To foster development of scientific knowledge needed to enhance the health, productivity, independence, and quality of life of persons with disabilities
- ♦ Located within the **National Institute of Child Health and Human Development (NICHD)**

So if you are looking for NCMRR – you have to look under NICHD

Other NIH Institutes that support Medical Rehabilitation Research

NINDS (Neurological Disorders & Stroke) e.g., spinal cord & brain injury, neurodegenerative disorders, Cerebral Palsy

NIAMS (Arthritis, Musculoskel & Skin) e.g., muscle, bone, skin

NIA (Aging) e.g., geriatric populations

NHLBI (Heart, Lung & Blood) e.g., exercise, cardiovascular

NIDCD (Deafness & Communication) e.g., speech, balance

NINR (Nursing Research)

NCI (Cancer)

NCCAM (Complementary & Alternative Medicine)

NIBIB (Biomedical Imaging & Bioengineering)

And beyond the NIH

- ♦ National Institute on Disability and Rehabilitation Research (NIDRR) located in Dept of Education
- ♦ National Science Foundation
- ♦ Center for Disease Control and Prevention (CDC) e.g., prevention, secondary complications
- ♦ Veterans Affairs (VA) e.g., treatment
- ♦ Department of Defense

And Foundations . . .

Muscular Dystrophy Assn, American Heart Assn, United Cerebral Palsy Foundation, Robert Wood Johnson Foundation, National Multiple Sclerosis, etc.

Applying to the NIH

Majority of funds go to *investigator-initiated* proposals - rather than responding to program initiatives

Funding for medical rehab research is largely driven by the number of quality applications NIH receives

NIH accepts proposals in three annual cycles, typically: early February, June, and October

Electronic submissions – leave time to deal with it!!!

From submission to funding: 9 months probably more for revisions

Support provided to *institutions* in name of investigator

Progression of Funding (NIH model)

- Training grants and fellowships
- Career development awards (K awards)
- Smaller foundation grants and pilot studies
- Co-investigator on R01, other major grants
- Principal investigator on major grant (R01)
- Involvement in larger collaborative studies

Research Project Award: R01

- ◆ Investigator-initiated applications (majority of NIH funding for basic and clinical research)
- ◆ Focus on specific set of aims
- ◆ Budget: no boundaries but typically \$200-300,000 per year
- ◆ May request up to 5 years;
- ◆ If funded, can later apply for competitive renewal

Small Grants: R03 and R21

- ◆ Pilot studies (feasibility); innovative research; high-risk; new methodology or technology
- ◆ New investigators especially encouraged
- ◆ Budgets \$100,000/ \$275,000, respectively, (direct costs) over 2 years
- ◆ Not renewable; may not be used to supplement already-funded projects

Small Business Tech Transfer (STTR R41/42) Small Business Innovation Res (SBIR R43/R44)

Innovative research, with potential for commercialization

- ◆ STTR:
 - Phase I: \$100,000 (1 year)
 - Phase II: \$500,000 (2 years)
- ◆ SBIR:
 - Phase I: \$100,000 (6 months)
 - Phase II: \$750,000 (2 years)

Special Research Initiatives

- ◆ **Program Announcements (PA)**
Highlights Institute(s) interest in specific area
- ◆ **Request for Applications (RFA)**
One-time set-aside for applications in specific area with dedicated review group
- ◆ **Request for Proposals (RFP)**
One time set aside for specific product (contract)

Training and Career Development

- ◆ Individual Fellowships
 - Graduate students (F31) or Postdoc (F32)
- ◆ Institutional Training Grants (T32)
 - Department support for PhD graduate students and/or Postdocs
- ◆ Career Development Mechanisms
 - New investigator in specific fields or clinician getting into research
 - Mentored: 3-5 yrs @ 75% effort
 - Application processes vary across NIH Institutes

Midcareer Investigator Award in Patient-Oriented Research (K24)

Supports mentoring of clinical researchers (to make someone a better *mentor* and assimilate other research approaches)

www.grants.nih.gov/grants/guide/pa-files/PA-04-107.html

Supplements to already-funded NIH research grants

To add qualified individuals at any level (high school through investigator) who:

- are from under-represented minorities
- come from disadvantaged backgrounds
- have disabilities
- re-entering research after family obligations

Contact NIH program director of funded grant

<http://grants1.nih.gov/grants/guide/pa-files/PA-05-015.html>

How an Application becomes a Grant – or at least tries

- ◆ Each round 15,000 applications arrive at NIH Central: “Receipt and Referral”
 - Which NIH Institute(s) support this area of research – should it get a top score?
 - Which study section has the most appropriate expertise?
- ◆ You can attach a cover letter to suggest appropriate Institute(s) and/or study section assignments

Center for Scientific Review

The “Judicial Branch” of the NIH

Over 100 standing study sections in following areas:

AIDS and Related Research	Hematology
Biobehavioral & Behavioral Proc	Immunology
Biological Chemistry and Macromolecular Biophysics	Infectious Diseases and Microbiology
Biology of Development and Aging	Integrative, Functional, and Cognitive Neuroscience
Bioengineering Sciences and Tech	Molecular, Cellular, and Developmental Neuroscience
Brain Disorders and Clinical Neuroscience	Musculoskeletal, Oral and Skin Sciences
Cell Biology	Oncological Sciences
Cardiovascular Sciences	Respiratory Sciences
Digestive Sciences	Risk, Prevention and Health Behavior
Endocrinology, Metabolism, Nutrition and Reproductive Sciences	Renal and Urological Sci
Genes, Genomes and Genetics	Surgical Science, Biomedical Imaging, & Bioengineering
Health of the Population	

Also a few peer-review committees associated with NIH Institutes

R01 applications are generally reviewed in the centralized “Center for Scientific Review” (CSR)

Institute study sections generally review:
RFAs and other one-time initiatives
Training and career-development applications
Other specialized support mechanisms

Institute study sections function similar to the peer-review panels of CSR

Application gets assigned to a Study Section

Study section has about two dozen reviewers, plus ad hoc expertise as needed

Scientific Review Administrator (SRA):
Checks applications for administrative issues
Makes reviewer assignments
Avoids "conflicts of interest" both positive and negative

Typical workload for study section:
50-80 applications per round

Prior to the Review Meeting

Each application assigned to three reviewers: primary, secondary, reader
unassigned reviewers may also read application

Sometimes, additional outside opinions sought

Assigned reviewers prepare detailed written critiques prior to the meeting, which are then shared with the entire committee electronically

These three critiques become the basis for the "summary statement"

NIH Review Criteria

Significance: important problem? Effect on the field?

Approach: conceptual framework, design, methods, & analyses

Innovation: Novel concepts, approaches or methods?
Are the aims original and innovative?

Investigator: PD/PI(s) appropriately trained?
Appropriate experience level?

Environment: Adequate scientific environment(s)?
Unique features, subject populations? Institutional support?

Additional criteria: Protection of human subjects;
Inclusion of women, minorities, and children;
Vertebrate animal research

At the Review Meeting

Triage process: Which applications are in the "upper half" and merit further discussion?

Triaged applications do not receive a priority score, but still get full benefit of written critiques

"Upper half" applications discussed (15-20' each)
Assigned reviewers highlight strengths/weaknesses
Rest of committee joins in discussion
Assign priority score: 1.0 (best) – 5.0 (worst)

To normalize scoring across study sections, the priority score gets translated into a percentile ranking

Meanwhile back at the Institutes . . .

Applications get second level of review from Institute Advisory Councils, but applications are rarely singled out for individual discussion

There is a limited amount of funds to support investigator-initiated research applications:
Institutes generally fund by percentile ranking, with minor adjustments based on high program priorities

Outcomes:

- ☺ Award notice !!!!
- ☹ Revise ?!?
- ⊖ Back to the drawing board

Talk to your Program official!

Winning over Reviewers, part 1

Develop a focused application, with explicit goals

Raise an interesting question (basic or clinical) and propose a direct response

Discuss likely outcomes and interpretations

When possible, use the most direct, appropriate, and current techniques to critically address the issues at hand

Provide a logical defense of your approaches and choices with alternatives

Winning over Reviewers, part 2

Briefly introduce the research field and cite the relevant literature (especially the papers of your likely peer-reviewers); but do not write a scholarly treatise

Discuss why hasn't this been done before and what is your unique angle

Include sufficient detail on techniques, outcome measures, plans for analysis

Describe collaborations (if appropriate); include appropriate statistical expertise

Discuss your subject and control populations

Winning over Reviewers, part 3

Write to your likely peer-review audience in a style that is logical and interesting

To make it more readable include diagrams, pictures, and tables (with adequate labels and legends)

Make sure your application is neat, accurate, and complete (show your standards)

Prepare for electronic submission and follow guidelines for page limits and appendices

Reviewers are not required to read appendices

Winning over Reviewers, part 4

Don't submit until it is your *best effort*

Respect your reviewers' time and efforts

You are starting a dialogue with reviewers and you only get three total chances

Human Subjects Research

- ◆ Define your subject population and discuss inclusion and exclusion criteria
- ◆ Power calculation; justify your numbers
- ◆ Work with your local IRB, but approval not required at time of NIH submission
- ◆ NIH policies require inclusion of women, minorities, and children, as appropriate
- ◆ HIPAA regulations for confidentiality
- ◆ Data and Safety Monitoring Board/Plan

Revisions: Be Persistent

Build in time for resubmissions

Make sure you understand the message in the summary statement; talk to staff!

Can you address the concerns raised by the reviewers?

Also use this as an opportunity to improve and update the application

You are encouraged to contact NIH staff

- As introduction, email your abstract and "specific aims" page
- We can discuss potential grant mechanisms, funding initiatives, and study section assignments
- Later, we can help interpret your summary statement
- But funding decisions are largely driven by the priority score you get from the study section

Useful NIH Websites

NIH Home page: www.nih.gov

National Center for Medical Rehab (in NICHD):
Including NCMRR-funded grants, RFAs/PAs
www.nichd.nih.gov/about/ncmrr/ncmrr.htm

CRISP (searchable database of all NIH-funded grants): www.commonscit.nih.gov/crisp/

Useful NIH Websites

NIH Guide (research initiatives, policy, etc.):
www.grants.nih.gov/grants/guide/index.html

Center for Scientific review
(study section descriptions and rosters):
www.csr.nih.gov

BECON (NIH Bioengineering Consortium):
www.becon.nih.gov/becon.htm

National Network of Medical Rehab Research Infrastructure Cores

Centralized research infrastructure for young faculty at the formative stage of their careers

Six centers across the country

State-of-the-art research facilities, mentorship, pilot grants, and other opportunities

www.ncmrr.org

Participating Centers

Medical Rehab Research Infrastructure Program in Muscle
Univ of Calif San Diego, Richard Lieber, PhD

National Capital Area Rehab Research Network Georgetown Univ and National Rehabilitation Hospital – Barbara Bregman, PT, Ph.D. & Joseph Hidler, Ph.D.

Integrated Molecular Core for Rehab Medicine Children's National Medical Center, Eric Hoffman, PhD & Susan Knoblach, PhD

Participating Centers

Engineering for Neurological Rehabilitation - Rehab Institute of Chicago, William Zev Rymer MD Ph.D

Center for Experimental Neurorehab Training – Univ of Pennsylvania and Univ of Calif Los Angeles, Michael Selzer, M.D., Ph.D. & Bruce Dobkin, MD, FRCP

Research Methods for Cognitive Rehabilitation - Moss Rehab Research Institute and the Univ of Pennsylvania, John Whyte, MD, Ph.D.

Goals of Rehabilitation Research

- ◆ Understand mechanisms of rehabilitation and recovery
- ◆ Promote new diagnostic and therapeutic approaches
- ◆ Modify and optimize current therapies to improve specificity or dosing regimens
- ◆ Adapt therapies to novel patient populations and extend to chronic phase
- ◆ Challenge assumptions of current practice

Goals of Rehabilitation Research

- ◆ Demonstrate safety and efficacy
- ◆ Extend clinical findings from the lab into real-world settings
- ◆ Explore potential secondary effects
- ◆ Longitudinal follow-up and lasting effects
- ◆ Evidence-based medicine to drive health-care management and policy

Unique Issues in Rehab Research

- ◆ Focus on *individual* rather than on cell, tissue, or organ
- ◆ Addresses longer time-frame
- ◆ Considers functional outcomes, participation, and quality-of-life
- ◆ Involves more complex relationships that cross several levels of conceptual analysis: pathology, impairment, function, disability
- ◆ Need to initiate collaborations among several professional disciplines

Unique Research Issues, cont.

- ◆ Conflicting goals among person with disabilities, family, caretaker, and clinician
- ◆ Goals and expectations evolve over time
- ◆ Should subjects be grouped by condition or functional limitations?
- ◆ Account for resources & environmental support Environmental factors can be positive or negative
- ◆ Ecological validity: dealing with treatments in "real-world" settings (e.g., home, community)

Current NCMRR Priority areas include:

- ◆ Improving functional **mobility**
- ◆ Promoting **behavioral adaptation** to functional losses
- ◆ Assessing the **efficacy and outcomes** to medical rehabilitation therapies and practices
- ◆ Developing improved **assistive technology**

Current NCMRR Priority areas include:

- ◆ Understanding **whole body system responses** to physical impairments & functional changes
- ◆ **Secondary conditions** relating to medical rehabilitation
- ◆ Developing **more precise** methods of **measuring** impairments, disabilities, and societal and functional limitations
- ◆ **Training** research scientists in the field of rehabilitation

What's Hot in Medical Rehab?

- Clinical Issues
- Secondary Complications
- Strategies and Mechanisms
- Cognitive and Behavioral issues
- Children and the Developing Brain
- Bioengineering
- Assessment and Outcomes

Clinical issues

- Weakness, paralysis, spasticity, tremors
- Movement disorders:
balance, coordination, gait
- Pain and sensory dysfunction
- Autonomic dysreflexia
- Bowel and bladder dysfunction
- Exercise and cardiovascular function

Secondary Complications

- Musculoskeletal changes: muscle atrophy, osteoporosis
- Obesity, inactivity, reduced fitness
- Skin ulceration and connective tissue dysfunction
- Increased susceptibility to infection
- Behavioral and psychosocial decline
- Accessibility and participation
- Increased morbidity and mortality
- Recurrence risk

Strategies and Mechanisms

- Prevention and reducing recurrence
- Improved diagnosis and prognosis
- Reducing initial pathology
- Minimizing collateral damage
- Reducing inflammation and scarring
- Promoting regeneration and neuroplasticity
- Adaptation and activity-mediated changes
- Developing alternative strategies

Cognitive and Behavioral Issues

- Executive function (decision-making)
- Attention
- Cognition and memory
- Visuospatial perception and neglect
- Communication disorders
- Aggression
- Depression
- Drug addiction and alcoholism

Children and the Developing Brain

- Increased vulnerability, but also increased potential for plasticity and recovery
- Growth trajectory: rapidly changing physical and behavioral repertoire
- Disorder can impede future development; interfere with "critical periods"
- Children react differently to trauma: physically, psychologically, emotionally
- Unique sensitivity to pharmacological and other therapeutic approaches

Bioengineering Research

- Orthotics, prosthetics, other assistive devices
- Neuroprosthetic interfaces
- Functional electrical stimulation (FES) and transcranial magnetic stimulation (TEM)
- Brain imaging (fMRI, DTI, PET, MEG, EEG)
- Robotics to provide therapy and improve diagnosis
- Wheelchairs and other mobility aids
- Improving control of the environment
- Speech, language and communication aids

Assessment and Outcome issues

- Importance of working across the domains of pathology, function, and/or disability
- Improving diagnostic & prognostic measures
- Assessment of "function", "disability", and "participation" in various environments (such as family, community, employment, education, recreation)
- Quality-of-life measures
- Reconciling needs of patient with those of family, caretaker, and/or clinician
- Goals/expectations may change over time
- Health-care constraints and policy issues